50th ERA-EDTA CONGRESS
MAY 18-21, 2013
Istanbul, Turkey
Abstracts
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WELCOME ADDRESS

Dear Colleagues and Friends,

We are extremely honoured to welcome you to Istanbul for the 50th Congress of the ERA-EDTA. We are also pleased to host all of you in Turkey for the third time. We sincerely believe that your contributions to the outstanding scientific programme which will be combined with the historical richness and the natural beauties of Istanbul, especially during The Golden Year Celebrations of ERA-EDTA, will be of great value.

Many people have worked very hard for the organization of this Congress in order to bring you the best from a scientific, technical and social point of view. First of all we would like to thank Prof. Rosanna Coppo for managing the scientific programme with a great effort and success and we hope that all the participants will comprehensively learn and be updated on all topics and points in their search for excellence in their careers. This outstanding scientific programme will be a good opportunity to discuss the hottest topics in the fields of clinical nephrology, hypertension, dialysis and kidney transplantation. Traditionally, CME sessions will be held before the official opening of the congress. We believe that these sessions will be very useful for nephrology fellows and particularly for young nephrologists.

A total number of 2,400 abstracts were submitted from many countries all over the world and this has seriously brought high quality to the organization. In this respect we deeply thank Prof. Markus Ketteler and all the members of Paper Selection Committee for their hard work in evaluating and choosing the free communications and the posters that will be presented at the Congress.

Istanbul, the only city built on two continents “where East meets the West”, guards the precious relics of the three empires, Roman, Byzantine and Ottoman, of which it has been the capital. It is a fascinating mixture of the past and present, old and new, modern and traditional with museums, churches, palaces, castles, mosques and bazaars, and inexhaustible sights of natural beauty. The New Convention Centre was opened in 2009 and is located at the heart of the city, only within 10 minutes walking distance to many exclusive hotels. Under the pleasant atmosphere of Istanbul, the third “Renal Run” will be organized during the Congress.

This city with her historical role of serving as a cultural melting pot over millenniums has the capacity of providing ideal settings for any action to be more purposeful, memorable and meaningful. We strongly believe that this congress will have a good impression in the memories of our esteemed guests.

Hoping that you will have a most memorable scientific and cultural experience in Istanbul, we extend our warmest regards to all participants to this Congress.

Best wishes.

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TEN BEST ABSTRACTS

The authors of the abstracts below will receive a diploma.

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PREDICTORS OF NUTRITIONAL RESILIENCE AND EFFECTS OF HOSPITALIZATION ON NUTRITIONAL PARAMETERS IN HEMODIALYSIS PATIENTS
Michelle Wong, New York, USA

SP624
EXTRACELLULAR VESICLES DERIVED FROM MESENCHYMAL STEM CELLS INHIBIT TUBULAR INJURY, T CELL PROLIFERATION AND PROMOTE REGULATORY T CELL DIFFERENTIATION THROUGH TRANSFER OF SPECIFIC RNAS: PROTECTIVE ROLE IN T-CELL-MEDIATED KIDNEY GRAFT REJECTION
Vincenzo Cantaluppi, Torino, Italy

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TIME DEPENDENT PODOCYTE SPECIFIC NFAT ACTIVATION MEDIATES BETWEEN MCD LIKE AND FSGS LIKE PHENOTYPES
Alexis Sloan, Miami, USA

MP034
EFFICACY OF Eculizumab in Atypical HEMOLYTIC UREMIC SYNDROME (aHUS) PATIENTS WITH OR WITHOUT PRIOR TRANSPLANT
Denis Fouque, Lyon, France

MP091
MESENCHYMAL STEM CELLS ATTENUATE RENAL INFLAMMATION, MICROVASCULAR RAREFACTION AND FIBROSIS IN A MODEL OF RENOVASCULAR HYPTERTENSION.
Mirian Boim, São Paulo, Brazil

MP552
SHORT AND LONG-TERM OUTCOMES OF THE HEMODIALYSIS SELF MANAGEMENT INTERVENTION RANDOMISED TRIAL (HED-SMART) – A PRACTICAL LOW INTENSITY INTERVENTION TO IMPROVE ADHERENCE AND CLINICAL MARKERS
Konstantina Griva, Singapore, Singapore

MP553
LEFT VENTRICULAR MASS IS A POWERFUL RISK FACTOR FOR ALL-CAUSE AND CARDIOVASCULAR DEATH IN END STAGE KIDNEY DISEASE (ESKD) PATIENTS ON DIALYSIS BUT DOES NOT CONTRIBUTE TO PROGNOSIS: AN ANALYSIS IN TWO EUROPEAN COHORTS.
Giovanni Tripepi, Reggio Calabria, Italy

MP554
PATIENT AND FACILITY-LEVEL VARIATION IN THE TIMING OF DIALYSIS INITIATION ACROSS CANADA: CANADIAN KIDNEY KNOWLEDGE TRANSLATION AND GENERATION NETWORK (CANN-NET)
Navdeep Tangri, Winnipeg, Canada

TO005
MIRNA LET-7E REGULATES STEM CELL DIFFERENTIATION TOWARDS RENAL LINEAGE
Georgina Hotter, Barcelona, Spain

TO006
HUMAN LIVER STEM CELLS CONTRIBUTE TO RENAL REGENERATION AFTER ACUTE INJURY
Ciro Tetta, Bad Homburg, Germany

EIGHT BEST ABSTRACTS PRESENTED BY YOUNG AUTHORS

The authors of the abstracts below will receive a grant of EUR 1,000, free congress registration and a diploma.

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PHOSPHATE IMPAIRS ENDOTHELIAL FUNCTION - A MECHANISM FOR INCREASED CARDIOVASCULAR RISK?
Kathryn Stevens, Glasgow, UK

SP053
CYSTEINE-RICH PROTEIN 61 MEDIATES KIDNEY FIBROSIS AFTER ISCHEMIA REPERFUSION INJURY
Chun-Fu Lai, Taipei, Taiwan Republic of China

SP260
PREDICTORS OF NUTRITIONAL RESILIENCE AND EFFECTS OF HOSPITALIZATION ON NUTRITIONAL PARAMETERS IN HEMODIALYSIS PATIENTS
Michelle Wong, New York, USA
SP648
CLINICAL RESULTS OF COMBINED AND SEQUENTIAL LIVER-KIDNEY TRANSPLANTATION: A SINGLE CENTER EXPERIENCE.
Francesca Simonato, Turin, Italy

MO004
STE20-LIKE KINASE SPAK DIFFERENTIALLY REGULATES Na-(K)-Cl COTRANSPORTERS ALONG THE DISTAL NEPHRON UNDER THE ENDOCRINE CONTROL OF AVP
Turgay Saritas, Aachen, Germany

MO036
INTRA-PERITONEAL VERSUS SYSTEMIC INFLAMMATION AND SURVIVAL IN PERITONEAL DIALYSIS: RESULTS FROM THE GLOBAL FLUID STUDY
Mark Lambie, Stoke on Trent, UK

MO045
THE DISCREPANCY BETWEEN BIOLOGICAL AGE AND CALENDAR AGE: A LARGE HISTOLOGY STUDY IN IMPLANTATION BIOPSIES.
Katrien De Vusser, Leuven, Belgium

BEST ABSTRACTS PRESENTED BY YOUNG AUTHORS

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LOW BIRTHWEIGHT AND LATER RENAL FUNCTION - THE ROLE OF ADULTHOOD OBESITY. RESULTS FROM THE 1946 BRITISH BIRTH COHORT STUDY
Dorothea Nitsch, London, UK

SO011
LONG TERM FOLLOW UP OF PATIENTS WHO RECEIVED REPEAT DOSE RITUXIMAB AS MAINTENANCE THERAPY FOR ANCA ASSOCIATED VASCULITIS (AAV)
Federico Alberici, Cambridge, UK

SO016
LOCAL SYNTHESIS OF CALCITRIOL BY 1aHYDROXYLASE IS INVOLVED IN VASCULAR CALCIFICATION INDUCED BY UREMIA.
Noelia Torremadé, Lleida, Spain

SO017
SOLUBLE a-KLOTHO LEVELS IN CKD
Silverio Rotondi, Rome, Italy

SO019
T-HELPER CELLS AND FIBROSIS-ASSOCIATED MACROPHAGES DOMINATE THE PERITONEAL INFLAMMATORY INFILTRATE IN EPS PATIENTS
S Habib, Rotterdam, Netherlands

SO020
THE PREDICTIVE VALUE OF PERITONEAL EFFLUENT MMP-2 AND PAI-1 IN PD PATIENTS WHO DEVELOP ENCAPSULATING PERITONEAL SCLEROSIS
Deirisa Lopes Barreto, Amsterdam, Netherlands

SO021
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A Abrahams, Utrecht, Netherlands

SO022
GADOLINIUM DEPOSITS IN THE PERITONEAL MEMBRANE-SECOND-HIT FOR DEVELOPMENT OF ENCAPSULATING PERITONEAL SCLEROSIS?
Joerg Latus, Stuttgart, Germany

SO028
MEDITERRANEAN DIET, KIDNEY FUNCTION, AND MORTALITY IN MEN WITH CHRONIC KIDNEY DISEASE
Xiaoyan Huang, Stockholm, Sweden

SO037
SOLUBLE FLT-1 CONTRIBUTES TO CARDIOVASCULAR DISEASE IN CKD
Giovana Di Marco, Münster, Germany

SO042
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Danilo Lofaro, Cosenza, Italy

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Chien-Hua Chiu, Kaohsiung, Taiwan Republic of China
SO057  NEPHRONECTIN IS A NOVEL PROTEIN ASSOCIATED WITH DIABETIC NEPHROPATHY
Shinya Nakatani, Osaka, Japan

SO061  BARRIERS TO IMPLEMENTING A FISTULA-FIRST POLICY IN EUROPE
SN van der Veer, Amsterdam, Netherlands

SO072  INCREASED PLASMA FIBROBLAST GROWTH FACTOR 23 IS ASSOCIATED WITH AN IMPAIRED RESPONSE TO ANTIPROTEINURIC THERAPY IN PATIENTS WITH CHRONIC KIDNEY DISEASE
Martin de Borst, Groningen, Netherlands

SP008  CLINICAL FACTORS PREDICTING RENAL OUTCOME IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD): RESULTS OF THE GENKYST REGISTRY
Emilie Cornec-Le Gall, Brest, France

SP065  CCAAT/ENHANCER-BINDING PROTEIN DELTA (CEBPd) IS A NOVEL HYPOXIA-INDUCIBLE FACTOR 1 (HIF-1) REGULATOR IN KIDNEY, WHICH REGULATES ITS PATHOGENESIS IN HYPOXIC AND/OR INFLAMMATORY KIDNEY INJURY
Junna Yamaguchi, Tokyo, Japan

SP068  MITOCHONDRIA-TARGETED APPROACHES TO PREVENT GENTAMYCIN TOXICITY
Stansilovas Jankauskas, Moscow, Russian Federation

SP069  SOLUBLE HEMOJUVELIN, AN EARLY BIOMARKER PROMOTES IRON DEPOSITION DURING ACUTE KIDNEY INJURY
Chiung-Ying Huang, Taipei, Taiwan Republic of China

SP111  IN ACUTE KIDNEY INJURY, INDOXYL SULFATE IMPAIRS ENDOTHELIAL PROGENITOR CELLS – MODULATION BY STATIN
Vin-Cent Wu, Taipei, Taiwan Republic of China

SP133  IS ANTIPROTEINURIC EFFECT OF ACE-INHIBITORS CONSTANT THROUGHOUT THE DAY?
Gaetano Lucisano, Catanzaro, Italy

SP340  THE LONG ACTING CALCIMIMETIC R-641 DOES NOT INDUCE ADYNAMIC BONE DISEASE IN CHRONIC KIDNEY DISEASE
Thilo Krueger, Aachen, Germany

SP438  SUBEROYLANILIDE HYDROXAMIC ACID ATTENUATES PERITONEAL FIBROSIS INDUCED BY CHLORHEXIDINE GLUCONATE IN MICE
Kumiko Io, Nagasaki, Japan

SP445  HEME OXYGENASE-1 ATTENUATES LIPOPOLYSACCHARIDE(LPS)-INDUCED TLR4 AND PROINFLAMMATORY SIGNALING IN HUMAN PERITONEAL MESOTHELIAL CELLS (HPMCS).
Kitae Bang, Daejeon, Korea

SP641  LONG TERM OUTCOMES OF HIGHLY SENSITIZED KIDNEY TRANSPLANT RECIPIENTS
Jude Yagan, Boston, USA

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Jeong Kye Hwang, Seoul, Korea

SP654  THE EFFECT OF MAGNESIUM SUPPLEMENTATION ON EARLY POST-TRANSPLANTATION GLUCOSE METABOLISM
Steven Van Laecke, Ghent, Belgium

SP655  LONG TERM GRAFT AND PATIENT SURVIVAL POST RENAL TRANSPLANTATION IN PATIENTS WITH A PRIMARY RENAL DIAGNOSIS OF GLOMERULONEPHRITIS
Rishi Pruthi, London, UK

SP659  ANTI-ENDOTHELIAL CELL ANTIBODIES (AECA) ARE ASSOCIATED WITH A WORSE EARLY RENAL TRANSPLANT FUNCTION
Miroslaw Banasik, Wroclaw, Poland
**SP661**
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Chantal Kopecky, Vienna, Austria

**SP667**
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Mariana Wohlfahrtova, Prague, Czech Republic

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LIMITED PROGNOSTIC VALUE FOR CHRONIC TRANSPLANT DYSFUNCTION BY URINARY MARKERS OF TUBULAR INJURY WHEN MEASURED WITHIN THE FIRST YEAR AFTER RENAL TRANSPLANTATION
Jesper Kers, Amsterdam, Netherlands

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Laura Cañas Sole, Badalona, Spain

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THE AVAILABILITY OF PRE-OPERATIVE GERIATRIC NUTRITIONAL RISK INDEX(GNRI) IN KIDNEY TRANSPLANT RECIPIENTS.
Mikiko Yoshikawa, Kobe, Japan

**SP685**
DETERMINANTS OF EARLY ACCESS TO THE WAITING LIST FOR PATIENTS OVER 60 IN ONE FRENCH AREA
Lise-Marie Pouteau, Nantes, France

**SP689**
STEROID AVOIDANCE OR WITHDRAWAL FOR PANCREAS AND PANCREAS WITH KIDNEY TRANSPLANT RECIPIENTS
Nuria Montero, Barcelona, Spain

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Aaltje Adema, Haarlem, Netherlands

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Deirdre Sawinski, Philadelphia, USA

**MO006**
INTEGRATED MESSANGER RNA AND microRNA PROFILES SUGGEST AN INTERFERON ALPHA SIGNATURE IN CHRONIC ANTIBODY-MEDIATED REJECTION (CAMR) OF KIDNEY TRANSPLANTATION
Paola Pontrelli, Bari, Italy

**MO017**
DELETION OF VON-HIPPEL-LINDAU PROTEIN CONVERTS RENIN PRODUCING INTO ERYTHROPOIETIN PRODUCING CELLS IN THE KIDNEY
Birgül Kurt, Regensburg, Germany

**MO037**
FIRST PERITONITIS EPISODE INFLUENCES PERITONEAL SIZE-SELECTIVITY TO MACROMOLECULES IN PERITONEAL DIALYSIS PATIENTS.
Anouk van Diepen, Amsterdam, Netherlands

**MO040**
RISK FACTORS FOR PROGRESSION IN CHILDREN WITH IgA NEPHROPATHY: DATA FROM A EUROPEAN COHORT
Roberta Camilla, Turin, Italy

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RENAL VASCULITIS

OUTCOME OF RENAL ANCA ASSOCIATED VASCULITIS (AAV) WITH COMPLEMENT HYPERACTIVATION SIGNS: A RETROSPECTIVE STUDY

Lucio Marenti, Lorenzo Signorini, Elisa Gnappi, Francesco P. Pilato, Augusto Vaglio, Lando Allegri and Carlo Buzio

Introduction and Aims: Studies in animal models suggest that complement activation is crucial in the pathogenesis of ANCA associated vasculitis (AAV); we revisited our renal vasculitis cases searching for clinical and histological patterns (such as thrombotic microangiopathy (TMA)) that would emphasize this association.

Methods: We retrospectively examined a series of 39 consecutive patients diagnosed with kidney biopsy as having AAV between 1990 and 2012. Patients had a mean follow-up of 86 months. When available we evaluated complement status and signs of hemolysis (LDH, haptoglobin, platelets count); moreover an independent pathologist, blinded for clinical data and renal outcome, revised all the available renal histology searching for TMA.

Results: Clinical parameters at admission are reported in Table 1. 10/39 patients died during follow up. 11/22 patients had a reduction of plasma levels of C3 (< 90 mg/dl) while plasma levels of C4 were in the normal range. 6/39 (15%) patients were identified as having clear signs of TMA. Plasma levels of C3 and the presence of associated TMA significantly related with a worse renal outcome (p<0.05) (Figure 1).

Conclusions: Our preliminary data suggests that both serum C3 consumption and TMA, as a consequence of AP hyperactivation, would determine a worse renal prognosis; consequently a precocious recognition of complement hyperactivation may allow an early treatment (i.e plasmapheresis, eculizumab) of acute renal failure in these cases.

ANALYSIS OF WHOLE-BLOOD MICRO-RNA PROFILES IN PR-3-ANCA POSITIVE VASCULITIS

Anna Bertram, Sujeetna Lovicj, Joon-Kweon Park, Jan U. Becker

Introduction and Aims: ANCA associated vasculitides (AAV) are characterized by a necrotizing inflammation of small vessels, high titer of autoantibodies, increased pro-inflammatory cytokines/chemokines secretion as well as enhanced shedding of membrane-bound molecules. In order to better understand the pathophysiology of this disease we aimed to analyze whole-blood microRNA (miRNA) profiles in proteinase-3 (PR3)-ANCA positive patients with active vasculitis and compared them with those of other renal diseases without vascular involvement.

Methods: For the analysis of the global miRNA profiles blood from 10 PR3-ANCA positive AAV patients was collected using PaxGene Blood RNA tubes and miRNA was isolated using Qiagen’s PAXgene Blood miRNA Kit. Blood samples from 10 patients with IgA nephropathy or membranous glomerulonephritis served as disease control group. For quality control RNA samples were analyzed using Agilent’s 2100 Bioanalyzer system. miRNA analysis was performed using Comprehensive Biomarker Center’s Genomique logo of Biochip MPEA homo sapiens based on Sanger miRBase version 16.0. For real-time qPCR RNA samples were reverse transcribed and analyzed on a LightCycler96 II System using SYBR-Green chemistry. Serum-derived ADAM17 was analyzed using ELISA.

Results: The global miRNA analysis of the whole-blood samples delivers high correlation within the two sample groups. Nonetheless, we also observed high correlations between groups. Nonetheless, we identified a group of more than 40 miRNA candidates that were significantly differentially expressed in the active AAV group compared to the disease controls. At least three of these miRNA candidates potentially target the metalloproteinase ADAM17 (TNF-alpha converting enzyme). We performed real-time qPCR analysis on three of these candidate miRNAs to technically validate the differential expression. Moreover, real-time qPCR revealed that ADAM17 mRNA but not ADAM10 or TIMP3 mRNA amounts were significantly increased in whole-blood samples of active PR3-positive AAV compared to samples from AAV patients in remission, disease controls or from healthy controls. In addition serum levels of ADAM17 protein were significantly enhanced in active AAV compared to controls. Hence, introduction of synthetic miRNA mimics, or transfection of specific miRNA inhibitors into human primary monocytes or granulocytes modulate expression and translocation of ADAM17.

Conclusions: In conclusion, we described a specific global whole-blood miRNA profile for PR3-ANCA positive AAV. We demonstrated that several of these miRNAs modulate expression and/or release of the pro-inflammatory sheddase ADAM17 that might account for increased shedding of membrane-bound proteins in AAV.

CZECH REGISTRY OF ANCA-ASSOCIATED VASCULITIDES 2013 - ON BEHALF OF THE CZECH NATIONAL CLINICAL REGISTRY OF AAV

Eva Jancova, Zdena Hruskova, Vera Lanska, Liliana Sedova, Renata Olsianská, Dalibor Jilek, Pavel Nemec and Vladimír Tesar

Introduction and Aims: The Czech Registry of ANCA (AntiNeutrophil Cytoplasmic Antibodies)-Associated Vasculitides (AAV) was established in 2009. We retroactively examined a series of 39 consecutive patients diagnosed with kidney biopsy as having AAV between 1990 and 2012. Patients had a mean follow-up of 86 months. When available we evaluated complement status and signs of hemolysis (LDH, haptoglobin, platelets count); moreover an independent pathologist, blinded for clinical data and renal outcome, revised all the available renal histology searching for TMA.

Results: Clinical parameters at admission are reported in Table 1. 10/39 patients died during follow up. 11/22 patients had a reduction of plasma levels of C3 (< 90 mg/dl) while plasma levels of C4 were in the normal range. 6/39 (15%) patients were identified as having clear signs of TMA. Plasma levels of C3 and the presence of associated TMA significantly related with a worse renal outcome (p<0.05) (Figure 1).

Conclusions: Our preliminary data suggests that both serum C3 consumption and TMA, as a consequence of AP hyperactivation, would determine a worse renal prognosis; consequently a precocious recognition of complement hyperactivation may allow an early treatment (i.e plasmapheresis, eculizumab) of acute renal failure in these cases.
Abstracts
Nephrology Dialysis Transplantation

SO010
METHOTREXATE VS CYCLOPHOSPHAMIDE AS MAINTENANCE THERAPY IN SEVERE EOSINOPHILIC GRANULOMATOSIS WITH POLYANGITIS: A SUBANALYSIS OF THE POWERCIME TRIAL

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Introduction and Aims: Standard therapy for severe eosinophilic granulomatosis with polyangiitis (EGPA) with poor-prognosis factors (FFS≥1) combines corticosteroids and cyclophosphamide (CYC) to induce remission, followed by a less toxic immunosuppressant. The randomized controlled trial Powercime (Maritati et al. in preparation) showed that CYC and methotrexate (MTX) are equally effective and safe as maintenance therapy for AAV (MPA, GPA, and EGPA). This subanalysis investigates the trial results in patients with EGPA.

Methods: We studied patients with active EGPA and FFS≥1, either at disease onset or relapse. All patients received the same remission-induction therapy, consisting of prednisone and CYC. At remission, patients were randomly assigned to continued CYC therapy (1.5–2 mg/kg/day) or to receive methotrexate (15 mg/week progressively titrated up to 25 mg/week) for 12 months. The primary end-point was relapse (time from remission to relapse).

Results: Of the 30 EGPA patients who entered remission, 13 were randomly assigned to CYC and 17 to MTX. Patients were followed for a median period of 48 months (IQR, 29-46.8). The median time to relapse was similar in the two groups, 24 months (IQR 16-29) in the CYC group and 22.5 months (IQR 19-24) in the MTX group (P=0.95). Five patients had one or more relapses (38.4%) in the CYC group and four in the MTX group (23.6%, P=0.51). During maintenance treatment there was one death in each group.

Conclusions: MTX appears to be effective as CYC for maintenance therapy in patients with severe EGPA; however these results do not seem to support the hypothesis that it is safer than CYC.

SO011
LONG TERM FOLLOW UP OF PATIENTS WHO RECEIVED REPEAT DOSE RITUXIMAB AS MAINTENANCE THERAPY FOR ANCA ASSOCIATED VASCULITIS (AAV)

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Introduction and Aims: Rituximab (RTX) is an established induction agent in AAV. We have previously shown that repeat dose of RTX for two years is a potential maintenance strategy. Relapse risk after repeat dose RTX discontinuation is not known. Methods: We report the long term follow up of patients who received a two year repeat dose RTX regimen for relapsing/refractory AAV (1g x 2 the first month, then 1g/6 months x 4).

Results: Sixty-nine patients completed the two years RTX course. 90% had GPA with prior disease duration of 60 months (IQR 21-120). During the treatment course 9/6 (13%) relapsed but completed the RTX course. Median post-treatment follow-up was 22.7 months (IQR 12.5-38.6). 58/69 (84%) have at least 6 months of follow-up after the last RTX dose. 25/58 (43%) relapsed after a median of 15.5 months. Figure 1 represents the Kaplan-Meier estimate of relapse free survival in all the population after the completion of RTX treatment; the overall median relapse free survival was 30.5 months (CI 95% 18.4-42.7). For treatment of relapse, 10 received RTX only; 10 RTX plus corticosteroids and five other agents. By 6 months, 21/25 (84%) had regained remission. 54/69 were ANCA negative at the end of the RTX course. 12/54 (22%) became ANCA positive during follow-up, of which nine (75%) relapsed a median of 1.6 months (0.5-4.6) after ANCA return. 15 remained ANCA positive after the RTX course, of which three (20%) relapsed. Thus, 12/25 (48%) had detectable ANCA at relapse. Of 56 patients (81%) with available B-cell counts, 42/56 (75%) had B-cell return a median of 11 months (IQR 9-13) after the RTX course. 17/25 (68%) had detectable B cells at relapse, and in 11/17 (65%) B cells had returned in the 6 months preceding relapse.

Conclusions: Following a two years RTX re-treatment course, relapses occurred in 43% after a further follow up of 22.5 months. Disease control was lower in patients seen following a single RTX course for relapsing GPA, and relapses were rapidly controlled by further RTX. A switch from ANCA negativity to positivity was a relapse predictor but ANCA was negative in one half of the relapses.

SO012
RITUXIMAB USE IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS: CLINICAL EFFICACY AND IMPACT ON IMMUNOLOGICAL PARAMETERS

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Introduction and Aims: Rituximab (RTX) has been reported as an effective therapeutic agent in (refractory) ANCA-associated vasculitis (AAV). We aimed to evaluate clinical efficacy of RTX in AAV along with its impact on humoral and cellular immunological parameters.

Methods: 18 RTX-treated patients with AAV (M/F: 11/7; median age 37.5, 15x PR3-ANCA, 3x MPO-ANCA; 16x refractory disease, 2x first-line therapy) were enrolled. Clinical response, ANCA, total serum IgG levels and cellular immunity parameters were examined in regular intervals after RTX administration.

Results: The patients were followed-up for a median of 26 months (range 3-82). 15 had follow-up ≥ 6 months. All patients achieved B cell depletion that lasted 3-24 months but no significant increase was noted in T cell or NK cell subpopulations. At 6 months, partial remission was achieved in 5/15 patients (33%), and complete remission in 8 patients (53%). The median prednisone dose (30.10 mg/d) and ANCA levels (17.2, 7.17 IU/mL) decreased by 6 months. Other immunosuppressives were withdrawn in all but 4 patients (78%). RTX retreatment was used in 9 patients (7x preemptive, 2x relapse). Six patients relapsed during follow-up, but none in the preemptively treated group. Three patients died of infectious complications. IgG levels at 3 months decreased below normal range in most patients but this was well tolerated. Despite B cell depletion, markers of T cell activity (higher percentage of HLA-DR+CD3+ cells and lower percentage of CD4+CD45RA+ naive T cells) persisted during the follow-up; IFN-γ production increased at 6 months compared to baseline (17.3 vs 41.5%) and no significant change was noted in the intracellular IL-10 and IL-12 production.

Conclusions: RTX is an effective induction and also maintenance therapy for AAV that helps to lower the glucocorticosteroids dose and withdraw cytoktonic drugs in most patients. Hypogammaglobulinemia was common but well-tolerated. Peripheral circulating T cells remained activated despite B cell depletion. Our results suggest a favourable effect of RTX on immune system regulatory potential (e.g. IL-10 production).
CKD-MBD - A

PHOSPHATE IMPAIRS ENDOTHELIAL FUNCTION - A MECHANISM FOR INCREASED CARDIOVASCULAR RISK?

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Introduction and Aims: Phosphate is an independent risk factor for cardiovascular disease although the mechanism of action is unclear. This study looks at the effect of altered phosphate concentration in rat resistance vessels and rat endothelial (ECs) and smooth muscle cells (SMCs).

Methods: Vessels were dissected from the mesentery of WKY rats and incubated in physiological saline solution (PSS) with normal (1.18 mM) or high phosphate concentration (2.5 mM). Some vessels were stored for cGMP measurement by ELISA. Vessels were mounted on a wire myograph and rested before vasoconstriction response to increasing concentrations of phenylephrine (PE) and vasorelaxation response to increasing concentrations of carbachol were measured (+/- ascorbic acid (AA)). Vessels were pre-constricted a second time with PE +/- AA and vasorelaxation response to sodium nitroprusside (SNP) was measured. Concentration-response curves were constructed for each vessel for PE, carbachol and SNP +/- AA. Area under the curve was calculated and comparisons were made between the vessels in high and normal phosphate concentration PSS and +/- AA. SMCs and EGs were grown in normal (0.5 mM) and high (3 mM) phosphate medium. Some cells grown in 0.5 mM phosphate media were treated for 48 hours with 3 mM media and vice versa. Nitric oxide (NO) was measured using the Griess reaction and VEGF by ELISA. Proliferation was measured with the MTT assay in the presence and absence of L-NAME and L-arginine.

Results: Vessels in high phosphate relax less well in response to carbachol and SNP (p<0.001 and p=0.029). AA significantly improved the initial relaxation response of vessels to carbachol in high phosphate concentration PSS. Maximum relaxation remained poorer than in vessels incubated in normal phosphate PSS. AA had no effect on the relaxation response to SNP. Vessels in normal phosphate produced more cGMP than vessels in high phosphate PSS (716 pmol/mg protein, QRR: 288-1541+33 pmol/mg protein, IQR: 191-500, p=0.026). Cells in high phosphate produced less NO (p<0.05). VEGF expression was not different in cells grown long term in high phosphate. However cells grown in normal phosphate conditions and exposed to high phosphate conditions expressed increased quantities of VEGF (p<0.001). Cell proliferation was increased in cells grown in high phosphate (p<0.001).

Conclusions: Elevated phosphate decreases endothelium dependent and independent vasoconstriction and reduces cGMP production in vessels. High phosphate cells produce less NO. This may explain the endothelial dysfunction observed in the vessels and the increased proliferation seen in cells exposed to high phosphate. Long term exposure to high phosphate does not affect VEGF expression but short exposure increases VEGF expression. This supports the concept that phosphate causes endothelial dysfunction and suggests cells might adapt to high phosphate if exposed over time. AA improves high phosphate does not affect VEGF expression but short exposure increases VEGF expression.

PLASMA PENTOSIDINE LEVELS ARE ASSOCIATED WITH OSTEOSTATIC ACTIVITY IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Introduction and Aims: Serum titrate-resistant acid phosphatase 5b (TRAcP5b) is a biomarker for osteclastic activity, which is not affected by renal function. Even in dialysis patients, bone biopsy data revealed that TRAcP5b was correlated with bone resorption status such as eroded surface and osteoclast surface. Pentosidine is one of advanced glycation end products (AGEs) and established as a biomarker of oxidative stress. Bone quality deterioration is related to abnormal bone collagen cross-links driven by AGEs in patient with diabetes or primary osteoporosis. However, the association between oxidative stress and bone turnover is still unclear. Our aim was to clarify the relationship between pentosidine levels, another component of bone quality, and bone turnover.

Methods: In this cross-sectional observational study, we enrolled 122 patients with chronic kidney disease (CKD) not yet on dialysis and 100 patients on dialysis in two nephrology departments. We measured plasma pentosidine and TRAcP5b levels. We employed multiple linear regression models with TRAcP5b as a dependent variable to examine if oxidative stress determines bone resorption status.

Results: In predialysis patients, estimated GFR (eGFR) was 27.3±13.3 mL/min/1.73m². In dialysis patients, the median dialysis vintage was 6 (interquartile range: 3, 14) years. Plasma pentosidine levels increased with progression of CKD [Figure 1] and were lower in patients with ACE-I or ARB than those without. In-TRAcP5b was positively associated with In-pentosidine (P<0.01) and In-PTH (parathyroid hormone) (P<0.001) levels after adjustment for age, sex, and eGFR in predialysis patients. Also in dialysis patients, In-TRAcP5b was positively related to In-pentosidine (P<0.03) and In-PTH (P<0.001) levels and dialysis vintage (P=0.048) after adjustment for age, sex, eGFR, and dialysis dose (K/UV).

DIETARY PHOSPHATE INFLUENCES RENAL EXTRACELLULAR MATRIX TURNOVER IN APOE NULL MICE

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Introduction and Aims: Patients with renal insufficiency commonly exhibit dyslipidaemia and hyperphosphataemia. However, the effects of hyperphosphataemia and hyperlipidaemia on renal pathology remain unclear. We investigated how dietary phosphate load influences the expression of extracellular matrix components and angiopoietin-1 in hyperphosphatemic ApoE null mice.

Methods: Male 8 week-old ApoE null mice received diet containing 0.3% (low phosphate, LP), 0.6% (normal phosphate, NP) or 2% (high phosphate, HP) phosphate (n=5-6/group). Following ten weeks of phosphate load kidneys were analysed for histology and mRNA expression.

Results: High phosphate load led to significant renal Ca x P deposition as shown by von Kossa staining (% positive: LP:0.03±0.02; NP:0.04±0.03; HP:1.17±0.46, p<0.05). This was accompanied by significantly increased renal TGF-β1 and collagen-I mRNA expression as compared to mice on normal and low phosphate diet (TGF-β1: LP:0.75±0.28; NP:0.75±0.14; HP:1.35±0.37; p=0.05; collagen-I: LP:0.85±0.14; NP:0.73±0.26, p=0.026). Some cells grown in 0.5% phosphate media were treated for 48 hours with 3 mM media and vice versa. Nitric oxide (NO) was measured using the Griess reaction and VEGF by ELISA. Proliferation was measured with the MTT assay in the presence and absence of L-NAME and L-arginine.

Results: We observed 4 fold increase in renal TGF-1 and 50% increase in TIMP-2 mRNA expression as compared to NP mice (TIMP-1: LP:1.86±0.51; NP:0.94±0.44; HP:6.83±0.10, p<0.05; TIP-2: LP:1.05±0.18; NP:0.90±0.36; HP:1.48 ±0.10, p<0.05). High phosphate load increased renal angiopoietin-1 expression by 70% as compared to mice on normal diet (Ang1: LP:0.79±0.18 ; NP: 0.94±0.10; HP: 1.67 ±0.43, p<0.05).

Conclusions: Our data show that hyperphosphataemia in hyperlipidemic mice may induce the expression of renal profibrotic and angiogenic molecules even without previous renal impairment.
Conclusions: In CKD patients, either not yet on dialysis or on dialysis, higher TRACP5b levels were associated with higher pentosidine levels. Our results indicated that pentosidine might enhance bone resorption independent of PTH.

LOCAL SYNTHESIS OF CALCITRIOL BY 1α-HYDROXYLASE IS INVOLVED IN VASCULAR CALCIFICATION INDUCED BY UREMIA

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Introduction and Aims: Vascular calcification is a complication of chronic kidney disease and one of the main predictors of increased morbidity and mortality in patients. Previous results of our group demonstrated that uremia deregulates proteins involved in vitamin D metabolism in vascular smooth muscle cells (VSMC), increasing the expression of 1α-hydroxylase and producing a local increase of calcitriol which could have a paracrine effect in the vessel wall. The objective of this study is to determine the role of the local synthesis of calcitriol on uremia-induced vascular calcification.

Methods: Wild type and 1α-hydroxylase KO mice (1αOHase KO) underwent 75% of renal mass reduction, were treated with high daily doses of calcitriol (400 ng/kg) for two weeks. At the end of the experiment, serum samples were collected and Ca, P and BUN were quantified. The artery was used to evaluate vascular calcification by calcium quantification and alizarin red staining. In vitro WT and 1αOHase KO VSMC were treated with healthy and uremic rat serum to evaluate its effect on calcification and in the expression of related genes.

Results: WT mice (n=8) show a significant weight loss and increased mortality when treated with high dose of calcitriol. However, 1α OHase KO mice (n=8) don’t lose weight and mortality is absent. Serum calcium levels (WT: 16.38 ± 4.8, KO: 15.18 ± 0.46 mg/dl), phosphorus (WT: 9.15 ± 0.42, KO: 8.43 ± 0.46 mg/dl), BUN (WT: 44.99 ±2.19, KO:46.13±4.02mg/dl), and 1,25D levels (WT: 150.21±14.71, KO: 123.8±14.71 pg/ml) increased in both in both calcitriol-treated groups. Furthermore, PTH levels decreased below normal values (WT: 29.25±0.84, KO: 30.48±0.70 pg/ml). Vascular calcium content significantly increased in the WT mice compared to 1αOHase KO mice (WT: 895,70±172,26; KO: 556.74±77.71 μgCa/mg protein, p<0.05). Similar results were observed with alizarin red staining and immunohistochemical detection of Runx2, which were increased only in WT mice. In vitro, WT VSMC treated with uremic serum also showed a significant increase in calcification that was not observed in 1αOHase KO cells (WT:3452.50 ± 498.07; KO: 510.72± 94.82 μgCa/mg protein, n=6 to 8, P<0.05).

Conclusions: These results suggest that local production of calcitriol by 1α-hydroxylase in the artery may mediate vascular calcification observed in uremia.
ENCAPSULATING PERITONEAL SCLEROSIS

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Introduction and Aims: Encapsulating peritoneal sclerosis (EPS) is a rare yet debilitating complication of peritoneal dialysis (PD). Although histological and clinical diagnosis is usually straightforward, a necrotizing peritonitis in a late stage of PD. Although histological and clinical diagnosis is usually straightforward, a necrotizing peritonitis in a late stage of PD, it is often not reversible and mortality is high. Therefore, the role of macrophages in the pathogenesis of EPS needs to be elucidated.

Methods: Peritoneal biopsies of 26 patients with EPS were obtained from the database of the Dutch EPS registry and compared to biopsies of 15 patients who were treated with PD but without developing EPS. Immunohistochemistry was performed using routine diagnostics on all biopsies using the primary antibodies CD3 (pan-T-cells), CD4 (T-helper cells), CD8 (cytotoxic T-cells), CD68 (macrophages) and CD163 (M2 macrophages). Stainings were thereafter analysed using digital image analysis (KS400), measuring % of area staining.

Results: Percentage of area surface staining for both CD3 and CD68 were higher in EPS patients in comparison to PD patients (resp. 1.49% (1.04-2.49) vs 0.26% (0.19-0.41), p < 0.001; and 4.08% (2.56-4.77) vs 0.37% (0.23-1.16), p < 0.001). EPS biopsies had a significantly higher percentage of area staining for CD4+ cells (1.47 (0.60-3.18)) as compared to CD8+ cells (0.66% (0.46-0.94), p < 0.05), while this difference was not present in the control group. Furthermore, area percentage of staining for CD68 was higher than that of CD3 in EPS biopsies (p < 0.001). The amount of area percentage staining for both CD163 and CD80 were higher in EPS biopsies than in control biopsies (p < 0.001).

Conclusions: This is the first study, in a large cohort of EPS patients, which elucidates the inflammatory response in the peritoneal biopsy of patients with EPS and compares it to that in the peritoneal biopsy of PD patients without EPS. Our findings suggest a prominent role for both T-helper cells and pro-fibrotic M2 macrophages in the development of EPS, which not only supports but also highlights the concept of peritoneal inflammatory and fibrotic mechanisms in the pathogenesis of EPS.

THE PREDICTIVE VALUE OF PERITONEAL EFFLUENT MMP-2 AND PAI-1 IN PATIENTS WHO DEVELOP ENCAPSULATING PERITONEAL SCLEROSIS

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Introduction and Aims: Encapsulating peritoneal sclerosis (EPS) is the most severe morphological complication that may occur in 3% of peritoneal dialysis (PD) patients. The clinical diagnosis is not possible in a late stage of PD. Although histological and clinical diagnosis is usually straightforward, a necrotizing peritonitis in a late stage of PD, it is often not reversible and mortality is high. Therefore, the role of macrophages in the pathogenesis of EPS needs to be elucidated.

Methods: Peritoneal biopsies were obtained from EPS patients and time-matched controls pointing to progressive peritoneal fibrosis and sclerosis. Risk estimations have to be made with regard to the levels of MMP-2 and PAI-1 in the years preceding the diagnosis of EPS.

Results: Elevated levels of PAI-1 were found in EPS patients, compared to the control group. Additionally, a significant increase of effluent PAI-1 (p=0.001) was present during longitudinal follow-up in the years prior to the diagnosis of EPS. Through analysis, levels of effluent PAI-1 are present in patients who develop EPS compared to time-matched controls pointing to progressive peritoneal fibrosis and sclerosis. Risk estimations have to be made with regard to the levels of MMP-2 and PAI-1 in the years preceding the diagnosis of EPS.
Encapsulating peritoneal sclerosis (EPS) often develops after withdrawal from peritoneal dialysis (PD). Termination of PD and Hemodialysis-related complications are supposed to be associated with significant morbidity. Previous exposition to gadolinium-based contrast agents during magnetic resonance imaging (MRI) has been linked to a disease called nephrogenic systemic fibrosis (NSF). Some authors discussed that EPS represents a localized form of NSF. Gadolinium was found in skin, myocardium, skeletal muscles, liver, lung and testis. In the present study, we investigated peritoneal biopsies from 5 late-stage EPS patients after exposure to gadolinium during MRI. Peritoneal biopsies of 5 late-stage EPS patients were investigated using conventional electron microscopy, ultrastructural analysis and immunostaining (Transforming growth factor β1, CD68 and CD34).

**Methods:** Peritoneal biopsies of 5 late-stage EPS patients were investigated under static conditions after stoppage of PD. Termination of PD and Hemodialysis-related complications are supposed to be associated with significant morbidity.

**Results:** Electron microscopy analysis of parietal peritoneum was positive for gadolinium in 1 out of 5 EPS patients. Immunoperoxidase staining of samples showed hot spots of arteriolar endothelial cells expressing CD34 and macrophages with expression of CD68. Inflammatory cells expressing TGF-β1 were present in all samples. Histopathological findings and baseline characteristics were not different between the patients, except for the homocystein levels, which were strongly elevated in the patient with gadolinium deposits in the peritoneal membrane. The gadolinium-positive patient had severe course of EPS requiring reoperation due to recurrent disease four-times.

**Conclusions:** Obviously, EPS represents a localized form of NSF. The severe course of the disease in the gadolinium-positive patient leads to the hypothesis that gadolinium deposits might act as an aetiopathogenic factor causing a “second-hit” in the development of EPS. This has to be elucidated in larger cohorts.

**Introduction and Aims:** Encapsulating Peritoneal Sclerosis (EPS) is a rare complication of peritoneal dialysis (PD) that is associated with significant morbidity.
and mortality in adults. There are scarce data for children. We performed a 10-year survey to determine the prevalence, risk factors and outcome for EPS in children.

**Methods:** Chronic PD patients in 14 dialysis units participating in the European Pediatric Dialysis Working Group between January 2001 and December 2010.

**Results:** Twenty-two cases of EPS were reported (prevalence 1.5%; 8.7 per 1000 patient-years on PD). Median PD vintage was 5.9 (1.6–10.2) in EPS and 1.7 (0.7–7.7) years in the remainder of the PD population (p<0.0001). EPS patients had a significantly higher peritonitis rate than non-EPS patients (p=0.02). EPS was diagnosed while the child was on PD in 17 (77%), after conversion to hemodialysis in 3, and after transplantation in 2. 15/17 (88%) developed ultrafiltration failure. The median interval between UF failure and presentation with bowel obstruction was 2.8 (0.02–5.8) months. Twenty (91%) had clinical and radiological signs of bowel obstruction. Enterolysis was performed in 14 and 19 received immunosuppression or tamoxifen. Nine required parenteral nutrition. At final follow-up 4.8 (1.3–8.7) years after EPS diagnosis, 3 patients have died, 11 have a functioning transplant and 8 are on hemodialysis.

**Conclusions:** The prevalence of EPS in European children on PD is comparable to that of adult PD patients, but mortality from paediatric EPS is significantly lower. A high index of suspicion is required for the diagnosis of EPS in children with a longer dialysis duration, high peritonitis rate and ultrafiltration failure.
HYPERTENSION AND OUTCOMES

**SO027** ALBUMINURIA IN PREDICTION OF CARDIOVASCULAR MORTALITY. ONE VERSUS MULTIPLE URINE SAMPLES IN THE SECOND HUNT STUDY, NORWAY

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Introduction and Aims: Albuminuria is an independent predictor of cardiovascular (CV) mortality, regardless of the presence of diabetes or hypertension. Still, only single urine samples are available in most previous studies and so far, there is no consensus of numbers of urine samples needed for risk prediction. This study examined the impact of increasing numbers of urine samples at different albuminuria cut-off levels for prediction of long-term CV mortality.

Methods: In a prospective cohort study from the population-based Nord-Tromsø Health Study (HUNT), Norway, we followed 9,158 adults with known diabetes, treated hypertension or randomly selected for 13 years. Albumin-to-creatinine ratios (ACR) in 3 morning urine samples were available from each participant. Adjusted hazard ratios (HR) for CV mortality on increasing number of positive ACR at different ACR cut-offs were assessed in Cox survival analyses, and predictive performance of models based on Framingham variables plus 1 versus 3 ACRs was evaluated.

Results: For levels above high-normal ACR range (i.e. cut-offs >1.0 mg/mmol), single urine sample was enough to demonstrate a significant association to CV mortality (HR 1.36, 95% CI 1.13-1.64, P = 0.001) in the total sample. This applied to all subgroups for cut-off levels ≥2.7 mg/mmol. For lower levels, 2 or 3 urine samples were needed for significance. There was neither improvement in discrimination (C-statistics 0.822 vs. 0.822; P=0.65) or calibration using 3 compared to 1 ACR value, nor did reclassification improve CV risk prediction (Net Reclassification Improvement 0.007 (-0.01-0.02)). However, considering ACR cut-offs below the high albuminuria (“microalbuminuria”) range, multiple ACR measurements might be superior.

Conclusions: Single urine ACR measurement will, in most clinical situations, be sufficient for CV mortality risk evaluation, since additional urine samples only improved diagnostic accuracy marginally.

**SO029** MEDITERRANEAN DIET, KIDNEY FUNCTION, AND MORTALITY IN MEN WITH CHRONIC KIDNEY DISEASE

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Introduction and Aims: A Mediterranean diet has been linked to reduced morbidity and mortality but in various populations but little is known with regard to kidney function in the community. We aimed to investigate whether adherence to a Mediterranean diet is associated with improved kidney function, cardiometabolic risk profile and reduced mortality risk in individuals with manifest chronic kidney disease (CKD).

Methods: Dietary habits were determined by 7-d dietary records in a population-based cohort of 1110 Swedish men (age 70 y), 506 of whom were considered to have CKD because of a glomerular filtration rate <60 ml/min/1.73 m2. A Mediterranean Diet Score (MDS) was calculated and participants categorized as low-, medium-, and high-adherents. Adequate reporters were identified with Goldberg cutoffs (n=597), and deaths were registered during a median follow-up of 9.9 years.

Results: As compared to low adherents, high adherents were 42% less likely to have CKD (adjusted OR 0.58, 95% CI (0.38-0.87), P for trend 0.04). During follow-up, 168 (33%) CKD individuals died. In these, no differences were observed regarding important cardiometabolic risk factors (BMI, waist circumference, blood pressure, blood lipids, glucose, insulin, inflammation or albumin) across adherence groups. In proportional hazards regression, a higher MDS adherence (every 2 point increase in MDS) was independently associated with 18% lower mortality risk. Sensitivity analyses showed stronger associations in individuals with adequate reported dietary intake.

Conclusions: Adherence to a Mediterranean-like dietary pattern correlates with better renal function in the community. A greater adherence to this diet independently predicts survival in individuals with manifest CKD.

**SO029** PREVALENCE OF HYPERTENSION AND LOW GFR IN OBESE CHILDREN: RESULTS OF A POPULATION-BASED FIELD STUDY, THE CREDIT-C STUDY

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Introduction and Aims: Obesity has risen dramatically in the Western world. Hypertension, metabolic syndrome, hyperlipidaemia, sleep disorders, and type 2 diabetes mellitus are weight-related disorders. In adults, obesity is associated with an increased risk of development and progression of kidney disease. Data at the epidemiological level are limited, both for children and adults. The aim of this study was to evaluate the effect of obesity on hypertension and glomerular filtration rate (GFR) among children in a field study in Turkey.

Methods: A population-based field study in which individuals were accessed by house visits throughout Turkey has been conducted (CREDIT-C). The study sample (3622 children; 5-18 years) was selected to represent Turkish population regarding to geographical region, gender and age (5 to 18 years). Obesity was defined as body mass index ≥95th percentile for age and gender. Schwartz formula was used to estimate GFR. Blood pressure (BP) percentile was determined according to age, gender and length.

Results: The prevalence of obesity, hypertension (≥95th percentile), and low GFR (<90ml/min/1.73m2) were 8.9%, 6.1% and 3.1%, respectively. GFR was <75ml/min/1.73m2 (1.2% vs. 0.7%) were higher among obese children, compared to non-obese group. Obesity increased risk for hypertension (OR 2.61, 95%CI 1.71-3.98; P<0.001). Systolic and diastolic blood pressure z-scores were higher among obese children (P<0.001).

Conclusions: In this population-based field study we showed a remarkable prevalence of obesity in children and its association with hypertension, and low GFR in Turkey. Strategies for the prevention and management of obesity are also important for developing countries and for children. Long term consequences of obesity during childhood in adult life merit further studies. The Study was supported by TUBITAK (The Scientific and Technological Research Council of Turkey).
ESAS AND IRON

SO300 CLINICAL PHARMACOLOGY OF THE ANTI-HEPCIDIN SPiegelMER® NOX-H94

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NOXXON Pharma AG Berlin Germany, 2Hammersmith Medicines Research London United Kingdom, 3Radboud University Nijmegen Medical Centre Nijmegen The Netherlands

Introduction and Aims: NOX-H94, a PEGylated anti-hepcidin L-RNA oligonucleotide, is in development for treatment of anemia of chronic disease (ACD). ACD is frequent in patients with renal failure, cancer, or inflammatory diseases. Caused by high serum hepcidin leading to ferroportin degradation it results in iron sequestration and iron restricted erythropoiesis. Targeting hepcidin may provide an efficacious, well tolerated alternative to current ACD treatments. Methods: NOX-H94 was studied after single and repeated IV and SC doses in healthy men and women. Cohorts of 8 subjects were randomly assigned to single IV doses of 0.3, 0.6, 1.2, 2.4, and 4.8 mg/kg NOX-H94 (n=6) or placebo (n=2), 2 cohorts received 5 qd IV doses of 0.6 or 1.2 mg/kg NOX-H94, one cohort received 8 qd SC injections of 0.5 mg/kg NOX-H94. The pharmacodynamics of NOX-H94 were further studied in the human endotoxemia model: 24 healthy young men received 2 ng/kg E. coli endotoxin (LPS) IV to provoke a systemic inflammatory reaction with induction of inflammatory cytokines and subsequent hepcidin, leading to hypoferraemia. Subjects were randomly assigned to single double blind IV treatment with 1.2 mg/kg NOX-H94 or placebo 0.5h post LPS. Cytokines and iron parameters were studied; serum iron change at 9h post LPS was the primary endpoint. Results: NOX-H94 doses 2.1 ± 2 mg/kg raised serum iron above placebo levels. NOX-H94 induced inflammatory reactions independently of treatment assignment. In the placebo group, iron (19±7.6 μg/L) initially increased until 3h post LPS; the time of hepcidin increase. Iron then decreased to a minimum of 8±2.9 μg/L at 12h. In NOX-H94 treated subjects, iron increased up to 8h post LPS (38±8.9 μg/L) and remained above baseline until 12h (28±9.6 μg/L). Iron concentrations were significantly different from 6 to 12h post LPS (p<0.0001, ANCOVA). Peak and systemic exposures (Cmax and AUC) were largely dose-linear. At 1.2 mg/kg IV Cmax was 2.2±0.3 μM, AUC was 30±6.2 μM×h; T1/2 was 24±10h. NOX-H94 did not accumulate after repeated doses. After SC injection of 0.5 mg/kg NOX-H94, Cmax was 0.12±0.03 nM 48h post dose and increased almost 3-fold after repeated dosing. Steady state was reached after 4 qd SC injections. NOX-H94 was well tolerated; mainly headache, fatigue, local reactions, and mild transaminase increases at high doses were observed. Conclusions: These clinical pharmacology studies demonstrated the inhibition of hepcidin by NOX-H94 in humans and showed dose-linear pharmacokinetics and a favourable safety profile. Based on these results, a phase II study in patients with ACD is ongoing.

SO301 SAFETY AND EFFICACY OF FERUMOXYTOL VS. IRON SUCROSE IN THE TREATMENT OF IRON DEFICIENCY ANEMIA (IDA) IN PATIENTS WITH NORMAL AND ABNORMAL RENAL FUNCTION

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AMAG Pharmaceuticals, Inc. Lexington MA United States

Introduction and Aims: IV iron plays an important role in the treatment of patients (pts) with IDA across all degrees of renal function, and in particular for pts with chronic kidney disease (CKD). The aim of this single-center, single-blind study was to assess the safety and pharmacodynamics of ferumoxytrol (FER), compared with iron sucrose (IS), in pts with IDA who had either CKD or in whom OI could not be used. Results: The study was conducted from September 2009 to May 2010 at 14 sites. Randomization was carried out in a 2:1 ratio (FER:IS) in 162 pts. 80 pts were assigned to FER and 82 to IS. All pts were on HD. Mean Hgb at Baseline (BL) was 9.4±1.3 g/dL; mean age 67±12 years; 56% were females; 16% were diabetic; 43% had CKD-201 (Hgb <10 g/dL and >7g/dL, TSAT<20%, eGFR<30ml/min; and history of unsatisfactory OI therapy or in whom OI could not be used). BL Hgb at entry was randomized to FER or IS (2 X 510 mg injections, 5±3 days apart) or IS (5 X 200 mg infusions/injections). Results: 162 pts were randomized in CKD-201 (80 FER; 82 IS); approximately 43% of pts were on HD. 605 pts were randomized into IDA-302 (406 FER; 199 IS). Demographics were well balanced between the 2 treatment groups in both studies. In IDA-201, the mean change in Hgb from BL to Wk 5 (primary endpoint), adjusted for BL Hgb and dialysis status, was 0.8±1.0±0.2 g/dL for FER-treated pts vs. 0.7±1.4±0.1 g/dL for IS-treated pts, meeting the pre-specified criteria for non-inferiority. In IDA-302, 84% of FER-treated pts had ≥2 g/dL rise in Hgb at anytime from BL (primary endpoint) vs. 81% of IS pts, thereby meeting the pre-specified criteria for non-inferiority. FER-treated pts had a mean increase in Hgb of 2.7±0.2, which was significantly greater than that for IS-treated pts (2.4±0.2; p=0.0124). The incidence of treatment emergent adverse events (AEs) is summarized below:

| Treatment | AEs of Special Interest | All Treatment Emergent AEs
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<td>AEs of Special Interest</td>
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* at any time from BL to Wk 5; † includes protocol-defined signs/symptoms of hypotension and hypersensitivity.

SO302 IRON DEFICIENCY, IRON IMMUNIZATION IN MACROPHAGES AND THEIR OVERLAP IN RENAL ANEMIA

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Introduction and Aims: Iron deficiency anemia (IDA) can be associated with inflammation-induced immunomodulation of iron in macrophages (anemia of chronic conditions - ACD) in renal anemia. This association could explain the ferritin and transferrin saturation index (TSAT) cut-offs recommended for iron deficiency diagnosis in chronic kidney disease (CKD), which are higher than in general population. Our aim was to investigate the role of iron indices, inflammation, hepcidin, erythropoietin in relation with the type of anemia diagnosed by bone marrow examination.

Methods: 167 anemic, iron and erythropoietin free, non-dialysis CKD patients entered this prospective single-center study. At bone marrow examination (aspiration, Perls’ and May Grünwald Giemsa stain) 4 patients were normal, 1 had erythrodiplasia, 15 IDA, 82 ACD and 65 IDA and ACD (IDA+ACD). Only IDA, ACD and IDA+ACD patients were retained in the final analysis (N=162, 52% males, median age 67 years, eGFR 14.2±9ml/min, Hb 9.4±1.3 g/dL; 23% with diabetes mellitus). Serum hepcidin and erythropoietin (Epo) were measured by ELISA, and ferritin, transferrin and CRP, immunoturbidimetrically. TSAT was calculated as the percentage of serum iron from total serum iron binding capacity. Data are presented as mean (median) and 95% confidence intervals of the mean (median).

Results: ACD was seen in 51%, the combined pattern IDA+ACD in 40%, while the ‘pure’ iron deficiency only in a minority (9%). Compared to ACD, patients with IDA had less severe anemia (9.5 [8.2-10.6]g/dL vs. 8.8 [8.4-9.3]g/dL) and a better renal function (eGFR 14.2±9ml/min, Hb 9.4±1.3 g/dL; 23% with diabetes mellitus). Serum hepcidin and erythropoietin levels were higher in IDA and ACD vs. IDA+ACD (P<0.05).

Conclusion: This study suggests that ACD is frequent in patients with renal failure, cancer, or inflammatory diseases. Caused by high serum hepcidin leading to ferroportin degradation it results in iron sequestration and iron restricted erythropoiesis. Targeting hepcidin may provide an efficacious, well tolerated alternative to current ACD treatments.
Conclusions: Iron deficiency and iron immobilization in macrophages are associated in a higher than reported proportion (40%) in renal anemia. As ferritin and TSAT in CKD patients with 'pure' iron deficiency are closer to those of general population but significantly different from those of ACD or IDA+ACD, the current cut-off probably reflect the underdiagnosed overlap between IDA and ACD. However, peripheral iron indices and even ferritin are of little help in distinguishing IDA or ACD from their overlap. As hepcidin and erythropoietin but not CRP differed between groups, hepcidin secretion seems driven by the erythropoietic activity, and not by inflammation, at least in this cohort with moderate inflammation.

SO033 HYPOPHOSPHATEMIA INDUCED BY INTRAVENOUS ADMINISTRATION OF FERRIC CARBOXYMALTOSE IN NONDIALYSIS CHRONIC KIDNEY DISEASE PATIENTS IS NOT MEDITATED BY FGF23

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Introduction and Aims: Some parental iron therapies have been found to be associated with hypophosphatemia. The mechanism of the decrease in serum phosphate is unknown. It has been suggested that fibroblast growth factor 23 (FGF23), reducing renal phosphate reabsorption and inhibiting 1α-hydroxilation of vitamin D, may play a role in the development of hypophosphatemia. The aim of this study was to examine the effect of i.v. ferric carboxymaltose (FCM) on phosphate metabolism and serum FGF23 levels in chronic kidney disease (CKD) patients.

Methods: This is a post-hoc analysis of a prospective study carried out in 47 nondialysis CKD patients (mean eGFR 28±10.4 ml/min/1.73 m²) with iron-deficiency anemia which received a single injection of 1000 mg of FCM. Markers of iron status (transferrin saturation and ferritin) and mineral metabolism (calcium, phosphate, 1,25-dihydroxyvitamin D, PTH and FGF23) were measured prior to and at week 3 and week 12 after FCM administration. Based on the measured levels of serum phosphate at week 3, patients were classified as hypophosphatemics and non-hypophosphatemics. There was no difference in mineral metabolism parameters between the two groups at baseline or during the study. Changes in FGF23 levels did not differ between groups.

Results: Serum phosphate levels decreased significantly after 3 weeks of FCM administration in nondialysis patients. There was no significant correlation between the decline in serum phosphate and FGF23 levels at week 3 and at week 12. Baseline FGF23 levels showed significant correlation with phosphate (r=0.28, p=0.05) but not with ferritin (r=−0.04, p=0.001), serum calcium (r=0.65, p=0.001), serum PTH (r=−0.48, p=0.001) and eGFR (r=−0.13, p=0.007) and hepcidin (r=−0.13, p=0.007) and hepcidin secretion was not significantly different between the hypophosphatemics and non-hypophosphatemics. There was no difference in mineral metabolism parameters.
CARDIOVASCULAR DISEASE IN CKD

SO036 ASSOCIATION OF MAGNESIUM LEVEL WITH REDUCED CARDIOVASCULAR MORTALITY IN INCIDENT DIALYSIS PATIENTS

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Introduction and Aims: Magnesium may have beneficial effects on vascular calcification. We therefore searched for epidemiological evidence to support the assumption of an independent favorable effect of magnesium on both all-cause and especially cardiovascular (CV) mortality in ESRD.

Methods: Magnesium level was determined in a prospective cohort study of incident dialysis patients in the Netherlands (the NECOSAD cohort). Association with all-cause and CV mortality at 1 and 3 years from start of dialysis was studied for tertiles of magnesium levels. Multivariate adjustments were made for sex, age, primary kidney disease, cardiovascular disease, diabetes, kidney function, body mass index, smoking status, and use of warfarin.

Results: 492 hemodialysis and 46 peritoneal dialysis patients were studied (63 ± 14 years, 58% male, 91% hemodialysis, 83% Caucasian). Diabetes was present in 25% of the patients. Mortality at year 1 and 3 after start of dialysis was 13% and 30% for all-cause and 6% and 15% for CV mortality respectively. Magnesium levels were 0.85 ± 0.08, 1.04 ± 0.05 and 1.26 ± 0.13 mmol/L in the three tertiles (upper limit of normal 1.1 mmol/L). In comparison with patients of the lowest magnesium tertile, patients of the highest tertile showed a lower baseline GFR (4.2±3.4 vs. 2.9±2.3 ml/min/1.73m²), higher PTH (21.8±21.8 pmol/L vs. 24.4±27.8 pmol/L) and lower Kt/V. All-cause mortality showed no significant association with magnesium tertiles in crude and adjusted analyses. The adjusted hazard ratios for cardiovascular mortality in the highest tertile as compared to the lowest tertile at 1 and 3 years after start of dialysis were 0.42 (CI 0.18-0.98) and 0.64 (CI 0.39-1.06) respectively.

Conclusions: Higher baseline magnesium level is significantly associated with lower CV mortality at one year after start of dialysis after multivariable adjustments. A similar trend was observed for year 3 CV mortality. Magnesium levels were not associated with all-cause mortality. Although a causal relation between higher magnesium level and improved CV mortality is not proven from our data, it does support that assumption.

SO037 SOLUBLE FLT-1 CONTRIBUTES TO CARDIOVASCULAR DISEASE IN CKD

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Introduction and Aims: SOLUBLE FLT-1 is strongly associated with cardiovascular burden. Soluble Flt-1, a VEGF antagonist, has been appeared to be elevated in CKD. However, data on whether sFlt-1 plays a causal role in CKD-associated heart dysfunction are still missing. We sought to determine 1) sFlt-1 as a biomarker in CKD-heart disease and 2) the direct effect of sFlt-1 on vascular remodelling and heart function.

Methods: Patient study: Serum sFlt-1 was determined in 586 patients of the Coronary Artery Disease and Renal Failure (CAD-REF) registry with angiographically documented CAD (>50% stenosis in at least one coronary artery) and CKD determined by estimated GFR (MDRD) and/or proteinuria. Animal study: Circulating sFlt-1 levels were raised in rats by delivery of recombinant sFlt-1 through oesophageal pumps. Control rats were treated with saline. Heart function and perfusion (contrast perfusion imaging) were assessed in vivo by high resolution echocardiography. Immunostaining with isoelectric B4 and picro Sirus were used to evaluate the capillary density and collagen deposition in the heart, while electron microscopy was used to determine ultrastructural changes.

Results: In the patient study, sFlt-1 levels were negatively correlated with GFR (p<0.001) and positively with proteinuria (p<0.01). Moreover, elevated sFlt-1 levels were associated with the New York Heart Association functional class (p<0.01), reduced left ventricular (LV) ejection fraction (p<0.003) and presence of left bundle branch block (p<0.005). Cumulative survival rate was slightly lower in patients in the 3rd and 4th quartile of sFlt-1 (180 pg/ml) (p=0.052). There was no association between sFlt-1 and CAD, suggesting that sFlt-1 may contribute to micro- rather than macrovascular disease in CKD. Corroborating these findings, sFlt-1-treated rats (sFlt-1: 434±97 vs. 195±39 pg/ml in control rats, mean±SD, p<0.05) displayed a 15%-reduction in the number of vessels/cardiomyocyte, while myocardial blood volume (perfusion imaging) were assessed in vivo by high resolution echocardiography. Immunostaining with isoelectric B4 and picro Sirus were used to evaluate the capillary density and collagen deposition in the heart, while electron microscopy was used to determine ultrastructural changes.

Conclusions: Our patient study confirms the inverse correlation between sFlt-1 and renal function, and supports a role for sFlt-1 in CKD-associated heart failure. Our animal study suggests that microvascular remodelling/disease in response to increased sFlt-1 levels may contribute to cardiomyocyte dysfunction, reduced ventricular contraction and loss of function in both rats and patients.

SO038 VITAMIN K ANTAGONISTS ARE AN INDEPENDENT RISK FACTOR FOR UREMIC FOOT AND DEATH AMONG DIALYZED PATIENTS

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Introduction and Aims: Foot ulceration (FU) and lower limb amputation, also defined as “uremic foot syndrome”, is a common complication in Hemodialyzed patients (HDpts). Its prevalence is high, because of the inflammation and vascular

CV-HD. All HD PBMC were also placed for 24 hours in culture terrain adding to each half sample of PBMC. miR-155 levels were quantified by TaqMan microRNA RT-PCR kit (Applied Biosystems, CA). Data were expressed as M155E and compared by unpaired t-test using Welch correction.

Results: PBMC miR-155 Relative Quantity (RQ) in CV HD was 0.34 ± 0.07 times higher than CV free HD (P=0.01). Analyzing PBMC miR-155 after PHA stimulation from all predialysis HDs, RQ was 1.79±0.59 times higher when compared to non stimulated HD PBMCs (P=0.019). No statistical difference was observed in miR-155 expression of non stratified HD PBMCs before vs. after hemodialysis.

Conclusions: These data show a significant down-regulation of miR-155 in PBMC from CV-HD when compared to CVFreeHD patients. Such evidence might encourage further studies aimed to analyse PBMC miR-155 expression as possible prognostic factor to predict cardiovascular risk in HD patients. Data on predialysis HD showing up-regulation after PHA stimulation are current purpose of additional investigation.

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Biomarkers of interest (albumin, magnesium, C-reactive protein, troponin T, homocysteine, interleukin-6, TNFα, IFG-23, fentin and dp-ucMGP). We used the Mann-Whitney test or independent samples t-test according to the distribution.

Results: The sample included 165 patients with the following clinical characteristics: median age was 74 y [63;80], mean BMI was 26.7 ± kg/m², median dialysis vintage 22 months [11;43], 44% were diabetic, 87% were hypertensive, 21% were smokers and 65% had cardiovascular antecedents. Among these patients, 143 were not treated by vitamin K antagonists and 22 were treated by acenocoumarol. Data about therapy was lacking in 2 patients. No statistical difference was observed in clinical and classical biological variables. Among biological variables, we found differences between treated and non-treated for dp-ucMGP: 3802 pM [2274;5322] versus 1280 pM [955;2178], p<0.0001, for b-ALP: 22 μg/L [17;34] versus 15 μg/L [10;23], p=0.004 and for P1NP: 330 pg/ml [173;519] versus 206 pg/ml [107;342], p=0.04, respectively.

Conclusions: In this study, we confirmed that levels of dp-ucMGP were strongly influenced by vitamin K antagonist therapy in hemodialysis. The moderate effect of vitamin K antagonist on b-ALP and P1NP deserve further studies.
Methods: unfavourable prognosis regarding graft survival, and assess whether these subgroups

Introduction and Aims: Improved perinatal care increased not only the survival rate but also the frequency of acute kidney injury (AKI) in newborns. We aimed to determine the frequency, etiology, clinical course and mortality of AKI in a third level neonatal intensive care unit (NICU).

Results: There were 677 patients (M/F: 392/285) and 94 (13.9%) had AKI of which 80% of patients with AKI were recorded.

Conclusion: AKI incidence in NICU was 14%, and 80% of AKI developed during the first week of life.

Introduction and Aims: Kidney transplantation (TX) is the treatment of choice for children on RRT. However, graft loss remains an important problem and therefore, the aim of this study is to identify subgroups of patients with markedely favourable or unfavourable prognosis regarding graft survival, and assess whether these subgroups are of added value to improve the prognostic power of conventional statistical analyses.

Methods: 5275 paediatric renal TX recorded in the ESPN/ERA-EDTA Registry were analyzed. 2 analyses were performed, the 1st on parameters known before TX including gender, age at TX, time on dialysis, pre-emptive TX, type of donor, and cause of renal failure. The 2nd considered also clinical measurements within 1 year after TX including eGFR, hb, blood pressure (BP) SDS and height. To evaluate 5-year graft survival, we used binary survival tree models to identify subgroups similar in graft survival and Cox regression to evaluate the prediction power of these models.

Results: 8 subgroups were identified in 1st analysis. The best survival was among patients on dialysis for less than 1.5 months (90.4%) while the poorest was among those adolescents at TX, on dialysis for a long time (51.7%). There were also differences among patients with age at TX between 4 and 13.5 yrs and low (86.9%) compared to high risk of recurrent diseases (97.3%, p<0.001) as well as in those older than 13, with short-term dialysis (0.1-2.2 yrs) and receiving a deceased donation, between males (82.7%) and females (68.6%, p<0.006). For the analysis including post-TX data, time on dialysis, recipient age, eGFR and diastolic BP identified 10 subgroups. The best graft survival (97.3%) was found among those on dialysis for less than 1.6 yrs before TX, eGFR ≥ 30 and younger than 8 yrs. Among older patients, the tree found a significant (p < 0.001) difference by diastolic BP: between 0.3 and 1.2 (95.6%), lower than -0.3 (85.9%) and higher than 1.2 SDS (85.3%). The subgroups with the worst 5-yr graft survival consisted of patients with long-term dialysis, eGFR < 64 and, respectively, aged between 11 and 14 at TX (46.5%) or older than 14 (34.7%, p<0.001). In Cox analyses inclusion of the subgroups as identified by the trees significantly (p<0.001) increased the predictive power of the model as compared to multivariate analyses containing the only the single parameters.

Conclusions: Long-term dialysis in combination with adolescent age as well as long term dialysis with impairment in graft function shortly after TX were independently associated with a worse renal graft outcome. The identification of these subgroups reveals interactions between factors and carries added value for early prediction of renal graft prognosis.

Introduction and Aims: The phosphatonin FGF23 suppresses tubular phosphate reabsorption (TPR) and the production of calcitriol. In addition to regulation of phosphate homeostasis in CKD it is biologically active and influences morbidity, progression of CKD and mortality. FGF23 effect is mediated by the co-receptor Klotho which was characterized as an anti-agent protein. Klotho can be measured as circulating sKlotho. Klotho is characterized by suppression of Klotho which is thought to be an early biomarker of renal dysfunction. Data of FGF23 and Klotho after KTX and its correlation to phosphate homeostasis are scarce, especially in children.

Methods: intact FGF23 and sKlotho were measured longitudinally over 1 year in serum of 33 children before and after KTX (age 9.7 ± 4.5 yrs). In addition parameter of phosphate homeostasis were determined.

Results: In comparison to pre Ktx FGF23 fell from 715±438 pg/l significantly to 158±224 ng/l after 1 year post KTX (p<0.001). sKlotho decreased initially from 143±1263 ng/l pre KTX to 584±159 ng/l on day 3 post KTX (p<0.001). From day 14 to 1 year post KTX a significant increase of sKlotho into the pediatric norm range (median 2406 (inter-quartil range 1710–3352) was noticed (pre KTx 143±1263ng/l vs. 1 year post KTX 2379±1266ng/l; p<0.006)). In a mixed model there was a significant association of serum-phosphate with sKlotho (p=0.026), creatinine and age (p<0.001, respectively), but not with FGF23. Only renal function correlated to TPR (p=0.014).

Conclusions: These are the first data on the dynamics of FGF23 and sKlotho in pKTx indicating a normalization of sKlotho and decrease of FGF23. Further studies are needed to elucidate the multiple interactions of these parameter on phosphate homeostasis and other biological actions, e.g. graft dysfunction.
**Transplantation - Basic**

**SO044 MOLECULAR MARKERS OF FIBROSIS BUT NOT ALLOIMMUNE RESPONSE IS ASSOCIATED WITH KIDNEY GRAFT DYSFUNCTION AFTER BORDERLINE CHANGES: GENOME-WIDE ASSOCIATION STUDY**

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**Introduction and Aims:** Borderline changes (BL) in kidney allograft biopsy represent diagnostic entity of unclear significance regarding the long term outcome. Using genome-wide association study the whole transcriptome in graft biopsy with BL was compared in patients with stable and deteriorated graft function in 24-months follow-up.

**Methods:** RNA was isolated from biopsies with BL diagnosed either early after transplantation (<2 months) (n=13) or from 3 months biopsies (n=15). Progressors were defined as having the increase in serum creatinine by at least 25% in 24 months. Isolated RNA was in vitro transcribed into cRNA and was hybridized to Illumina Human HT-12 v4 Expression BeadChip. Genes were normalized and genes with statistically significant expression differences were identified. The enrichment of deregulated genes in biological processes was analyzed using DAVID database. The microarray analysis results were validated in 64 patients with BL using 28 genes chosen as highly differentially expressed by RT-qPCR.

**Results:** The annotation enrichment analysis for genes up-regulated in progressors with early BL compared to stable patients at 24-months revealed among the most significant categories: immune system process (p=6.5E-14), defense response (p=3.1E-10), response to wounding (p=2.3E-08) and inflammatory response (1.1E-07). Pathway mapping found two up-regulated (Cytokine-cytokine receptor interaction and Nod-like receptor signaling) and one down-regulated (Aldosteron-regulated sodium reabsorption) pathways in progressors compared to non-progressors. The most significant gene ontology terms enriched in progressors with BL at 3 month biopsy were fibrinogen complex (p=2.7E-04), cell surface binding (1.6E-03) and extracellular region part (p=5.9E-03). RT-qPCR validation confirmed statistically significant expression of SAA1 (serum amyloid A1) and FGA (1.6E-03) and extracellular region part (p=5.9E-03). RT-qPCR validation confirmed statistically significant expression differences were identified. The enrichment of deregulated genes in biological processes was analyzed using DAVID database. The microarray analysis results were validated in 64 patients with BL using 28 genes chosen as highly differentially expressed by RT-qPCR.

**Conclusions:** Molecular phenotype of BL characterized by different regulation of genes associated with fibrosis but not with alloimmune response is associated with the increased risk of progression at 24 months.

**SO045 PERIPHERAL BLOOD MONONUCLEAR CELLS (PBMCs) PHOSPHOPROTEIN ANALYSIS: A NEW TOOL TO INVESTIGATE ANTIBODY-MEDIATED CHRONIC GRAFT REJECTION**

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**Introduction and Aims:** Chronic antibody-mediated graft rejection (AMCR) represents one of the main causes of kidney transplant failure. The molecular mechanisms underlying this event are still poorly defined deeply influencing the potential therapeutic strategies. Further, specific markers for an early diagnosis of AMCR are currently missing. In the attempt to identify potential diagnostic markers and to elucidate the signaling pathways involved in the pathogenesis of AMCR, we analyzed the PBMCs phosphoproteome to identify cellular signaling networks differentially activated in patients with AMCR.

**Methods:** PBMCs were isolated from whole blood samples of 5 biopsy-proven AMCR according to Banff 2007 consensus, 5 renal transplant recipients with normal graft function and histology (t-CTRL), and 5 healthy subjects (CTRL). Phosphoproteins were isolated by precipitation with lanthanum ions and separated by two-dimensional gel electrophoresis. Image Master Software was used to standardize the PBMCs phosphoproteome maps and to list the differentially expressed protein spots among the 3 groups. MALDI-TOF-MS/MS analysis was used to identify the phosphoproteins.

**Results:** Phosphoproteins were obtained with an overall yield of 5.6±4.4% for healthy subjects and of 3.6±2.8% for patients. 2-DE phosphoproteome maps of PBMCs of normal and pathological samples were standardized. Image analysis of sycopy red-stained gels detected 550±78 (mean±SD) protein spots (CV=26%) in healthy individuals, 499±83 protein spots (CV=35%) in AMCR patients and 402±22 protein spot (CV=10%) in t-CTRL patients. By densitometric analysis of the reference gels, we preliminarily recognized 8 protein spots whose density was significantly increased in AMCR patients compared to CTRL and t-CTRL (a and b boxes), and 4 protein spots whose density was increased in all patients compared to CTRL (b box). Further, 3 spot trains, for a total of 13 protein spots, were significantly more expressed in t-CTRL compared to AMCR and CTRL (c and d boxes).

**Conclusions:** Our preliminary results suggest that PBMC phosphoproteome analysis might help to distinguish biopsy-proven AMCR patients from healthy subjects and renal transplant recipients with a stable renal function. In addition, the identification of differentially phosphorylated protein spots may indicate potential therapeutic targets for this condition.

**SO046 THE NUMBER OF B CELL EPITOPES AS A POSSIBLE TOOL TO IMPROVE THE PREDICTIVE VALUE OF HLA DONOR-SPECIFIC ANTIBODIES DETECTED BY FLOW BEADS ASSAYS**

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**Introduction and Aims:** Approximately 20% of patients harbour anti-HLA donor-specific antibodies (DSA) detected by single antigen flow beads (SAF) at transplantation, yet only one-third will develop acute antibody-mediated rejection (AAMR). Therefore, surrogate biomarkers are needed to improve the predictive value of DSA.

**Methods:** We retrospectively assessed from a multi-center cohort of 1958 kidney transplant recipients whether the total number of eplet mismatches (MM) targeted by DSA might be an independent predictor of AAMR and death-censored graft loss (DCGL).

**Results:** We identified for analysis 148 patients (14%) with DSA at transplantation using SAFB assays. For each of them: 1) the total number of eplet MM targeted by DSA was determined using HLA Matchmaker and Matchit softwares; 2) DSA maximum and cumulative median fluorescence intensity (MFI) were recorded. Among the 148 DSA+ patients, 30 (20.3%) developed 1y AAMR and 23 experienced DCGL by the end of follow-up (median: 40 months). While most DSA+ patients had no targeted eplet (DCGL).
SO047

EXPRESSION OF SKIN-HOMING RECEPTORS IN THE DIFFERENT CD4+ T CELL SUBSETS OBTAINED BY ASPIRATION CYTOLOGY OF THE RENAL GRAFT VERSUS PERIPHERAL BLOOD

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Introduction and Aims: Monitoring the CD4+ T cell subsets, including the Treg cells (CD4 CD25highCD127low) and the conventional CD4+ T cells (CD4CD25lowCD127low), may help optimize the management of kidney transplant recipients. The expression of the chemokine receptors CXCR3 and CCR4 in these cells may provide valuable information about the functionality of these cells in the kidney graft.

Methods: In a prospective study of 27 kidney transplant recipients (aged 53.5±15 years; 19 men and 8 women) with no acute rejection we measured by flow cytometry the expression of the receptors CXCR3 and CCR4 in Treg cells and conventional CD4+ T cells in samples obtained from both fine needle aspiration cytology (FNAC) of the graft and from the peripheral blood at 1 and 6 months post-transplantation.

Results: Whereas in peripheral blood samples we detected a significant increase in the percentage of Treg with a high expression of the skin-homing CCR4 in these cells may provide valuable information about the functionality of these cells in the kidney graft. 

SO048

THE INFLUENCE OF SIROLIMUS ON RENAL MAGNESIUM HANDLING, ON RENAL EGF EXPRESSION AND ON THE MAGNESIUM CHANNEL TRPM6

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Introduction and Aims: In literature there is some discrepancy concerning renal magnesium loss as a side-effect of sirolimus. Moreover, the underlying mechanisms still remain unclear. Disturbances in magnesium homeostasis however, can have serious consequences. Recently it has been demonstrated that fine-tuning of magnesium reabsorption takes place in the distal convoluted tubule by active transcellular transport via the magnesium channel TRPM6. Epidermal growth factor (EGF) stimulates TRPM6 activation. This study investigated in vivo the role of EGF in sirolimus-induced magnesium disturbances and its relation to TRPM6.

Methods: A daily dose of 0.6 mg/kg sirolimus was given subcutaneously to 12 male Wistar rats during 4 weeks, while on a standard diet. Serum and urine magnesium, sodium, potassium and creatinine levels were determined. Real-time RT-PCR analyses were performed to study the renal mRNA expression levels of TRPM6, EGF, EGFR, PAI-1 and TGF-β. Infiltration of macrophages in the glomerulus and interstitium were quantified by using immunohistochemistry (anti-ED1). Signs of tubular injury or fibrosis were evaluated by using histological staining. Results were compared to 12 control rats.

Results: The sirolimus rat model was characterised by sufficient blood sirolimus levels in the sirolimus-treated group (17.98±6.37 vs. 1.27±0.13 μg/ml) nor FE Mg2+ (3.63±1.33% vs. 4.84±2.65%). The mRNA level of TRPM6 did not significantly differ between the two groups either (mean Relative Quantification (RQ) 1.20±0.13 vs. 1.04±0.28). mRNA levels of EGF and EGFR were increased in the sirolimus-treated group (mean RQ 2.01±0.91 vs. 1.20±0.93 and 1.95±0.78 vs. 1.20±0.72 respectively). mRNA expression of PAI-1 did not differ among groups (1.41±0.59 vs. 1.04±0.29), TGF-β was significantly upregulated in the sirolimus-treated group (1.39±0.32 vs. 1.03±0.26). Histological and immunohistochemical analysis did not show severe tubulitis damage, fibrosis or inflammation respectively.

Conclusions: This study revealed no sirolimus-induced renal magnesium loss in vivo in the rat. Sirolimus increased the mRNA expression of EGF and EGFR however apparently without affecting TRPM6 and renal magnesium handling significantly.
Diabetes - Clinical

**SO055** Effects of Diet-Induced Insulin Resistance on Basal and Insulin-Stimulated Rates of Renal Cortical Mitochondrial Pyruvate Dehydrogenase/Tricarboxylic Acid Flux in Awake Rats

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**Introduction and Aims:** Obesity and metabolic syndrome (MET-S) are associated with an increased prevalence of kidney disease. Despite being a major metabolically active organ surprisingly little is known about renal substrate preferences in the fasting state and whether this substrate preference is affected during insulin stimulation or altered by insulin resistance.

**Methods:** To address these fundamental questions we applied a novel LC-tandem mass spectrometry method to estimate basal and insulin-stimulated rates of renal cortical mitochondrial pyruvate dehydrogenase (PDH) flux/tricarboxylic acid (TCA) flux in vivo. Rats were fed a standard diet or a high-fat diet to induce whole-body insulin resistance and were infused with [1-13C] glucose for 120 minutes under basal or under hyperinsulinemic-euglycemic clamp conditions. At the end of the clamp studies animals were euthanized, the kidney cortex was excised and freeze-clamped. Relative rates of PDH/TCA flux were assessed by the ratio of [4-13C] glutamate/[3-13C] alanine.

**Results:** Using this approach we found that the relative PDH/TCA flux in the basal state was 30±9% and that it increased by 150% (P = 0.01) during insulin stimulation where the kidneys surprisingly derived the majority of their energy from glucose oxidation (74±10%). Furthermore, insulin resistance did not alter the basal PDH/TCA flux (37±7%), but completely abrogated insulin-stimulated increases in PDH/TCA flux (36±7%) reflecting severe renal cortical insulin resistance.

**Conclusions:** These data demonstrate for the first time that the kidneys have a high degree of metabolic flexibility switching from predominantly fat oxidation in the basal state to predominantly glucose oxidation during insulin stimulation in vivo. Furthermore, these data demonstrate that the kidney is susceptible to lipid-induced insulin resistance, which may play an important role in the progression of obesity and MET-S associated renal disease.

**SO056** Crucial Roles of Mitochondrial Morphogenesis in Diabetic Nephropathy

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**Introduction and Aims:** Growing evidence has shown that mitochondrial morphology is altered in several pathological contexts. Mitochondrial morphogenesis was regulated by a balance between fusion and fission. Key proteins required for mitochondrial fusion include mitofusin 1 (Mfn1) and mitofusin 2 (Mfn2) and those for mitochondrial fission include dynamin related protein (Drp1) and Fis1. Although some of these fusion and fission factors have been identified in kidneys, their roles in diabetic kidneys are unknown. This study aimed to investigate the roles of mitochondrial fusion/fission proteins in diabetic nephropathy. We also aimed to treat the glucose-induced renal injuries by shaping the mitochondria in experimental models.

**Methods:** Diabetic mice were induced by feeding them with high fat high sucrose (HFHS) diet. Immunohistochemistry was employed to delineate the expression patterns of Mfn1, Mfn2, Drp1 and Fis1 in both control diet and HFHS diet fed, age and gender matched mice. Cell (HK2) culture models were used to investigate the function of mitochondrial fusion/fission proteins. Western blot was used to examine the impacts of glucose on the expression of mitochondrial fusion/fission proteins. RNAi techniques including shRNA and siRNA were used to investigate the function of Mfn1 and Fis1 in HK2 cells cultured in the presence or absence of glucose. Mitochondrial morphology were stained by mitotracker and analyzed by confocal microscopy. TUNEL assay was used to examine the cellular apoptosis in glucose treated wild type and Mfn1-depleted HK2 cells.

**Results:** The expressions of Mfn1 and Mfn2 were reduced whereas those of Drp1 and Fis1 were enhanced in the renal tubules of HFHS-fed mice. Glucose led to up regulation of Mfn1, Mfn2 and Fis1. It also caused mitochondrial fragmentation in HK2 cells. Mfn1-depleted cells were more susceptible to glucose-induced mitochondrial fragmentation and cellular apoptosis. SiRNA targeting Fis1 were able to rescue the glucose-induced mitochondrial fragmentation and cellular apoptosis in Mfn1-depleted cells.

**Conclusions:** Our results demonstrated that mitochondrial fusion proteins, Mfn1 and Mfn2, were almost depleted whereas fission protein, Fis1, was over-expressed in the renal tubules of diabetic mice. In vitro studies suggested that glucose drives the mitochondria to fission which eventually led to mitochondrial fragmentation and cellular apoptosis. Mfn1 played a protective role in these injuries. Silencing of the mitochondrial fission protein, Fis1, could be a novel strategy to treat glucose-induced mitochondrial fragmentation and cellular apoptosis.

**SO057** Nephronectin is a Novel Protein Associated with Diabetic Nephropathy

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**Introduction and aims:** Proteome analysis is a new technology which can be used to identify disease-specific proteins. In the present study, we performed proteome analysis of diabetic glomeruli in human autopsy cases to identify new proteins which are related to diabetic nephropathy.

**Methods:** We performed proteome analysis for laser microdissected glomeruli from paraffin-embedded tissues of patients with diabetic nephropathy (n=10) and those of non-diabetic patients (n=10). Immunohistochemistry of identified proteins of renal
biopsy was performed in a total of 190 patients. The percentage of immunoreactivity-positive areas in the glomeruli was analyzed, using an image analyzer.

Results: There were 55 up-regulated and 45 down-regulated proteins that were differentially expressed in glomeruli of diabetic patients, compared to those of non-diabetic patients. Nephrocin, which is an integrin α6β1 ligand and functions as a assembly of extracellular matrix, was found to be up-regulated. Nephrocin-immunoreactivity was clearly, strongly positive in the mesangial expansion of diabetic nephropathy (n=18), whereas nephrocin-immunoreactivity was negative in IgA glomerulonephritis, membranoproliferative glomerulonephritis, lupus nephritis, membranous glomerulonephritis, minor glomerular abnormalities, and crescentic glomerulonephritis. Nephrocin was stained weakly in sclerotic lesions, such as focal segmental glomerulosclerosis and hypertensive nephropathy. The percentage of nephrocin-positive areas in the glomeruli from diabetic nephropathy patients (15.1±4.7%) was significantly higher than that for other various types of patients (10.8±3.8%). The percentage of nephrocin-positive areas in the glomeruli (β=0.23, p<0.001 and β=0.16, p=0.045, respectively).

Conclusions: Nephrocin is a novel component of the increased mesangial matrix in diabetic glomerulosclerosis. We conclude that nephrocin staining could be a useful and novel tool for the diagnosis of diabetic glomerulosclerosis.

**SO058 CLINICAL DEVELOPMENT OF CCR2 ANTAGONISTS CCX140-B AND CCX872-B**

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Introduction and Aims: The C-C chemokine receptor 2 (CCCR2) and its ligand MCP-1 (also called CCL2), enable monocyte/macrophage migration to sites of inflammation. Several studies have pointed to an important role of MCP-1 and CCR2 in diabetic nephropathy (DN). Chemocentryx discovered two potent small-molecule, orally active, specific CCCR2 antagonists, CCX140-B and CCX872-B. Both show pharmacologic activity in mouse models of DN. Specifically, our CCCR2 antagonists reduce albuminuria and hyperglycemia, and improve renal histologic parameters such as glomerular size, glomerular basement membrane thickness, mesangial matrix deposition, podocyte number, and interstitial macrophage infiltration. CCX140-B is in Ph2 and CCX872-B in Ph1 clinical development.

Methods: Here we summarize results from the CCX140-B and CCX872-B clinical trials. Seven CCX140-B clinical trials, 4 Ph1 and 3 Ph2, have been conducted. Doses of 0.05 mg to 15 mg CCX140-B once daily have been studied. Clinical trials have been conducted globally. CCX140-B is being developed for treatment of patients with DN. Two Ph2 clinical trials in up to 290 patients with DN have been conducted. The main efficacy endpoint in these trials is the change from baseline in urinary albumin excretion. A Ph1 clinical trial has been conducted with CCX872-B in 40 healthy volunteers. The dose range tested is 3 to 300 mg CCX872-B.

Results: A total of 448 subjects have been enrolled in CCX140-B trials, with 289 randomized to receive CCX140-B. A Ph2 clinical trial in 159 subjects with type 2 diabetes showed that 10 mg once daily CCX140-B, compared to placebo, was effective in reducing fasting plasma glucose and HbA1c over a 4-week dosing period. The four Ph1 clinical trials showed that the plasma exposure of CCX140-B was dose-proportional, with T1/2 ranges from 4 hrs to 5,105 hrs. There was no gender or food effect on CCX140-B plasma exposure. An integrated safety analysis from all completed clinical trials showed that CCX140-B was well tolerated, with no significant safety concern. The incidence of the most commonly observed adverse events was similar for CCX140-B compared to placebo: headache (10% for CCX140-B, 12% for placebo) and fatigue (7% for CCX140-B, 5% for placebo). No increased risk of infection was observed. CCX872-B was well tolerated at all doses studied. The T1/2 ranges from 2 to 3 hrs, Cmax ranged from 148 ng/mL to 320000 ng/mL at 300 mg CCX872-B. AUC0-24 ranges from 28.30 to 94 mg/hr/mL to 27000000 ng/hr/mL, and 1/2 was approximately 35 hrs.

Conclusions: Clinical development of two CCR2 antagonists CCX140-B and CCX872-B is progressing well. Both molecules have been well tolerated and safe in clinical trials. CCX140-B has shown efficacy in a Ph2 trial in type 2 diabetes and results from two clinical trials in DN are anticipated in 2013.

**SO059 THE POSTPRANDIAL RESPONSES OF GLUCOREGULATORY GUT INCRETIN HORMONES IN NONDIABETIC PATIENTS WITH END-STAGE RENAL DISEASE**

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Introduction and Aims: The glucose metabolism is disturbed in patients with end-stage kidney disease (ESKD), who have a high prevalence of prediabetes. The underlying pathophysiology is unclear and the postprandial responses of insulinotropic gut incretin hormones are unexplored; we aimed to evaluate the separate impact of severe uraemia and prediabetes.

Methods: Participants were separated into three groups: ESRD patients with normal (N=10) or impaired (N=10) glucose tolerance and healthy control subjects (N=11). Glucose tolerance was evaluated using an oral glucose tolerance test followed by a standardised 4h-liquid meal test at a separate day. Plasma glucose, insulin and incretin hormones (glucagon-like peptide 1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP)) were measured repeatedly during the meal test.

Results: Fasting glucose and glucose excursions were comparable between groups (P=0.59). Patients with ESRD exhibited higher fasting levels of GIP and GLP-1 compared with controls. Relative to fasting values, postprandial GIP responses in the two ESRD groups were lower (P=0.005), whereas absolute postprandial GLP-1 responses were higher compared with controls (P=0.002). Postprandial insulin responses were reduced (P=0.035) in ESRD patients. None of the variables differed between the two ESRD subgroups.

Conclusions: Nondiabetic ESRD patients were characterized by a reduced postprandial insulin response despite an increased absolute GLP-1 response and a decreased relative GIP response. This implies involvement of the incretin system in the pathogenesis of the disturbed glucose metabolism in ESRD patients and it seems to be caused by the uraemic state per se.

**SO060 LACTIC ACIDOSIS DURING ACUTE KIDNEY INJURY: IS METFORMIN AN INNOCENT BYSTANDER OR THE CULPRIT?**

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Introduction and Aims: Whether metformin intoxication during Acute Renal Failure (ARF) can lead to Lactic Acidosis (LA) is debated. The aim of this study is to evaluate the risk of developing LA during ARF in diabetic patients with a previously normal renal function. In particular, we have assessed if the use of metformin has exposed these patients to a greater risk and if this risk was related to the dose of metformin taken at home.

Methods: We retrospectively enrolled all the diabetic patients who were discharged from January 1st, 2007 to December 31st, 2011 with the ICD-9 diagnosis code of "ARF" from our Institution. We after excluded patients with CKD, defined by the presence of a previous serum creatinine of >1.5 mg/dL or the presence of pathological or morphological abnormalities. At the end of the selection process, 131 patients were isolated. Clinical and biochemical data at the admission in the Emergency Department and major clinical outcomes were collected. LA was defined as both pH <7.35 and lactate levels >5 mmol/L. For statistics, Fisher’s and Student’s tests and logistic regression using Stata v12 were employed.

Results: In our cohort, 79 patients were taking metformin (Group A, average dosage 1700mg/d) and 52 patients were taking any other oral antidiabetic agent and/or insulin (Group B). There were no differences in baseline characteristics between groups at admission. Acidosis occurred more frequently in patients taking metformin (50.6 vs 32.6%, p-value 0.091), who showed lower pH (7.33 ±0.15 vs 7.39 ± 0.10, p=0.099) and higher lactate levels (4.3 ± 3.2 mmol/L vs 1.67 ± 1.08, p=0.001). Serum creatinine was significantly higher in Group A (3.99 ± 2.7 vs 3.09 ± 1.8 mg/dL, p=0.03). On a regression logistic analysis, creatinine increase was related to pH decrease but not to
lactate increase, while the daily dose of metformin was strictly correlated to both acidosis and lactate levels. LA occurred in 19 patients in the Group A and no cases were observed in Group B. There were no differences in mortality, hospital stay and need for dialysis.

**Conclusions:** In our experience, diabetic patients with a previously normal renal function had an increased risk to develop LA during ARF if they were taking metformin. However, in these patients serum creatinine was significantly increased, a condition that could explain by itself the worse pH. Therefore, we applied a model of logistic regression analysis to consider the role of both metformin and ARF itself as causes of increased lactate levels and decreased pH. The development of acidosis was related both to the degree of ARF and the daily metformin intake, while increased lactate levels were related only to the daily metformin intake. This explains why we observed worse metabolic acidoses in patients taking metformin. Moreover, the evidence that LA occurred only in this group underlines a causal relationship between metformin accumulation and lactate production during ARF.
VASCULAR ACCESS

**SO061 BARRIERS TO IMPLEMENTING A FISTULA-FIRST POLICY IN EUROPE**

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Introduction and Aims: All guidelines recommend an arteriovenous fistula (AVF) as preferred bloodstream access. Still, many patients in Europe receive haemodialysis (HD) via a permanent catheter. This ERPB initiated study explored potential barriers related to attitude, organisation and reimbursement that may explain non-adherence to this fistula-first (FF) policy.

Methods: We developed an electronic survey with 35 items regarding factors potentially affecting choice and quality of HD access. Via national renal societies, we invited 61 experts from 37 countries in the ERA-EDTA community to provide national data on access preference, care delivery and reimbursement.

Results: In total, 44 experts (72% response rate) from 33 countries participated. The majority were nephrologists (89%) from public centres (86%) with ≥15 years of clinical experience (75%). Attitude Many respondents (84%) believed that a FF policy was justified by the current evidence base. However, only 36% expected an AVF to be a durable access in ≥80% of prevalent HD patients. When being presented different clinical cases, experts from 29 countries indicated that an AVF would be attempted in ≥80% of 40-yr old patients without comorbidities. In 9 countries this was believed to be the case in 75-yr olds with comorbidities. A FF policy was promoted in 23 countries. Organisation Centralisation of HD access care was formally facilitated by service providers in 4 countries; this was informally arranged by groups of centres in 18 countries, and not at all in 11. The time between the request and the actual procedure for AVF creation was longer than for catheter placement in 21 countries and similar in 12. In many countries nephrologists were among those responsible for placing catheters (n=24), but this was seldom so for creating AVFs (n=7). Educational meetings on HD access were organised in 27 countries; 2 provided certified training. In 17 countries there was a formal multidisciplinary approach to HD access care in at least part of the centres. Reimbursement In 19 countries facilities received a fee per created access. In 13 of them the fee for AVF creation was higher than for placing permanent catheters (n=2), but this was seldom so for creating AVFs (n=7). Educational meetings on HD access were organised in 27 countries; 2 provided certified training. In 17 countries there was a formal multidisciplinary approach to HD access care in at least part of the centres. Reimbursement In 19 countries facilities received a fee per created access. In 13 of them the fee for AVF creation was higher than for placing permanent catheters; in 5 this fee was paid directly to clinicians.

Conclusions: Our study showed a positive overall attitude towards a FF policy, which became less apparent when applied to older and sicker patients. Future guidelines should thus be more specific about which patients could benefit from this policy. Reimbursement seemed to favour AVF. Besides limited access to dedicated and certified clinicians to create AVFs, we identified lack of formal care centralisation as a potential organisational barrier. Encouraging collaboration in HD access care might be warranted.

**SO062 HEMODIALYSIS TUNNELED CENTRAL VENOUS CATHERS: FIVE YEARS OUTCOMES ANALYSIS**

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Introduction and Aims: Tunneled central venous catheters (TCVC) are considered inferior to fistulas and grafts in all nephrology guidelines. However, they, are being increasingly used as haemodialysis vascular access. The purpose of this study was to document the natural history of TCVC to determine the rate and type of catheter replacement.

Methods: This was a prospective study of patients who are undergoing hemodialysis (HD) with TCVC on our renal unit between January 2008 and December 2012. Standard protocols, according to European Renal Best Practice (2007, 2010), detailing all aspects of preventive nursing care, early diagnosis, were well established. All catheters were inserted in the internal jugular vein (right 91%). Complete data was available on 141 patients (age 73 ± 10 year) who used 154 TCVC. Criteria for catheter removal were (1) persistent bloodstream infection (repetitive blood culture 1 week after completion of antibiotic therapy); (2) detection of an outbreak of CRBS; or (3) catheter dysfunction (inadequate blood flow rate - Qb < 250 ml/min) for three consecutive treatments. Event rates were calculated per 1,000 catheter days; TCVC cumulative survival was estimated according Kaplan Meier analysis.

Results: Catheter replacement occurred in 15 patient (0.29 per 1,000 days), catheter dysfunction with loss of patency was the main cause of replacement (0.18 per 1,000 days), typically within 12 months of catheter insertion. A total of 53 CRBS events in 36 patients were identified (0.82 per 1,000 days). There were 17 organisms isolated. The most common organisms were Gram-positive, comprising 62% of all species. Among Gram positive pathogen isolated, most frequently were the Staphylococcus Aureus. Staphylococcus Aureus of which 85% were meticillin resistant. Among Gram-negative (58% ESBL positive) most frequently were pseudomonaciace and enterobacteriace. The vast majority of CVC infections (87%) were cleared by systemic antibiotics associated with lock therapy. TCVC cumulative survival was 91% at 1 year, 88 % at 2 years and 85 % at 4 years.

Conclusions: Our data showed a high survival rate of TCVC in patient undergoing HD, with low incidence of catheter dysfunction and CRBS. Careful application of standard protocols in the dialysis staff contributed to achieve this results. These data justify TCVC use for hemodialysis vascular access, even as a first choice, especially in patients with exhausted peripheral access, abrupt failure or lack of a native arteriovenous fistula and in patientwith limited life expectancy.

**IS FETUIN-A A BIOMARKER OF VASCULAR ACCESS (VA) FUNCTION IN CHRONIC HEMODIALYSIS (HD) PATIENTS?**

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Introduction and Aims: The objective monitoring of VA function should be performed by measuring the blood flow (Qb) and Co(2) values in patients (pts) with VA. We have previously reported that the VA function is impaired (lower Co(2) and Qb) in patients with VA. The aim of this prospective observational study was to investigate the relationship between serum
Conclusion: The functional VA profile is related to serum fetuin-A levels at baseline. Lower serum fetuin-A levels at baseline are associated with VA failure during the follow-up.

SO065 VASCULAR ACCESS CALCIFICATION RATHER THAN OVERALL CALCIFICATION SCORE IS A PREDICTOR OF ARTERIO-VENOUS FISTULA SURVIVAL

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Introduction and aims: Functional, long-lasting vascular access (VA) is essential for maintaining effective long-term haemodialysis. It has been shown that the most reliable VA are autogenous arteriovenous fistulas (AVFs) as compared with arteriovenous grafts (AVG) and tunnelled catheters. Given the importance of the role that AVFs have in maintenance of HD treatment, there is a constant need to find other causes of their functional failure.

Methods: This retrospective study included 181 patients treated by chronic HD for more than 6 months. Patients with AVG and vein catheter were included as first VA and patients with primary failure of first VA were excluded from further analysis. Beside general data analysis include the last data from the medical records at the time of investigation: HD vintage, characteristics of dialysis membrane, blood flow rate during HD, mineral metabolism indices and the use (and dose) of vitamin D analogues. Blood flow rate during HD was less than 250 ml/min in 38 (23.2%) patients, 250 ml/min in 55 (33.5%) and above 250 ml/min in 71 (43.3%) consecutively. For scoring of the calcification we used Adrago score supplemented by the calcification score of VA region (ulnar artery, radial artery and shunt).

Results: There were no significant difference in 1-, 5- and 10-year AVF survival in regard to age, underlying renal disease, vitD usage, presence of hypertension and diabetes, dialysis membrane type, blood flow rate and serum Ca/P. Figure 1 and Table 1 show survival of first functional AVF in patients with different AVF calcification score which was statistically significant (p=0.009).

However, 1-, 5- and 10-year AVF survival was not influenced by overall calcification score (85.4%, 73.2% and 65.9% in patients with score from 0 to 3; 96.8%, 74.1% and 67.3% in patients with score from 4 to 7 and 87.1%, 74.2% and 63.2% in patients with score from 8 to 11; p=0.614). Results of multivariate logistic regression have shown that only serum PTH over 650 pg/mol is independent factor that influence survival of AVF (p=0.026, OR=0.134).

Conclusions: Our study has shown that more prominent vascular access calcification score have protective effect on first functional AVF. In spite of traditional opinion, our research has shown that high iPTH level is an independent factor that influence on AVF survival rate.

SO065 Table 1.

<table>
<thead>
<tr>
<th>Vascular access calcification score</th>
<th>1-year survival</th>
<th>5-years survival</th>
<th>10-years survival</th>
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<tr>
<td>0</td>
<td>88.9%</td>
<td>77.8%</td>
<td>68.9%</td>
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<tr>
<td>1</td>
<td>87.9%</td>
<td>60.6%</td>
<td>56.8%</td>
</tr>
<tr>
<td>2</td>
<td>90.5%</td>
<td>75.9%</td>
<td>54.8%</td>
</tr>
<tr>
<td>3</td>
<td>92.3%</td>
<td>92.3%</td>
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SO066 SERUM SCLEROSTIN LEVELS, ARTERIOVENOUS FISTULA CALCIFICATION AND ARTERIOVENOUS FISTULA SURVIVAL IN PREVALENT HAEMODIALYSIS PATIENTS

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Introduction and Aims: Arteriovenous fistula (AVF) is prone to recurrent stenosis and thrombosis. Sclerostin, a novel protein secreted by the osteocytes, has been recently shown to be associated with renal osteodystrophy. This prospective study was designed to determine if there was an association between serum sclerostin levels, AVF calcification and one year AVF survival.

Methods: 350 haemodialysis patients were included and followed for 12 months. AVF calcification was evaluated by computed tomography as described previously by Agaston et al. AVF surveillance was conducted by clinical and ultrasonographic evaluation. AVF dysfunction is diagnosed on angiographic basis.

Results: Patients with calcified AVFs had higher serum sclerostin levels than patients with not (1841±1516 vs. 1261±1173 pg/ml; p=0.002). Serum sclerostin levels were correlated with AVF calcium score (r=0.417, p=0.002). One year AVF survival was reduced in patients with calcified AVFs (HR for AVF thrombosis: 1.28; 95% CI, 1.12–1.38; p=0.030). Patients with 25-hydroxy D3 levels greater than median value (21.6 microg/L; Group 1) were associated with an increase in AVF survival, compared to patients with 25-hydroxy D3 levels greater than median value and receiving calcitriol (Group 2), patients with 25-hydroxy D3 levels lower than median value and receiving calcitriol.
calcitriol (Group 3) and finally patients with 25–hydroxy D3 levels lower than median value and not receiving calcitriol (Group 4) (Log rank: p<0.0001). One year AVF survival was lower with increasing serum sclerostin quartiles (log rank, p=0.003). Multivariable-adjusted regression analyses revealed that only presence of AVF calcification (B=2.88; p=0.027) was independently associated with decreased one-year AVF survival.

Conclusions: Presence of AVF calcification but not increased serum sclerostin levels, appear to be independently associated with AVF survival among prevalent haemodialysis patients.
BIOMARKERS

SO067 HIGH LEVELS OF COMBINED SERUM FREE LIGHT CHAINS ARE ASSOCIATED WITH POOR OUTCOMES IN CHRONIC KIDNEY DISEASE

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Introduction and Aims: The stratification of chronic kidney disease (CKD) patients, to identify those at high risk of poor outcomes, requires tests that individually assess kidney function, kidney injury and systemic inflammation. Due to the limitations of the individual markers, here we evaluate a marker of immune status and kidney function, combined polyclonal serum free light chains (cFLC), as a tool for independent risk stratification in patients with CKD.

Methods: Data were available for 908 patients with stage 3-5 CKD enrolled into the Chronic Renal Insufficiency Standards Implementation Study (CRISIS; Salford Royal NHS, UK). At baseline, the population had a median age of 66 years (range 21-92), and 62% were male. 32% were diabetics and 58% had a history of cardiovascular disease. Sera collected at patient recruitment were assessed for cFLC (cFLC=FLC, Freelite®, The Binding Site Group Ltd) levels. The results were compared to routinely measured clinical biomarkers. Renal replacement therapy (RRT) was defined as initiation of dialysis or kidney transplantation. Kaplan-Meier survival analysis were performed to compare time to death between subgroups based on the presence or absence of monoclonal FLC in serum (κ/λ > 1.65 for κ, < 0.26 for λ, FREELITE™). The Binding Site™) and/or urine. FLC clearance and fractional excretion (FE) was calculated for each sample. Urinary light chain concentrations was obtained using antisera anti-total light chain (free + bound, Siemens Healthcare Diagnostics™).

Results:

- Sensitivity of monoclonal FLC recognition was 89.6 and 91.1 % with serum κ/λ ratio and 67.0 and 68.3% by uFE, for κ and λ respectively.
- Monoclonal FLC was present in urine but not in serum in 5.4% of κ and in 4.7% of λ samples. In both groups, serum FLC concentration was very low and FE was more than 4 times higher than in groups where FLC was present in serum but not in urine (median FE 3.59 vs 0.77% for κ, 0.79 vs 0.14% for λ).
- Serum FLC concentration corresponding to uFE positivity, ranged from 0.1 to 15700 mg/L for κ and from 5.8 to 4350 mg/L for λ.
- In each group, FLC clearance was strongly correlated to FE (R² from 0.82-0.99) but not with creatinine clearance.
- Neither FLC concentration nor the FLC Clearance, nor FE was related to creatinine clearance.

Conclusions: The results of our study confirm the indication to use serum κ/λ as an alternative to uFE for earlier recognition of monoclonal CLL, adding, however, the awareness that this criterion loses about 5% of cases both for κ that for λ, due to increased FE. The wide range of serum FLC concentration corresponding to uFE positivity, demonstrates that doesn’t exists a Tim for FLC and that tubular reabsorption, and therefore the excretion of FLC, depends on their qualitative and not quantitative characteristics. Finally, our study shows that FLC clearance depends on tubular function and not from GFR.

SO068 URINARY EXOSOMAL microRNA AS POTENTIAL BIOMARKERS OF CHRONIC KIDNEY DISEASE

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Introduction and Aims: Recent findings indicated that aberrant miRNA expression could activate signaling pathways that lead to progression of kidney fibrosis. Exosomes are small membrane vesicles that could be isolated from urine secreted from all nephron segments. Exosome-associated miRNAs with stability resistant to RNase. Here we sought to observe for the first time whether urinary exosomal miRNA could serve as novel biomarkers of chronic kidney disease (CKD).

Methods: Urine samples were collected from 17 CKD patients who underwent kidney biopsy (2 diabetic nephropathy, 4 focal segmental glomerulosclerosis, 6 immunoglobulin-A nephropathy, 5 membrane nephropathy) and 7 healthy controls. Urinary exosomes were isolated from urine sample by differential ultracentrifugation (2000g for 20 min, 13,500g for 20 min and 200,000g for 60 min). Pellet exosomes were formed by electron microscopy and immunogold staining of exosome marker. microRNA was extracted with miRNasy micro Kit (Qiagen). Members of miR-29, miR-200 family shown previously to reduce renal fibrosis and RNU6B as endogenous control were detected by real-time quantitative PCR. The correlation among miRNAs and clinical parameters and histology were analyzed by the Spearman correlation test. The renal fibrosis was monitored by histological scoring of Mascon staining.

Results: Electronic microscopy verified a typical shape of urinary exosome with average size of 65 1 25.9nm and was positively immunogold labelled with anti-CD9 and AQP. The level of urinary exosomal miRs (miR-29a, 29c, 29r, miR-200a, 200b, 200c) were significantly lower in CKD patients compared with healthy controls (p<0.05). The level of urinary exosomal miRNAs did not correlate with serum creatinine levels. However, miR-29c and miR-200b correlated with eGFR significantly (r=0.576, p<0.016; r=0.520, p=0.033 respectively). And miR-29a, 29c, 29r, miR-200b, 200c correlated inversely with blood urea nitrogen (BUN) significantly (r=-0.696, r=-0.719, r=-0.663, r=-0.590, r=-0.504 respectively, p<0.05). Interestingly, miR-29a, 29c, miR-200b correlated inversely with degree of tubulointerstitial fibrosis (r=-0.557, r=-0.555, r=-0.613 reactively, p<0.05). Moreover, all 6 miRs could discriminate CKD from controls with AUC of 0.796 (p<0.05) when analyzed with the receiver operating characteristic (ROC). And miR-29a and miR-29c could classify kidney biopsy subgroups based on at least one uIFE positivity (Hydrazyme™, Sebia™). Each group of paired samples was then divided into 4 subgroups based on the presence or absence of monoclonal FLC in serum (κ/λ > 1.65 for κ, < 0.26 for λ, FREELITE™). The Binding Site™) and/or urine. FLC clearance and fractional excretion (FE) was calculated for each sample. Urinary light chain concentrations was obtained using antisera anti-total light chain (free + bound, Siemens Healthcare Diagnostics™).

Conclusions: The data suggest that levels of urinary exosomal miRNA are significantly downregulated in CKD patients and could reflect renal function and

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degree of histological fibrosis. This is the first study to show that urinary exosomal miRNA may serve as stable and noninvasive biomarker of CKD and further studies are needed to validate its biomarker potential.

**SO070 A BIOINFORMATICS ANALYSIS OF RENAL MiRNA - AND MRNA-EXPRESSION SIGNATURES IN PROGRESSIVE CHRONIC KIDNEY DISEASE**

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**Introduction and Aims:** MicroRNAs (miRNAs) significantly contribute to the pathophysiology of chronic kidney disease (CKD) progression via negatively affecting mRNA expression but their association with clinical outcome remains poorly understood. In this study we analysed renal miRNA- and mRNA expression in stable and progressive nephropathies using a novel systems biology approach.

**Methods:** Large scale miRNA and mRNA expression profiling was performed on cryo-cut biopsy sections from 43 cases of proteinuric kidney diseases. Significantly differentially expressed miRNAs between progressive (doubling of serum-creatinine or end-stage renal disease) and stable (all other) cases were determined, and inversely correlated mRNA expression profiles were identified. These miRNA-mRNA pairs were further characterized.

**Results:** In progressive subjects 12 miRNAs (miR-140-3p, -148a, -190, -192, -194, -204, -206, -216b, -30d, -30e-3p, -532-3p) were significantly downregulated and the corresponding upregulated mRNAs were involved in inflammatory response, cell-cell interaction, metabolism, apoptosis, and intracellular signalling. Ten of these miRNAs were correlated with serum-creatinine at time of biopsy and at follow-up, and all 12 miRNAs correlated inversely with the degree of arteriolar hyalinosis and tubular atrophy/intertstitial fibrosis. The corresponding significantly upregulated mRNA targets were further analyzed using bioinformatics network analysis. Two molecular subnetworks holding in total 8 mRNAs were identified being of major relevance.

**Conclusions:** We identified differentially expressed renal miRNA- and mRNA-profiles in progressive chronic kidney disease. These miRNAs and mRNAs were associated with inflammatory pathways, and the degree of expression correlated with renal disease severity, suggesting an important role of these miRNA/mRNA-pairs in the pathogenesis of renal disease progression.

**SO071 CIRCULATING BIOMARKER PROFILE CHARACTERIZES PATIENTS WITH RETROPERITONEAL FIBROSIS AND CONCOMITANT URETER OBSTRUCTION - AN EPIDEMIOLOGICAL STUDY**

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**Introduction and Aims:** Retroperitoneal fibrosis (RPF) is a rare chronic disease marked by fibrotic tissue formation in the retroperitoneum which frequently results in ureteral obstruction and symptoms of impaired kidney function. The diagnosis of RPF is an elaborate process involving imaging and biopsy. Therefore, a search for soluble biomarkers is being described.

**Methods:** Serum samples from patients with manifested RPF (n=46, Else Kröner-Fresenius-Register) and age and gender matched controls (n=32) were analyzed for biomarkers representing fibro-inflammatory tissue remodeling (MCP1, calprotectin, MMP2, PTEN, tenascin C, TGFβ1, CTGF, osteopontin e.g.), or tissue injury response (NGAL, TIMP-1, MMP9 e.g.) as well as markers of renal failure.

**Results:** RPF patients have been grouped according to imaging (MRI) figures and laparoscopy findings to low (n=18) and high (n=28) fibrotic tissue burden for the analyses. Distinct differences to controls and the grade of RPF tissue burden were identified by the fibro-inflammatory markers calprotectin (controls 0.96 +/- 0.61 μg/ml, low RPF 2.87 +/- 2.51 μg/ml, high RPF 3.54 +/- 2.28 μg/ml, p < 0.001) and CRP (controls 8.33 +/- 1.34 μg/ml, low RPF 11.41 +/- 6.3 μg/ml, high RPF 27.2 +/- 6.3 μg/ml, p<0.001), whereas MCP-1, MMP2 and TGFβ1 did not show significant differences among the groups. Circulating fibrosis biomarkers are highly increased in RPF patients e.g. collagen NPIII (controls 220.7 +/- 693.9 ng/ml, low RPF 268.2 +/- 80.9 ng/ml, high RPF 329.3 +/- 90.6 ng/ml, p<0.001) or tenascin C (B-domain) (controls 504.0 +/- 143.2 ng/ml, low RPF 727.2 +/- 143.0, high RPF 1038.4 +/- 322.7, p< 0.001). Similar proportions show the fibrosis biomarkers MMP 9, TIMP-1, and tenascin C (C-domain). Tissue injury response markers like osteopontin and NGAL also increase with severity of RPF disease. However, as this is also known for CKD patients, these two markers fail for diagnostic discrimination. A prime classifying biomarker dissecting RPF from CKD is the rather unusual ratio of cystatin C and creatinine in RPF patients (cystatin C controls 0.92 +/- 0.13 μg/ml, low RPF 1.66 +/-0.42 ng/ml, high RPF 1.65 +/- 0.53 μg/ml p<0.001; creatinine: 10.2 +/-1.42 μg/ml, low RPF 10.80 +/- 3.10, high RPF 14.48 +/-11.80 μg/ml, p<0.05).

**Conclusions:** Biomarkers indicating tissue remodeling processes like MMP-9, NPIII, tenascin C, and TIMP-1 are significantly elevated in RPF patients. These markers and significantly increased cystatin C levels at normal creatinine levels shape a biomarker profile which is characteristic for RPF patients.

**SO072 INCREASED PLASMA FIBROBLAST GROWTH FACTOR 23 IS ASSOCIATED WITH AN IMPAIRED RESPONSE TO ANTIPROTEINURIC THERAPY IN PATIENTS WITH CHRONIC KIDNEY DISEASE**

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**Introduction and Aims:** Renin-angiotensin-aldosterone system (RAAS)-blockade by ACE inhibition (ACEi) or angiotensin receptor blockade (ARB) is the cornerstone of chronic kidney disease therapy, by reducing proteinuria and blood pressure. High phosphate levels are associated with reduced ACEi efficacy, but the underlying mechanism is unclear. The phosphaturic hormone fibroblast growth factor 23 (FGF23) is upregulated with phosphate retention, and may affect the RAAS. We evaluated whether higher FGF23 levels are associated with an impaired response to intensification of RAAS-blockade-based therapy.

**Methods:** We measured plasma C-terminal FGF23 levels by ELISA and several other phosphate-related parameters in a previously conducted trial with a rotation design (Slagman et al. BMJ 2011;343:d4366). In this trial, 51 patients with non-diabetic chronic kidney disease therapy, by reducing proteinuria and blood pressure. High phosphate levels are associated with reduced ACEi efficacy, but the underlying mechanism is unclear. The phosphaturic hormone fibroblast growth factor 23 (FGF23) is upregulated with phosphate retention, and may affect the RAAS. We evaluated whether higher FGF23 levels are associated with an impaired response to intensification of RAAS-blockade-based therapy.

**Results:** In the trial, 51 patients with non-diabetic proteinuric nephropathy were treated with background ACEi (lisinopril 40 mg/day) during regular sodium diet (ACEi+RS) (Slagman et al. BMJ 2011;343:d4366). In this trial, 51 patients with non-diabetic proteinuric nephropathy were treated with background ACEi (lisinopril 40 mg/day) during regular sodium diet (ACEi+RS). Subsequently, we analyzed changes in proteinuria according to FGF23 levels at baseline (ACEi+RS) during subsequent 6-week study periods where antiproteinuric therapy was intensified by addition of an ARB (valsartan 320 mg/day; ACEi+ARB+RS), dietary sodium restriction (ACEi+LS), or both (ACEi+ARB+LS). Multivariate regression analysis was used to study the association between FGF23 levels and changes in proteinuria in response to therapy intensification.

**Conclusions:** We included 51 patients with a creatinine clearance of 69 [50-108] ml/ min (median [1st-3rd quartile]). Antiproteinuric therapy intensification resulted in...
stepwise reduction of proteinuria (ACEi+RS: 1.92 [0.87-3.40] vs ACEi+ARB+LS: 0.67 [0.37-1.40] g/d, p<0.0083) at the expense of a decline in creatinine clearance (ACEi+RS: 69 [50-108] vs ACEi+ARB+LS: 59 [42-77], p=0.0083). Plasma FGF23 levels tended to increase with intensified antiproteinuric treatment. At baseline, proteinuria was similar in tertiles of FGF23. Patients in the lowest FGF23 tertile (80-131 RU/mL) at baseline responded stronger to therapy intensification during ACEi+ARB+LS (residual proteinuria 0.3 [0.2-0.6] g/d) compared to those in the highest tertile (211-556 RU/mL) (residual proteinuria 0.8 [0.5-1.4] g/d) (p<0.05). In multivariate analysis, baseline FGF23 predicted residual proteinuria during ACEi+ARB+LS (standardized β -0.241, p=0.02) independently of baseline proteinuria and creatinine clearance. Systolic (SBP) and diastolic (DBP) blood pressure, serum phosphate, phosphate excretion, 1,25(OH)2-vitamin D, PTH, NT-proBNP, BMI, age and gender did not contribute to the model. FGF23 did not predict SBP or DBP reduction.

Conclusions: Higher baseline FGF23 levels are independently associated with resistance to intensification of antiproteinuric therapy. Future studies should address whether reduction of FGF23 levels may enhance RAAS-blockade efficacy.
CKD-MBD - B

**MO007** TREATMENT OF SECONDARY HYPERPARATHYROIDISM IN THE EVOLVE TRIAL

Tilman Druzeke, on behalf of the EVOLVE Writing Committee

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Introduction and Aims: Secondary hyperparathyroidism (HPT) is common in patients on maintenance hemodialysis and often progresses despite treatment with vitamin D sterols and phosphate binders.

Methods: The EVOLVE trial randomized 3883 patients with moderate to severe secondary HPT with a median plasma intact parathyroid hormone (PTH) concentration of 693 pg/mL (normal range 11–72 pg/mL) to treatment with cinacalcet or placebo. The majority of patients also received vitamin D sterols and phosphate binders. Patients were followed for up to 64 months. We assessed the rates of parathyroidectomy (PTX), switching to commercial cinacalcet, and progress to severe unremitting HPT (defined as PTH values >1000 pg/mL and serum total calcium >2.6 mmol/L on two consecutive occasions, or iPTH > 1000 pg/mL and serum total calcium >2.6 mmol/L on one occasion with prescription of commercial cinacalcet).

Results: In the group randomized to placebo (n=1935) nearly 70% received vitamin D sterols and 90% phosphate binders throughout the trial. Nonetheless, 278 (14.4%) patients had surgical PTX, with a median (p10, p90) iPTH level of 1873 (760, 3706) pg/mL before surgery, 443 (22.9%) patients started commercial cinacalcet with a median iPTH of 1108 (455, 2310) pg/mL, and 470 (24.3%) progressed to severe unremitting HPT with a median PTH of 1510 (810, 2991) pg/mL. Substantial selection bias was evident in patients who either underwent PTX, were prescribed commercial cinacalcet, or progressed to severe unremitting HPT, with these outcomes differing widely by age, sex, region and comorbidity. The unadjusted relative hazard in the cinacalcet vs. placebo group for PTX was 0.44 (95% CI 0.36-0.54), for provision of commercial cinacalcet 0.41 (95% CI 0.35-0.48), and for progression to severe unremitting HPT with hypercalcemia 0.43 (95% CI 0.37-0.50).

Conclusions: Severe unremitting HPT developed frequently in patients randomized to placebo in EVOLVE, despite the use of conventional therapy with vitamin D sterols and phosphate binders, prompting PTX or motivating the off-protocol use of commercial cinacalcet. Randomization to cinacalcet resulted in a nominally significant reduction in the occurrence of these events.

**MO008** COSMOS: ABNORMALITIES IN THE MAIN BONE AND MINERAL BIOCHEMICAL PARAMETERS ARE ASSOCIATED WITH HIGHER RISK OF MORTALITY

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Introduction and Aims: Chronic kidney disease mineral and bone disorders are important complications of CKD and are associated with a higher risk of mortality. The objective of this study was to assess the association of serum calcium (Ca), phosphorus (P) and parathyroid hormone (PTH) with mortality in the European COSMOS study.

Methods: COSMOS is a 3-year, multicenter, open-cohort, prospective study carried out in adult chronic hemodialysis (HD) patients from 20 European countries. At baseline and every 6 months, demographics, comorbidities, drug prescription, monthly serum biochemical parameters of the previous six months and clinical outcomes were collected. Mean biochemical parameters of the previous 6 months were calculated and categorized in several categories. Cox proportional hazard regression with time-dependent covariates was used to study the association between mortality rate and serum Ca, P and PTH. The Hazard Ratios were adjusted (aHR) by for demographics, centre funding (public/private), country, comorbidities, therapies and biochemical parameters (Ca, P, PTH, albumin and haemoglobin).

Results: A total number of 4500 patients were randomly recruited for COSMOS at baseline. During the 3 years of follow-up, 2297 new patients (less than 1 year on HD) were additionally recruited to replace those dying or leaving the study by other reasons (total number of patients 6797). Patients with no follow-up data or lacking information on biochemical parameters were excluded, making a total number of 6295 patients available for the analysis (4313 [68.5%] randomly selected and 1982 [31.5%] replacements). Both, high and low serum P and PTH were significantly associated with a higher risk of mortality, whereas high serum Ca but not low serum Ca was associated with an increased risk of mortality (Table).

Conclusions: In COSMOS, a representative European HD population, abnormalities in serum PTH and P and a higher Ca were associated with a higher risk of mortality. Study supported by Amgen and Fundación Renal Fígo Álvarez de Toledo.

**MO009** TISSUE CONTENT OF PHOSPHORUS IN CKD-MBD. IS CKD-MBD A STATE OF TISSUE PHOSPHORUS DEPLETION?

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Introduction and Aims: CKD-MBD is considered a state of phosphate loading. It is postulated that in CKD5D renal excretion of phosphate is maintained at the expense of rising serum FGF23, which increases fractional glomerular excretion of phosphate. However, it is not until CKD 4 that elevation of serum phosphate is regularly seen. High levels of FGF23 are associated with adverse outcomes such as progression of CKD and LVF. There is speculation that use of phosphate binders in early CKD3D might result in lower FGF23 levels and a reduction in associated adverse outcomes. Clear evidence for progressive phosphate accumulation with progressive loss of kidney function does not exist; yet studies are already being conducted on the basis of this assumption. However other studies suggest that CKD may not be a state of positive phosphate balance (Munro P et al 2012). Total tissue phosphorus can be measured by simple laboratory techniques. Twenty-three isotopes of phosphorus are known, including all possibilities from P24 up to P46. Only P31 is stable and hence can be measured. We report the results of a pilot study to estimate the phosphorus content in skin biopsy samples from 20 dialysis patients selected for radiological evidence of vascular calcification, and 10 control subjects without CKD.

Methods: Dialysis patients with radiological evidence of vascular calcification, and control subjects without CKD, were invited to take part and give written informed consent. Each subject underwent a forearm skin biopsy under local anaesthetic. Samples were acid-digested and inorganic phosphate measured to estimate the content of phosphorus-31. Tissue content of Calcium-43 was also estimated. Serum calcium, phosphate, albumin, alkaline phosphatase and PTH levels were measured.

Results: Mean skin P31 in the biopsy samples from dialysis patients(n=15) was 298mcg/g as compared with 364mcg/g in controls(p=0.23).No correlation was seen between tissue content of phosphorous-31 and Serum creatinine. Tissue content of Calcium-43 was also estimated. Serum calcium, phosphate, albumin, alkaline phosphatase and PTH levels were all measured.

Conclusions: Our preliminary data show no significant difference in skin phosphate levels between subjects and controls, and do not support the assumption that CKD is a state of tissue phosphate loading, at least in skin. Indeed there is a trend towards lower skin phosphate levels in the dialysis patients with vascular calcification compared to controls. The positive correlation between the tissue levels of Ca43 and P31 suggest that phosphorous in tissue exists in combination with Calcium. Further sample analysis is on-going and will increase the reliability of the preliminary results.
MO009

THE RELATIONSHIP BETWEEN RENAL OSTEODYSTROPHY AND FIBROBLAST GROWTH FACTOR-23 IN HEMODIALYSIS PATIENTS

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Introduction and Aims: The studies on the association between fibroblast growth factor-23 (FGF-23) and mineral metabolism disorders occurred in chronic kidney disease together with cardiovascular outcomes aroused interest about the relationship between renal osteodystrophy and FGF-23. In this study, we aimed to investigate the relationship between FGF-23 and renal osteodystrophy assessed by dynamic bone biopsy findings in chronic hemodialysis patients.

Methods: Among the 207 prevalent hemodialysis patients who underwent bone biopsies, plasma intact FGF-23 levels were measured in 180 patients who had plasma samples stored at -80°C.

Results: The mean age of patients in the study group was 57.8 ± 14.4 years. The mean plasma level of FGF-23 was found as 257 ± 387 pg/ml (14.8-1297). FGF-23 plasma levels were positively correlated with serum phosphate levels (r=0.440, p<0.001), serum calcium levels (r=0.394, p<0.001), serum creatinine level (r=0.365, p<0.001) and calcium-phosphate product (r=0.482, p<0.001). While FGF-23 plasma levels were negatively correlated with serum alkaline phosphatase levels (r=-0.231, p=0.003), it was not correlated with serum parathyroid hormone levels (pre-iCa value of 0.18 mmol/L). Using DCC -0.06 to +0.8 mmol/L; a neutral iCa balance was maintained with a mean DCC ± 0.1 mmol/L (from 1.15 ± 0.08 to 1.35 ± 0.1 mmol/L); 0.09 ± 0.08 mmol/L (from predialysis: 1.14 ± 0.07 to postdialysis: 1.13 ± 0.07 mmol/L) with a DCC of 1.25 mmol/L; 0.09 ± 0.08 mmol/L (from predialysis: 1.13 ± 0.07 to 1.22 ± 0.07 mmol/L) with a DCC of 1.5 mmol/L and 0.19 ± 0.07 to 0.25 ± 0.07 mmol/L (from predialysis: 1.12 ± 0.07 to 1.35 ± 0.1 mmol/L) with a DCC of 1.75 mmol/L. The delta iCa values (from pre- to postdialysis) were -0.01 ± 0.06 mmol/L (from predialysis: 1.14 ± 0.07 to postdialysis: 1.13 ± 0.07 mmol/L) with a DCC of 1.25 mmol/L; 0.09 ± 0.08 mmol/L (from 1.13 ± 0.07 to 1.22 ± 0.07 mmol/L) with a DCC of 1.5 mmol/L; and 0.19 ± 0.07 to 0.25 ± 0.07 mmol/L (from 1.12 ± 0.07 to 1.35 ± 0.1 mmol/L) with a DCC of 1.75 mmol/L. The delta iCa was dependent on baseline iCa and whether HDF was used, but not dependent on the session time. Delta iCa was correlated with DCC - pre-iCa (0.37 ± 0.2 mmol/L; -0.06 to +0.8 mmol/L); a neutral iCa balance was maintained with a mean DCC - pre-iCa value of 0.18 mmol/L. Using DCC - iCa, a neutral calcium balance (median value, 2.2 mmol/L) was achieved using a DCC of 1.38 mmol/L (1.3 mmol/L if HDF was used). Delta PTH (%) was correlated with delta iCa (r² = 0.42; p < 0.001).

Conclusions: Using our individualized DCC strategy, a DCC of 1.5 mmol/L was found to provide a positive intradialytic iCa balance for most patients. This positive balance is larger when HDF is used. The calcium balance is also dependant on predialysis iCa levels and inversely correlated with intradialytic PTH variations. The HD session time does not affect the calcium balance. 1- Jean, G et al, NDT 2012.
RENNAL FIBROSIS AND PROGRESSION

MO012

PIB-4050, A NOVEL FIRST-IN-CLASS ANTI-FIBROTIC COMPOUND, INHIBITS CTGF, α-SMA AND COLLAGEN EXPRESSION IN UUO MODELS AND REDUCES KIDNEY FIBROSIS IN 5/6-NEPHRECTOMIZED AND DOXORUBICIN-INDUCED NephROPTICITY MODELS

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Introduction and Aims: Interstitial fibroblasts are the principal effector cells of organ fibrosis. Transforming growth factor (TGF-β) -activated myofibroblasts express α-smooth muscle actin (α-SMA), secrete connective tissue growth factor (CTGF) that functions as a downstream mediator of TGF-β action on fibroblastic cell types, and are important in the synthesis of collagen I. The aim of this study was to investigate the effect of PIB-4050, a first-in-class anti-fibrotic compound, on CTGF, α-SMA and collagen I expression in TGF-β1-stimulated human fibroblasts (normal human dermal fibroblasts (NHDF)).

Methods: The effect of PIB-4050 on the mRNA expression of fibrotic markers was analyzed by qPCR in TGF-β1-stimulated NHDF and in kidney from models of ESRD (5/6-nephrectomized rats) and AKI (dxorurbin-induced nephroptoticity in mice).

Results: Activation of NHDF fibroblasts by TGF-β1 resulted in a strong increase in mRNA expression of CTGF (30 times), α-SMA (10 times) and collagen I (2.5 times). PIB-4050 significantly reduced TGF-β1-induced overexpression of CTGF (78%), α-SMA (85%) and collagen 1 (21%) mRNA in NHDF to the control level (untreated/no TGF-β-stimulation). This is also translated at the protein level, as TGF-β1-induced CTGF production is also significantly inhibited by PIB-4050 in NHDF. Furthermore, in non-stimulated NHDF, PIB-4050 reduced basal CTGF (60%), α-SMA (40%) and collagen I (25%) mRNA expression. These results correlate with in vivo inhibition of CTGF, α-SMA and collagen I mRNA expression observed in different models of kidney fibrosis. In 5/6-nephrectomized rats (CKD/ESRD model), oral administration of PIB-4050 (200 mg/kg) significantly decreased the mRNA expression of CTGF (50%), α-SMA (30%) and collagen I (50%) in the remnant kidney. In doxorurbin-induced nephroptoticity (AKI model), oral administration of PIB-4050 (100 mg/kg) significantly decreased the expression of CTGF, α-SMA and collagen I mRNA expression close to the control level (no doxorurbinic).

Conclusions: These results indicate a direct effect of PIB-4050 on fibroblasts as observed by an inhibition of CTGF, α-SMA and collagen I mRNA expression, and this is translated by a reduction of fibrosis in the kidney.

MO013

THE ROLE OF CALRETICULIN IN RENAL FIBROSIS

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Introduction and Aims: Renal fibrosis is a key component of several kidney diseases, leading eventually to renal failure; however, the involved mechanisms are largely unknown. Using a classical proteomic approach on the Unilateral Ureteral Obstruction (UUO) rat model, we have found Calreticulin, a multifunctional Ca²⁺-binding protein, to be significantly upregulated both at the early and the late stages of fibrosis, especially in tubular epithelial cells. This work is focused on unraveling the role of Calreticulin in renal fibrosis, with studies both on cell culture systems and animal models.

Methods: In order to further explore the role of calreticulin overexpression in the development of fibrosis, cell culture systems and animal models were used.

Results: Calreticulin overexpression in renal proximal tubular epithelial cells (HK-2) led to significant reduction of E-cadherin as well as increase of vimentin and vinculin expression, without induction of α-SMA or collagen I, implicating a tendency for non-complete transformation of the epithelial cells. However, typical epithelial matrix proteins like fibronectin and collagen IV were significantly upregulated. Moreover, Calreticulin-overexpressing cells showed increased motility and cellular stress, reduced proliferation and increased sensitivity to apoptosis. These characteristics were also confirmed in the Calreticulin-overexpressing L-Eng+ human L-Endoglin (L-ENDOGLIN) cell line and in kidney models of experimental ESRD.

Conclusions: The findings described above strongly suggest that Calreticulin may be a novel important mediator of the fibrotic process and that its regulation expression might be a future target of anti-fibrotic pharmacological interventions.

MO014

L-ENDOGLIN OVEREXPRESSION INCREASES RENAL FIBROSIS AFTER UNILATERAL URETERAL OBSTRUCTION

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Introduction and Aims: Transforming growth factor - (TGF-β) plays a pivotal role in renal fibrosis. Endoglin, a 180 KDa membrane glycoprotein, is a TGF-β β 3-receptor which is overexpressed in several models of chronic kidney disease but its function in renal fibrosis remains still unclear. Two membrane isoforms generated by alternative splicing have been described, L-Endoglin (long, the most abundant isoform) and S-Endoglin (short) that differ from each other in their cytoplasmic tails. The aim of the present study was to assess the effect of L-Endoglin overexpression in renal tubulo-interstitial fibrosis.

Methods: For this purpose, a transgenic mouse which ubiquitously overexpresses human L-Endoglin (L-ENDG+) was generated and unilateral ureteral obstruction (UUO) was performed in L-ENDG+ mice and their wild type littermates. The degree of fibrosis was assessed by morphometric techniques and by the expression of fibrosis-related molecules (collagens, fibronectin) and the number of myofibroblasts. Renal fibroblasts were isolated and cultured from L-ENDG+ and WT mice, and the fibrogenic potential of L-ENDG+ fibroblasts was assessed by measuring collagen I and fibronectin production.

Results: Obstructed kidneys from L-ENDG+ mice showed higher tubulo-interstitial fibrotic area and higher amounts of extracellular matrix proteins, such as type I collagen and fibronectin, than obstructed kidneys from WT mice. However, the higher increase of renal fibrosis observed in L-ENDG+ mice is not due to a major abundance of myofibroblasts, as similar levels of α-smooth muscle actin were observed in obstructed kidneys from both mice types. Western blot analysis showed that levels of p-Smad1 and p-Smad3 were higher in O than in NO or sham kidneys, being these levels significantly higher in O kidneys from L-ENDG+ than in those from WT animals. Accordingly, the number of p-Smad1-stained nuclei was higher in L-ENDG+ than in WT mice. Western blot analysis revealed that collagen I and fibronectin production was higher in L-ENDG+ fibroblasts than in wild type fibroblasts.

Conclusions: Our results suggest that L-Endoglin overexpression potentiates the activation of Smad1 and Smad3 pathways and this effect is associated to higher renal fibrosis development, probably based on a higher pro-fibrotic potential of L-ENDG+ fibroblasts.
Introduction and Aims: Psychological disorders such as anxiety and depression are strong predictors of life expectancy and have important impact on quality of life. Surprisingly enough, these factors have received little attention in autosomal dominant polycystic kidney disease (ADPKD). ADPKD is the most common hereditary disorder in nephrology and is frequently diagnosed based on family history and imaging diagnostics, well before the onset of subjective symptoms and complications of the disease. Due to its genetic conditionings, patients suffering from this disease have to face a remarkable psychological burden during their life. The study aimed to determine whether the knowledge about the course and possible consequences of the disease, as well as, medical surveillance, affects the perception of anxiety, depression and decision making process in asymptomatic ADPKD patients.

Methods: We included 50 (N=50) patients in asymptomatic stage of ADPKD with eGFR > 60 ml/min according to MDRD formula. Patients completed a set of psychological questionnaires Courtland Emotional Control Scale (CECS), Acceptance of Illness (AIS) as well satisfaction with Life Scale (SWLS), before the control visit at the clinic. All the measures are commonly used and validated psychological assessment tools. Controls (N= 50) were recruited from healthy population and were age and gender matched. We used t-Student tests for statistical analysis of obtained data.

Results: As t- Student test for independent samples revealed patients with ADPKD present remarkable higher anxiety and depression suppression level than healthy controls. Both results are statistically significant at p<0.001. Moreover, patients life satisfaction is also significantly lower than in the healthy group ( p= 0.002).

Conclusions: Asymptomatic ADPKD patients had high disease acceptance. Anger perception in this group was comparable with controls. However, we found surprisingly low perception of depression and anxiety among studied patients. It indicates the tendency for suppression and avoidance mechanisms, and reflects high psychological costs of the disease awareness and acceptance.

Introduction and Aims: Autosomal dominant polycystic kidney disease (ADPKD) paved the way for the elucidation of cilia-related disorders (ciliopathies) and notably most ciliopathies have a renal cystogenic component. Some clinical and molecular overlap exists between ADPKD and von Hippel-Lindau (VHL) syndrome and tuberous sclerosis (TSC). Ciliopathies are clinically and genetically very heterogeneous with involvement of practically all organs. Frequent manifestations besides cystic kidney disease are retinal degeneration, cardiac defects, situs inversus, polydactyly, other skeletal features, and defects of the central and peripheral nervous system. These can occur isolated or as part of syndromes, such as Bardet-Biedl, Joubert, Meckel, Jeune, and Ellis-van-Creveld syndrome. Variable expressivity and overlaps between different entities often make it difficult to give a clear clinical diagnosis. Genotype-phenotype correlations are usually not convincing and mutations in the same gene can cause very different phenotypes. In general, it is the rule of life style (SWLS), that the genes general to be considered as disease-relevant in a patient with suspected ciliopathy. Second-site modifiers are expected to exert an aggravating effect in an epistatic way. In this scenario, altered dosage of disease proteins may disturb cell homeostasis and network integrity contributing to early and more severe disease expression.

Methods: We designed an NGS (next generation sequencing) based panel for all ciliopathies that allows the parallel investigation of 258 genes (in total 4637 exons) known or hypothesized to cause cilia-related disorders in a time- and cost-efficient manner.

Results: Patients were analyzed with an average coverage of currently more than 100x. We present our experiences from the analysis of more than 300 unrelated families from a broad spectrum of cilia-related disease phenotypes in which we have used our NGS-panel and identified convincing disease-related mutations in different genes corroborating our hypothesis. In most patients we could clearly detect the underlying disease mutation(s). Notably, we were also able to identify new genes for cystic and polycystic kidney disease as well as for some syndromic ciliopathies.

Conclusions: The novel genetic testing approach presented here considerably improves genetic diagnostics of (poly)cystic kidney disease and other ciliopathies and deserves increased attention in genetic counselling and the management of affected families.
Methods: EXIST-2 (NCT00790400), a randomized, double-blind, phase 3 trial, assessed the efficacy and safety of everolimus, an oral mTOR inhibitor, for treating renal AML in patients with TSC or sporadic LAM. Patients were randomized 2:1 to receive everolimus 10 mg/day (n=79) or placebo (n=39) and stratified by TSC and enzyme-inducing anti-epileptic drugs use, and sporadic LAM. The primary endpoint was the proportion of patients with confirmed ≥50% reduction in sum of volumes of all target AML (defined as ≥1 AML ≥3 cm in longest diameter) relative to baseline. Secondary endpoints included time to AML progression and skin lesion response rate (patients ≥1 skin lesion at baseline [n=114]). Adverse events (AEs) were monitored at every visit.

Results: As of 10-14-2011, median treatment duration was 48 and 45 weeks for everolimus and placebo arms, respectively. Everolimus continued to demonstrate superiority over placebo for AML response rate. The AML response rate was 45.6% (36/79 95% confidence interval [CI] 34.3%-57.2%) for everolimus compared with 0% (0/39 95% CI 0.0%-9.0%) for placebo (difference 45.6% [95% CI 27.5%-61.8%]). At week 48, 80.5% of patients in the everolimus arm had ≥30% AML shrinkage compared with 5.6% of those in the placebo arm. Median time to AML progression was 11.1 months for placebo and not yet reached for everolimus. Everolimus was superior to placebo in time to AML progression (hazard ratio [HR] 0.10; 95% CI 0.03-0.36). No additional patients progressed in the everolimus arm; however, an additional 4 patients progressed in the placebo arm since the original analysis. Skin lesion response rate (complete or partial response according to Physician’s Global Assessment criteria) continued to be higher for everolimus than placebo (32.5% [95% CI 22.2-44.1]) vs 0% [95% CI 0-9.5], respectively). Discontinuations in the double-blind period were the same in the everolimus arm, but had increased by 4 patients in the placebo arm since the initial analysis (n=3 disease progression, n=1 withdrawal of consent). The majority of adverse events (AEs) continued to be grade 1 or 2; however, the incidence of serious AEs was slightly higher than initially reported, particularly in the placebo arm (everolimus 20.3%, placebo 23.1%).

Conclusions: Everolimus treatment continued to demonstrate a clinically significant reduction in AML volume compared with placebo and showed a safety profile consistent with previous reports.
EXTRACORPOREAL TECHNIQUES AND ADEQUACY

MOO20 THE TYPE OF VASCULAR ACCESS IS AN INDEPENDENT DETERMINANT OF THE CONVECTIVE VOLUME IN POST-DILUTION HEMODIAFILTRATION: RESULTS FROM THE CONVEXTIVE TRANSPORT STUDY (CONTRAST)

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Introduction and Aims: Hemodiafiltration (HDF) is increasingly used as a means of improving the clearance of middle-weight molecular substances in patients with end stage renal disease. Post hoc analysis of two large randomized controlled trials in which HDF was compared with HD, revealed that patients treated with HDF had a lower mortality risk. The aim of this study was to determine which factors influence the achieved convection volume in patients treated with post-dilution online (ol) HDF.

Methods: IN CONTRAST, a total of 318 patients were treated with HDF at 6 months. Three patients were excluded because they were probably treated with pre-dilution olHDF. The remaining 315 patients receiving post-dilution olHDF were selected for this cross-sectional on-treatment analysis. Data on clinical characteristics and treatment-related parameters were collected at 6 months after randomization. Determinants of convection volume were analysed using multivariable linear regression. Treatment time, blood flow rate and hematocrit (Ht) were added upfront into the model. Results were considered statistically significant when p<0.05.

Results: Patients were predominantly males (60%) with a mean age of 64 ± 14 years and a median dialysis vintage of 1.8 (0.1-19.0) years. Twenty-seven percent of patients had diabetes and 43% cardiovascular disease at baseline. The main vascular access was arteriovenous fistula (AVF, 79%), followed by graft (15%) and central venous catheter (6%). Mean convective volume (CV) of HDF was 198 ± 4.4 L and filtration fraction was 26.0 ± 5.7%. Multivariable analysis showed that treatment time (regression coefficient (B) = 0.08 L per min (95%CI 0.07-0.10)), blood flow rate [B = 0.05 L per ml/min (95%CI 0.05-0.06)], dialysis vintage [B = 0.14 L per year (95%CI 0.03-0.247)], male gender [B = 0.43 L vs. female (95%CI 0.02-1.40)] and albumin [B = 0.13 L per g/L (95%CI 0.04-0.224)] were positively related to CV, while Ht [B = -0.11 L per % (95%CI -0.19–0.033)] and AVF [B = -1.25 L vs. other vascular access (95%CI -2.08–0.42)] were negatively associated to CV. Differences were not observed between lower and upper arm AVFs.

Conclusions: In this study both AVF and Ht were inversely and independently related to the convection volume, while treatment time and blood flow rate showed a positive relationship. Whether optimization of these parameters to increase convection volume is feasible in clinical practice is a subject for further research.

MOO21 MIXED PRE-POST DILUTION HEMODIAFILTRATION: A COMPARISON OF SOLUTE ELIMINATION WITH PRE- AND POSTDILUTION MODES

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Introduction and Aims: Several studies showed that online HDF can enhance the removal of toxins compared to hemodialysis. Postdilution HDF (post HDF) is considered as the most effective mode, but it may cause decrease of solute clearance and dialyzer clotting due to hemocoagulation, high blood viscosity and resistance to flow. Pre dilution HDF (pre HDF) can ensure better rheological and hydraulic conditions, whereas its toxin removing efficiency is relatively lower. Mixed pre-dilution hemodiafiltration (mixed HDF) is a newly developed technology which may combine the advantages of two dilutions of HDF. The study is to compare the differences of three HDF modes in solute removal.

Methods: A Fresenius 5008 dialysis system (Fresenius Medical Care, Bad Homburg, Germany) was used and 42 stable patients were enrolled in the study. Each patient underwent three HDF modes: pre HDF (infusion rate, Qi =200ml/min), mixed HDF (initial Qi = calculated by hematocrit, effective blood flow rate and plasma flow rate of the patients) and post HDF (Qi =80ml/min). Each mode includes three consecutive treatments and 1-week wash out of high-flux dialysis was performed between every two modes. In mixed HDF, the ratio of pre - post dilution was adjusted to maintain mean TMP within 250–300mmHg continuously. At the third treatment of each mode, blood samples were taken before and after and dialysis and wasted dialysate was collected to determine the concentration of urea, phosphate(P), Rmicroglobulin(βM), interleukin-6(IL-6), advanced oxidation protein products(AOPP), advanced glycosylation end products(AGEs) and albumin(ALB).

Results: Mixed HDF provided a high volume exchange (40±2.44L/session). EKTV was similar in mixed HDF and post HDF, which was significantly higher than that in pre HDF(1,62±0.29 and 1.63±0.29 vs 1.50±0.27. p=0.000 and 0.000). Serum βM after dialysis was significantly lower in mixed HDF and post HDF than that in pre HDF(3.34 ±0.54 and 3.32±0.54 vs 3.93±0.79, p=0.000 and 0.000). The mean dialyse clearances (KDCO) of βM, IL-6 in mixed HDF were significantly higher than those in pre and post HDF(21.47±6.5 vs59.55±2.78 and 76.54±2.71, p=0.000 and 0.025; 243.95 ±26.13 vs 97.87±18.23 and 210.22±38.91, p=0.000 and 0.000), while serum P after dialysis was obviously lower(0.68±0.17 vs 0.75±0.18 and 0.73±0.18, p=0.000 and 0.006). Kp, of AOPP was significantly higher in pre HDF and mixed HDF than post HDF(166.01±33.03 and 159.81±35.47 vs 144.19±25.74,p=0.002 and 0.025). Serum AGES after dialysis was found significantly lower in pre HDF and mixed HDF compared with that in post HDF(21.38±3.16 and 20.56±3.28 vs 37.75±5.08, p=0.000 and 0.000). Although the albumin leakage was highest in mixed HDF (4.8±2.0g), albumin serum before and after dialysis was not significantly different among three modes.

Conclusions: Mixed dialution HDF seems to be a good HDF alternative that allows a better removal of molecules than post and HDF. While its side effect of albumin loss appears to be within an acceptable range for HDF. It may provide an ideal choice of online HDF in the near future.

INFLUENCE OF HIGH CONVECTION VOLUMES IN REMOVAL PERFORMANCES OF ON-LINE HEMODIAFILTRATION (HDF)

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Introduction and Aims: Recent prospective trials suggest that on-line hemodiafiltration (HDF) improves survival, provided that it reaches high convective volumes. However, while these results await confirmation, there is scant information on the consequences of modifying convection correction in vivo. We wanted to characterise the influence of convection volume on the removal performances of on-line post-dilutional HDF.

Methods: Twelve dialysis patients were treated with 2.3 m² Amembris® dialysers, and 28 consecutive treatments and 1-week wash out of high-flux dialysis was performed (KUF max and 40% over conditions respectively (NS). The maximum in vivo ultrafiltration coefficient (KUF max), KUF max and 40% over the KUF max setting) for 1 week each. Continuous sampling of spent dialysate was performed in all dialysis sessions and total mass of urea, creatinine, and total proteins were measured. SDS-PAGE scanning of the removed proteins and ELISA measurements of R2M, retinol binding protein, light chains of immunoglobulins, a1-antitrypsin and albumin, were performed.

Results: The total mass of urea removed was 512±42, 494±45, 491±44 and 471±38 mmol/session in HD, under KUF max and over conditions respectively (NS). The corresponding KUF values were 1.72±0.05, 1.78±0.05, 1.77±0.05 and 1.78±0.05 (NS). Protein removal, both, calculated from the SDS-PAGE pattern and by ELISA measurements of specific proteins (Figure 1), differed with convection increase. B2M removal was 242.35, 274±35, 266±24 and 283.35±23 mg /session (NS) while albumin removal was 1161.24, 2444±39, 559±49 and 1052±178 mg/session respectively (p<0.001).

Conclusions: While removal of small mol wt uramic compounds did not significantly change with increased convection correction in HDF, a clear change in the cut-off pattern was observed: the highest correction was associated with a significant increase in proteins mostly in the range of albumin and over. HDF performed at KUF max convection volumes are associated with significant increases in middle molecules while albumin removal is <600 mg/treatment session. Increasing the convection volumes over the KUF max situation results in albumin losses >1 g/treatment session, which might be an unwanted effect of HDF.
Abstracts

MO023 DETERMINANTS OF BETA-2 MICROGLOBULIN (β2-m) LEVELS IN PATIENTS ON LONG-TERM HAEMODIALYSIS/TRANSFILTRATION (HDF), COMPUTATIONAL TECHNIQUE ANALYSIS OF THE RECORDS FROM A LARGE DATA-BASE SYSTEM (EUCLID)

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Introduction and Aims: Secondary analyses of large trials (CONTRAST & Turkish Study) suggested that improved survival may be obtained in on-line HDF with larger amount of volume exchange. Moreover, serum β2-m basal levels were shown to predict mortality in dialysis RRT patients (Cheung et al., HEMO Study, JASN 2006). Thus, major focus of the present work was to attempt to disclose the factor(s) patient- and treatment-related which mainly affect β2-m levels in patients on chronic RRT with on-line postdilution HDF with an unsupervised approach based on a new computational technique.

Methods: A retrospective study was performed on medical data of 2743 patients undergoing chronic RRT with HDF, assisted in the European analysis facilities of an international provider. A homogeneous set of values of relevant clinical and biochemical indicators was extracted from a common database (Euclid). A total number of 7780 β2-m measurements associated to 77 other clinical parameters were included in our analysis. A Self Organizing Maps (SOM) algorithm, based on a neural net, was implemented to extract information from this complex and multidimensional dataset. SOM is a computational technique that allows projecting high-dimensional datasets to a two-dimensional space (map) while preserving the similarity relations existing in the original dataset. By means of SOM maps it is thus possible to detect expected as well as unexpected relationships among the variables under study with an unsupervised approach, meaning that no a priori hypotheses need to be formulated by the user; results are, therefore, unbiased. SOM outcomes have been also validated with statistical tests.

Results: The analysis of SOMs maps highlighted 4 clusters showing an inverse correlation between levels of Exchange Volume and β2-m, confirmed by the regression analysis (P<0.001). The 4 clusters correspond to 4 subpopulations treated with different amounts of exchange volume (Liter/treatment): A: <14, between 14 and 19, between 19 and 24, and >24. Within these subpopulations the mean ± SD β2-m levels (mg/L) were, respectively, as follows: 25.3±8.4, 24.1±8.1, 23.0±7.8, 22.2±6.8. These subpopulation means were significantly different as verified with ANOVA testing (p<0.001).

Conclusions: With a new unsupervised approach we have confirmed in this study that lower β2-m levels may be achieved in HDF patients by increasing volume exchange. If progressively lower β2-m basal levels predict progressively lower mortality rates in RRT patients, as suggested by the HEMO study (Cheung, JASN 2006), it may be inferred that the greatest benefits in terms of patients outcome may be achieved in on-line HDF by achieving the maximum possible volume exchange on an individual basis and that a general adequate amount does not exist.

MO024 PRACTICAL GUIDANCE FOR PREDICTING CHANGES IN PREDIALYSIS SERUM PHOSPHORUS CONCENTRATION AFTER ALTERING THE HAEMODIALYSIS PRESCRIPTION BASED ON A PSEUDO ONE-COMPARTMENT KINETIC MODEL

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Introduction and Aims: The KDIGO Work Group recommends increasing dialytic phosphorus removal in the treatment of CKD-stage 3D patients with persistent hyperphosphatemia; however, guidelines to achieve enhanced phosphorus removal by using daily haemodialysis (HD) therapies have not been formulated. We evaluated whether kinetic modeling of phosphorus using a pseudo one-compartment model could provide guidance for predicting changes in predialysis serum phosphorus concentration after altering the HD prescription.

Methods: Modeling of intradialytic and postdialytic rebound kinetics of serum phosphorus during thrice weekly HD treatments (treatment (Tx) time median of 210 [183, 239] minutes, 25th percentile, 75th percentile) on 774 patients from the HEMO Study has previously allowed determination of the phosphorus mobilization clearance (87 [65, 116] mL/min) and central distribution volume of phosphorus (9.4 [7.2, 12.0] L) (Agar et al, Nephrol Dial Transplant 2012). In this study, a pseudo one-compartment kinetic model was used to predict changes in predialysis serum phosphorus concentration after altering the HD prescription.

Results: Initial analyses showed that the decrease in predialysis serum phosphorus concentration from thrice weekly to daily HD therapies assuming equal weekly Tx times was strongly correlated to the thrice weekly predialysis serum phosphorus concentration (R=0.814, P<0.001 for 4 Tx per week, R=0.832, P<0.001 for 5 Tx per week, R=0.815, P<0.001 for 6 Tx per week). Further analyses showed that the percent decrease in predialysis serum phosphorus concentration spanned a narrow range and was relatively independent of the thrice weekly predialysis serum phosphorus concentration and patient-specific kinetic parameters (see tabulated results for all 774 patients).

Conclusions: This study suggests that practical guidance can be developed based on a pseudo one-compartment kinetic model for predicting the decrease in predialysis serum phosphorus concentration after altering the HD prescription. The extension of this guidance when dietary phosphorus intake, oral phosphate binder use and dialyzer phosphorus clearance are altered during daily HD therapies can also be achieved using this approach.

MO025 HOW TO ADAPT HEMODIALYSIS STRATEGIES TO REMOVE PROTEIN-BOUND SOLUTES MORE ADEQUATELY: A KINETIC ANALYSIS

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Introduction and Aims: Patients with renal failure retain a large variety of solutes, of which urea is commonly applied as adequacy marker. Urea kinetics were however found not representative for the removal of other small water soluble solutes. Several protein-bound solutes (PBS) are known to exert (cardio)vascular damage, and might be as interesting to focus on from a kinetic point of view. We therefore studied the kinetics of PBS with different % protein binding (%BP). Based on these findings, adequacy of different hemodialysis (HD) strategies in removing PBS was calculated.

Methods: This study included 10 stable hemodialysis patients undergoing high flux HD. Blood samples were collected from inlet blood line at start, and after 15, 30, 60, 120, and 240min, and from outlet blood line at 30 and 120min. Total and free concentrations of hippuric acid (HAA), indoxyl sulfate (IS), indole acetic acid (IAA),

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Percent Decrease in Predialysis Serum Phosphorus (median [25th percentile, 75th percentile])

<table>
<thead>
<tr>
<th>Tx per Week</th>
<th>Equal Weekly Tx Time (207 minutes)</th>
<th>Equal Weekly Tx Time Plus 1 hour/Tx (447-567 minutes)</th>
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<tr>
<td>4</td>
<td>5.7 [4.3-6.9]</td>
<td>25.3 [23.8-27.3]</td>
</tr>
<tr>
<td>5</td>
<td>10.1 [7.9-12.1]</td>
<td>32.2 [30.4-34.1]</td>
</tr>
<tr>
<td>6</td>
<td>13.7 [10.9-16.3]</td>
<td>37.8 [35.8-39.8]</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Protein</th>
<th>%BP</th>
<th>Kinetic Model</th>
<th>Phosphorus Clearance</th>
<th>Hemodialysis Prescriptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAA</td>
<td>84</td>
<td>One-compartment</td>
<td>0.814</td>
<td>4 Tx per week</td>
</tr>
<tr>
<td>IS</td>
<td>19</td>
<td>One-compartment</td>
<td>0.832</td>
<td>5 Tx per week</td>
</tr>
<tr>
<td>IAA</td>
<td>9</td>
<td>One-compartment</td>
<td>0.815</td>
<td>6 Tx per week</td>
</tr>
</tbody>
</table>
3-carboxy-4-methyl-5-propyl-2-furanpropionic acid (CMPF), p-cresylsulfate (PCS), and p-cresylglucuronide (PCG) were determined to calculate dialyzer clearance (K) and %PB at start. Per solute, a two-pool kinetic model was fitted to the measured serum concentrations, calculating the plasmatic volume (V₁), total distribution volume (V₂tot), and inter-compartment clearance (K₁₂); solute generation and ultrafiltration were determined independently. The calibrated kinetic models were further used to calculate mass removal (MR) and time-averaged concentrations (TACs) during standard HD (3x4h), frequent HD (6x2h) with blood flow Q₃00 and extended thrice weekly HD (3x8h) with Q₃150.

Results: K (range:0-152mL/min) correlated well with %PB (range:13-100%) (R=−0.984; P<0.001). Kinetic parameters V₁, V₂tot, and K₁₂ of IS and PCS, known to share the same binding site on albumin and having similar %PB (93-94%), were correlated (R=0.89; P=0.001, R=0.84;P=0.002, and R=0.84;P=0.002, respectively). Significant differences for V₁ were found between PCG (13%PB) versus IAA (70%PB), IS, and PCS (all P<0.01), and for V₂tot and K₁₂ between PCG versus IAA and PCS (all P<0.05). HA (40%PB) showed intermediate results, while CMPF (100%PB) was not found to be removed from the patient. More frequent HD resulted in 10-25% higher MR and -4 to 13% lower TACs compared to standard HD, while extended HD resulted in 6-14% higher MR and 0-15% lower TACs.

Conclusions: In conclusion, the removal of PBS is rather complex, since they differ in dialyzer clearance depending on their %PB, as well as in their kinetic transport in the patient. Among individual PBS the kinetic pattern may be strongly different, so that data from one molecule cannot automatically be extrapolated to the other. More frequent HD seems more beneficial than extended HD for the removal of PBS, although impact seems rather limited to those solutes with the highest %PB.
Heart and Bone in CKD - A

Introduction and Aims: Animal studies showed that non-oxidized PTH (n-oxPTH) is bioactive, whereas oxidation of PTH at methionine residues results in loss of biological activity. In the present study we analyzed the effect of n-oxPTH on mortality in hemodialysis patients.

Methods: For determining associations among PTH levels and mortality in hemodialysis patients we performed a prospective cohort study in 340 prevalent hemodialysis patients which were followed up for 5 years. PTH was measured by means of the third generation intact-PTH immunoassay system, either directly (total intact parathyroid hormone, iPTH) and after prior removal of oxidized PTH molecules from the samples using specific monoclonal antibodies raised against the oxidized human PTH.

Results: Hemodialysis patients (224 men/116 women) had a median age of 66 years, median time on dialysis was 266 days (IQR, 31 to 1209 days), and median dialysis dose (kt/V) was 1.2. 170 patients (50%) participated in a follow up time of 5 years. Median n-ox-PTH levels were higher in survivors (7.2 ng/mL) compared to patient that died (5.0 ng/mL; p=0.002). Survival analysis showed an increased survival in the highest n-ox-PTH tertile compared to the lowest n-ox-PTH tertile (Chi square 14.3; p=0.008). Median survival was 1172 days in the highest n-ox-PTH tertile, whereas it was only 453 days in the lowest n-ox-PTH tertile. Multivariable-adjusted Cox regression showed that higher age increased odds for death, whereas n-oxPTH and hemoglobin concentrations reduced the odds for death. In this model, the iPTH category did not affect the odds for death, indicating that the amount of n-ox-PTH but not iPTH predicted patients’ survival in the entire study population. A further model analyzing only patients with iPTH above the normal range (>70 ng/ml) revealed that mortality in this subgroup depended protein oxidation on PTH but not on n-ox-PTH. N-oxPTH had no impact on mortality in patients with high iPTH, whereas iPTH was associated with all-cause mortality when only analyzing patients with iPTH >70 pg/mL. Additionally, we find stratified iPTH levels according to international guidelines into five categories representing very low (<20ng/L), low (20 to 65ng/L), medium (65 to 150ng/L), target (150 to 300ng/L), and high (>300ng/L). Survival analysis showed that patients with target iPTH levels had longer median survival compared to the other categories.

Conclusions: In conclusion, the predictive power of n-oxPTH and iPTH on all-cause mortality differs substantially. Since the classical iPTH assay detects mainly oxidized, biologically inactive PTH, clinical decisions based on iPTH measurements might be misleading.

Heart Failure in the Evolve Trial

Introduction and Aims: Increased levels of parathyroid hormone (PTH), calcium and phosphorus can cause arterial calcification and arteriosclerosis, which predispose to left ventricular hypertrophy and heart failure. We designed the EVOLVE trial to test the hypothesis that the calcimimetic cinacalcet (+ conventional therapy for secondary hyperparathyroidism (shPT)) would reduce the risk of mortality and cardiovascular events in patients on hemodialysis with moderate to severe shHT.

Methods: The EVOLVE trial randomized 3883 patients with moderate to severe shHT with a median plasma intact parathyroid hormone concentration of 693 pg/ml (normal range 11–72 pg/ml; treatment with cinacalcet or placebo. The majority of patients received vitamin D steroids and phosphate binders. Time to the composite event comprising all-cause mortality or non-fatal cardiovascular events (myocardial infarction, hospitalization for unstable angina or hospitalization for peripheral revascularization events) were followed for up to 64 months. To determine whether cinacalcet reduced the risk of heart failure, we examined it’s effect on this outcome after adjusting for baseline risk factors, using an intent-to-treat analysis and Cox regression.

Results: The unadjusted hazard ratio (HR) in the cinacalcet vs placebo group for the primary composite end-point was 0.93 (95% CI 0.85-1.02). After adjustment for baseline variables it was 0.88 (95% CI 0.79-0.97). There were 236 (12.2%) heart failure events in patients randomized to placebo and 206 (10.6%) in patients randomized to cinacalcet (unadjusted HR=0.82, 95% CI 0.68-0.99) (p=0.034). The adjusted HR for heart failure (cinacalcet vs placebo) was 0.76 (95% CI 0.63–0.93). Using a prespecified lag censoring analysis where data were censored 6 months after patients discontinued study drug, the HR was 0.72 (95% CI 0.58–0.88). Significant predictors of heart failure independent of the treatment effect were older age, region, history of heart failure and hypertension, other cardiac diseases, lower baseline hemoglobin level, higher HDL, and tobacco use.

Conclusions: In the pre-specified intent-to-treat analyses accounting for baseline factors, randomization to cinacalcet resulted in a statistically significant 24% reduction in heart failure events in patients on hemodialysis with shHT.

The Calcimimetic R-641 with an Extended Duration of PTH Suppression Significantly Reduced Vascular Calcification and Serum FGF23 in Experimental Chronic Kidney Disease

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Introduction and Aims: Secondary hyperparathyroidism, characterized by increased PTH and FGF-23, contributes to vascular calcification in chronic kidney disease (CKD). Calcimetics lower parathyroid hormone (PTH) secretion and serum calcium levels by activating the calcium-sensing receptor in the parathyroid gland. Here we investigated whether administration of a calcimimetic, PTH or the combination (calcimimetics-PTH) influences vascular calcification and serum levels of FGF23 in a rat CKD model.

Methods: CKD was induced in rats by adenine (0.75%H) diet for 4 weeks, followed by normal diet and treatment for 4 weeks with either vehicle, PTH-(1-34), R-641-vehicle, or R-641+PTH-(1-34) and compared to rats fed control diet throughout the experiment. R-641 (10 mg/kg) or vehicle were administered (p.o.) every third day. In the R-641+PTH group each R-641 dose was followed 48 hrs later by 80 μg/kg PTH s.c. Blood samples were collected; vascular calcification was assessed by measurement of calcium content in aortic walls. PTH-(1-84) and FGF23 serum levels were measured by ELISA.

Results: Compared to healthy controls, adenine significantly increased serum urea, creatinine and aortic calcium content. In adenine fed animals, R-641 reduced aortic calcium content compared to vehicle (9 ± 3 vs 65 ± 57 μg/g, respectively, p<0.05, ANOVA). Serum PTH was lower in R-641 treatment groups compared to CKD, vehicle rats (773 ± 277 vs. 3464 ± 2576 pg/ml, p<0.05, ANOVA). Adenine diet induced an increase in FGF23 serum levels (1.4 ± 0.2 vs. 198.4 ± 95 ng/ml, p<0.05, ANOVA); R-641 treatment resulted in significantly lower values (71.4 ± 6 ng/ml, p<0.05, ANOVA). PTH administration did neither change vascular calcium content in CKD nor FGF23 serum levels in CKD alone or with R-641 co-administration.

Conclusions: After 4 weeks treatment, R-641 significantly reduced vascular calcification and lowered serum FGF23 levels in experimental CKD. PTH injection had no influence on vascular calcification or FGF23 serum levels.
PARATHYROID HORMONE-MEDIATED CHONDROCYTE TRANSITION OF ENDOTHELIAL CELLS PROMOTES MEDIAL CALCIFICATION IN EXPERIMENTAL SECONDARY HYPERPARATHYROIDISM

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Introduction and Aims: Secondary hyperparathyroidism (SHPT) is a common complication of uremia, which is closely associated with development of arterial media calcification (AMC). Previous studies have shown that heterotopic chondrogenesis contributes to AMC. In this study, we firstly demonstrated that elevation of PTH could induce the transition of endothelial cells into chondrocyte-like cells in experimental SHPT.

Methods: Uremia-related SHPT was induced by feeding rats an adenine diet (0.75%) for 4 weeks followed by high phosphorous diet (1.03%). Vascular calcification was checked by von Kossa staining and cartilage matrix was stained by alcian blue. Cultured human aortic endothelial cells (HAECs) were treated with PTH and then changed to chondrogenic differentiation medium. Endothelial, mesenchymal and chondrocyte markers were examined by immunohistochemistry, immunofluorescent staining, real-time PCR and western blot.

Results: After 4 weeks of adenine diet, serum creatinine (Scr) and PTH concentrations significantly increased over time compared with control (p<0.05). At 4 weeks after adenine withdrawal, mild to moderate aortic media calcification could be detected. Eight weeks after the establishment of CRF, von Kossa staining showed severe media calcification in the aortas. And there was significant cartilage matrix accumulation in the aortas of SHPT group compared to control, which was correlated with increased serum PTH levels. Immunohistochemical observation showed that SHPT downregulated the expression of endothelial marker CD31, and enhanced the translocation of CD31 from the aortic intima to media. Confocal microscopy further revealed the colocalization of CD31 and chondrocyte marker SOX9 in the aortic media of SHPT group. Further analysis showed the downregulation of CD31 accompanied with the increased protein expression of mesenchymal markers (α-SMA and FSP1) and chondrocyte markers (SOX9 and COL2A1). Exposure of cultured HAECs to PTH could significantly upregulate the expression of FSP1 and α-SMA and downregulate the levels of CD31 in concentration-dependent and time-dependent manners (p<0.05). Meanwhile, double staining showed a co-localization of CD31 and FSP1. After treatment with 100 nM PTH for 48 h, cells were grown in chondrogenic culture media for 7 days. We demonstrated the expression of SOX9 and COL2A1 significantly increased.

Conclusions: Elevation of PTH could directly contribute to the development of media calcification in CRF via endothelial to chondrocyte-like cell transition.

DIFFERENTIAL EFFECTS OF VITAMIN D RECEPTOR ACTIVATORS ON PULSE WAVE VELOCITY IN MAINTENANCE HEMODIALYSIS PATIENTS

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Introduction and Aims: Vascular calcification (VC) represents an important contributor to the high rate of cardiovascular mortality in end-stage renal disease (ESRD). Parathyroid hormone (PTH) and vitamin D play a critical role in regulating VC. This is a randomized, 12-months prospective study. Eligible 80 subjects (32 female, age: 50.0 ± 14.9 years) out of 250 MHD patients were included. Patients with parathyroid hormone (PTH) levels above >300 pg/mL were randomized and treated according to one of 4 groups: a) total serum calcium < 10.5 mg/dL, serum Ca × P <75 and PTH level between 300-800 pg/ml were randomized to receive either paricalcitol (n=20, group 1) or calcitriol (n=20, group 2), b) normalized total serum calcium < 10.5 mg/dL, serum Ca × P<75 and PTH level >800 pg/ml were randomized to receive either paricalcitol plus cinacalcet (n=30, group 3) or calcitriol plus cinacalcet (n=20, group 4). In addition to demographic and laboratory parameters, vascular calcification (PWV) were assessed at the beginning and end of the study.

Results: There were no differences in means of demographic characteristics of all groups. Although baseline P levels were similar in all groups after 4 months P levels of group 2 and 4 were significantly higher than the paricalcitol based treatment groups (p<0.05). Patients in group 3 and 4 had significantly higher Ca levels at the first 4 months of study (p<0.01) however in following 8 months these levels were statistically similar in all groups. When PTH levels were assessed and compared to basal values we observed a significant increment in group 2 and group 4 at the end of the study (p=0.002, 0.006, respectively). PWV significantly increased in Group 2, compared to the other groups (6.8 ± 1.6 m/sn to 8.1 ± 1.7 m/sn) at the end of the study (p=0.013). Additionally, we found that in calcitriol based treatment groups (Group 2 and 4) PWV significantly increased during the follow-up period while there was not significant change in PWV in paricalcitol based treatment groups (7.2 ± 2.0 m/sn to 8.0 ± 3.3 m/sn vs. 7.8 ± 3.1 m/sn to 7.5 ± 2.6 m/sn) (p=0.047).

Conclusions: In MHD patients with established SHPT, we demonstrated differential effects of calcitriol and paricalcitol on parathyroid hormone control and vascular calcification. We suggest that in clinical practice, the use of paricalcitol may allow for a wider therapeutic window with effects beyond SHPT management and may explain the increased survival advantage with paricalcitol treatment.
**PERITONEAL DIALYSIS - CLINICAL**

**MO032**  
**PERITONEAL ULTRAFILTRATION IN REFRACTORY HEART FAILURE: A COHORT STUDY**

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Introduction and Aims: Heart failure (HF) is a progressive and lethal disease with a high prevalence: in the entire US population it was 2.4% in 2008. A similar situation has been described in Europe. HF is often characterized by the presence of a vicious circle between heart and kidney. As a consequence of venous congestion and reduced renal perfusion, glomerular filtration rate (GFR) reduces and renin-angiotensin and sympathetic nervous system increase their activity. Therefore, sodium delivery to the distal tubule as well as the effects of natriuretic peptide, decrease, leading to the diuretic resistance and acute cardiac decompensation. Acutely decompensated HF in patients with diuretic resistance is often treated with extracorporeal ultrafiltration. After the resolution of the acute episode, peritoneal ultrafiltration (PUP) has been proposed for the long-term management of severe HF. The aim of this study was to evaluate the use of PUF in the chronic treatment of refractory HF in patients without end stage renal disease.

Methods: This was a multicenter, retrospective study (10 Nephrology Units throughout Italy) investigating the use of PUF as a therapy for severe HF, even if the patient didn’t need dialysis for his level of GFR. All consecutive patients with severe congestive HF, treated with PUF between January 1, 2006 and December 31, 2010, and with a follow up of at least 6 months, were included in this study. Patients were referred to the nephrologist only after adequate cardiological therapy, including extracorporeal ultrafiltration for acutely decompensated HF, resolving therefore the possible diuretic resistance. Patients needing PUF for any other indication than chronic fluid overload (ESRD with GFR < 6 ml/min, uremic symptoms, severe hyperkalemia, oliguria or acute HF) were excluded. Fluid overload was defined per center practice, including clinical assessment, chest X-ray and echocardiography.

Results: Forty-eight patients (39 men and 9 women, aged 74±9 years) were included: 30 patients underwent one nocturnal icodextrin exchange, 5 patients required two daily exchanges and 13 patients performed 2-4 sessions per week of automated peritoneal dialysis. During the first year renal function remained stable (from 20.8±1.0 ml/min/1.73m² to 22.1±3.6 ml/min/1.73m²), while pulmonary artery systolic pressure decreased from 45.5±9.18 to 40±6.99 mmHg (p=0.003) with a concomitant significant improvement in the NYHA functional status. Hospitalization days decreased from 43 ±33 (before starting PUF) to 11±17 days/patient/year (p=0.001). The incidence of peritonitis was 1 episode per 45-month patient. Patient survival was 85% at one year and 56% at two years.

Conclusions: This study confirms the satisfactory results of PUF in chronic HF in a consistent number of elderly patients.

**MO033**  
**NON-THYROIDAL ILLNESS - A NOVEL RISK FACTOR FOR CORONARY CALCIFICATION AND ARTERIAL STIFFNESS IN DIALYSIS PATIENTS?**

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Introduction and Aims: Low triiodothyronine levels, as part of the non-thyroidal illness spectrum, are common in dialysis patients and have been associated with increased (cardiovascular) mortality rates. We hypothesized that an increased vascular calcification may intercalate this relationship.

Methods: A prospective observational study was conducted in 84 peritoneal dialysis patients from the Stockholm region. Free triiodothyronine (fT3), thyroxine (fT4) and coronary artery calcium (CAC) scores (n=66) were assessed by cardiac computed tomography (CT) scans. Surrogates of arterial stiffness (n=74) included aortic diastolic and systolic blood pressure (BP), pulse pressure, augmentation pressure and Buckberg’s subendocardial viability ratio (SEVR) assessed by pulse waveform analyses. Patients were consequently followed for events of death and censoring.

Results: Both median CAC scores (1.527 vs. 4.38; p=0.013) and arterial stiffness surrogates, such as aortic pulse pressure (52±3 vs. 40±2 mmHg; p=0.086) were substantially higher in individuals with low fT3 levels (median value). These associations persisted in multivariate logistic and linear regression analyses. During a median (IQR) follow-up of 32 (22-42) months, 24 patients died. Both fT3 levels below the median value (HR:crude 2.7 [95%CI: 1.1-6.6] and CAC scores above the median value (HR:crude 5.8 [95%CI: 1.7-20.1]) associated strongly with mortality.

Conclusions: This study shows associations between fT3 levels, arterial stiffness and coronary artery calcification in PD patients. We hypothesize that the association between this hormonal alteration and mortality may, in part, be mediated by promotion of accelerated vascular calcification.

**THE RELATION BETWEEN FIBROBLAST GROWTH FACTOR-23 WITH ECHOCARDIOGRAPHIC PARAMETERS AND INTIMA-MEDIA THICKNESS OF CAROTID ARTERY IN PERITONEAL DIALYSIS PATIENTS**

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Introduction and Aims: Fibroblast growth factor 23 (FGF–23) is a phosphorus-regulating hormone. In chronic kidney disease (CKD), circulating FGF–23 levels are markedly elevated and independently associated with mortality. Left ventricular hypertrophy and atherosclerosis are potent risk factors for mortality in patients with CKD, and FGF–23 have been implicated in the pathogenesis of both myocardial hypertrophy and atherosclerosis. The aim of this study was to test that whether elevated FGF–23 levels might be associated with carotid artery atherosclerosis and left ventricular mass index (LVMI) in continuous ambulatory peritoneal dialysis patients (CAPD).

Methods: In this cross-sectional study, 61 subjects with CAPD (29 women and 32 men, mean age 46.9±13.3 years, mean CAPD vintage: 69.5±39 months) underwent echocardiograms to assess LVMI and carotid artery atherosclerosis was assessed by measuring the intima-media thickness (IMT) of the common carotid arteries using a B-mode Doppler ultrasound. Serum FGF–23 concentrations were measured with intact FGF–23 human enzyme-linked immunosorbent assay kit. According to the median levels of serum FGF–23 the patients were divided into two groups (FGF–23 high and low groups).

Results: Patients with high FGF–23 levels had significantly higher LVMI compared to patients with low FGF–23 levels (150±39 g/m² vs. 128±35 g/m²; p=0.02). However there was no difference in carotid IMT between two groups (0.079±0.02 cm vs. 0.080±0.02 cm, p=0.856). Significant positive correlation were recorded between increased serum FGF–23 levels and LVMI (r = 0.023) but serum levels of FGF–23 were not correlated with carotid IMT in these patients.

Conclusions: FGF–23 is associated with LVMI in patients with CAPD. Whether increased FGF–23 is a marker or a potential cause of myocardial hypertrophy and atherosclerosis in patients with end-stage renal disease requires further study.

**ARTERIAL STIFFNESS IN PERITONEAL DIALYSIS PATIENTS: AFFECTING FACTORS AND EFFECT ON MORTALITY**

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Introduction and Aims: Arterial stiffness is a common problem in patients with end-stage renal disease and a predictor of adverse events. In this study, we aimed to evaluate the factors affecting arterial stiffness and also to examine the effect of arterial stiffness on mortality.

Methods: Sixty-seven peritoneal dialysis (PD) patients, 41 female and 26 male, were included in the study. Mean age was 46.9 ± 12.6 years and mean duration of PD was 28.5 ± 22.6 months. Arterial stiffness was assessed by ankle-brachial pulse wave velocity. Two pulse wave measurements six months apart for each patient were averaged. The factors affecting pulse wave velocity was examined by a stepwise linear regression analysis, and the effect of pulse wave velocity on 4-year mortality was evaluated by logistic regression analysis.

Results: Mean pulse wave velocity was 8.51 ± 2.64 m/sec. Pulse wave velocity was positively correlated with age (r=0.519, p<0.001), co-morbidity score (r=0.493, p<0.001), the presence of diabetes mellitus (r=0.540, p<0.001), the presence of...
coronary artery disease (r=0.570, p<0.001), systolic blood pressure (r=0.536, p<0.001), pulse pressure (r=0.582, p<0.001), serum proBNP level (r=0.521, p<0.001) and C-reactive protein level (r=0.369, p=0.002), and negatively correlated with serum prealbumin level (r=-0.503, p<0.001) and the use of ESA (r=-0.322, p=0.008). In stepwise linear regression analysis, serum C-reactive protein level was most important determinant of pulse wave velocity. Fifteen patients died during the follow-up. Mean pulse wave velocity in patients who died was significantly higher than that of the patients who surviving (10.43 ± 3.26 vs. 7.78 ± 2.08 m/sec; p<0.001). The most important predictor of mortality was pulse wave velocity in logistic regression analysis (p=0.009, RR=1.32). With every 1 m/s increase in pulse wave velocity, relative death risk increased by 1.32 fold. Co-morbidity score, the presence of coronary artery disease, the levels of serum proBNP and prealbumin were also factors independently affecting mortality.

Conclusions: Increased pulse wave velocity is an important predictor of mortality in PD patients. Inflammation and volume overload reflected by serum proBNP level were most important determinants of increased pulse wave velocity. Regular screening of markers of inflammation and the approaches preventing inflammation, and strict volume control can contribute to the improvement of arterial stiffness.

**MO035 Figure 1:**

**MO036 INTRA-PERITONEAL VERSUS SYSTEMIC INFLAMMATION AND SURVIVAL IN PERITONEAL DIALYSIS: RESULTS FROM THE GLOBAL FLUID STUDY**

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**Introduction and Aims:** Systemic inflammation, as evidenced by circulating inflammatory cytokines such as IL-6 predicts worse survival in dialysis patients. Intrapertitoneal IL-6 is an established determinant of peritoneal transport characteristics in peritoneal dialysis (PD) patients, which has also been linked to patient survival. We sought to determine the link between systemic and local intraperitoneal inflammation and establish their independent effects on patient survival.

**Methods:** The Global Fluid Study is a multi-national multicentre prospective incident and prevalent cohort study with up to 8 years follow-up. Data included demography, comorbidity, modality, prescription, membrane function, and dialysate and plasma IL-1β, TNF-α, IFN-γ and IL-6 measured by electrochemiluminescence. Stratified unadjusted and adjusted Cox models with robust standard errors for clustering by centres were used for survival analysis of dialysate and plasma cytokines. Proportional hazards were checked.

**Results:** 426 survival endpoints occurred in 559 incident and 358 prevalent patients from 10 centres in Korea, Canada and the UK. On univariable analysis, plasma IL-6 and TNF-α and dialysate IL-6 were significantly associated with survival in incident and prevalent groups (with a trend to significance for dialysate IFN-γ). After adjustment for age, gender, residual renal function, peritoneal solute transport rate, comorbidity, BMI, duration of PD and albumin, plasma IL-6 and TNF-α in incident and plasma IL-6 in prevalent groups were independent predictors of patient survival.

**Conclusions:** This is the first study to demonstrate that local intraperitoneal inflammation does not affect patient survival unless via systemic inflammation. Plasma TNF-α provides additional predictive information over plasma IL-6 in incident PD patients.

**MO037 FIRST PERITONITIS EPISODE INFLUENCES PERITONEAL SIZE-SELECTIVITY TO MACROMOLECULES IN PERITONEAL DIALYSIS PATIENTS**

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**Introduction and Aims:** Preservation of peritoneal membrane quality in peritoneal dialysis (PD) patients is required to maintain these patients on long-term PD. Recurrent peritonitis has been hypothesized to alter peritoneal transport status by inflammatory damage, but only few studies determined the importance of this phenomenon by measurement of transport kinetics, and reported inconsistent results. Little or no evidence is available on the impact of the first peritonitis episode. The objective of this study was to investigate the importance of the first peritonitis episode by comparison of peritoneal transport before and after the infection.

**Methods:** We analyzed prospectively collected data from 709 incident PD patients aged >18 years old treated in a tertiary-care university hospital between 1990 and 2010. Standard Peritoneal Permeability Analyses (SPA) data within the year before and within the year (but not within 30 days) after the first peritonitis were compared. SPA data included the mass transfer area coefficient of creatinine, glucose absorption and protein clearances of β-2 microglobulin (β2m), albumin, IgG and α-2-macroglobulin (α2m). From these clearances the restriction coefficient to macromolecules (RC) was calculated. Also parameters of fluid transport were determined: transcapillary ultrafiltration, lymphatic absorption and free water transport.

**Results:** Of 709 patients, 507 experienced a first peritonitis episode. Of these, 92 peritonitis episodes were preceded and followed by a SPA within one year. No changes in peritoneal transport of low molecular weight solutes and fluid kinetics were found. However, a discreet but significant decrease in the transport of macromolecules was seen: median difference in post- and preperitonitis values: IgG: -5 μL/min (p=0.01), α2m: -2 μL/min (p=0.02), albumin: -4 μL/min (p=0.04). Accordingly, the RC to macromolecules increased after peritonitis: 0.07, p<0.001. This is the first study to demonstrate that local intraperitoneal inflammation does not affect patient survival unless via systemic inflammation. Plasma TNF-α provides additional predictive information over plasma IL-6 in incident PD patients.
PAEDIATRIC NEPHROLOGY - B

MO038 INDICATORS OF FIBROSIS IN CHILDREN WITH CHRONIC KIDNEY DISEASE

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Introduction and Aims: Matrix metalloproteinases (MMPs), their tissue inhibitors (TIMPs), adherence molecules and heat shock proteins (hsps) may play an essential role in the process of renal fibrosis. Recent animal studies have shown that the inhibition of selected MMPs and hsps may slow down the progression of fibrosis or even reverse it. However, the data concerning such influence in adult patients with chronic kidney disease (CKD) on conservative treatment are scarce and there are no results of such investigation in children. The aim of the study was to assess the concentrations of Hsp90α, sE-selectin, MMP-2, TIMP-1 and TIMP-2 in the predialysis CKD children and to analyze the potential relations between these parameters.

Methods: 65 children enrolled in the study were divided into those with CKD stage 3-4 (CKD I) and CKD stage 5 not yet on dialysis (CKD II). 30 age-matched subjects served as controls. The serum concentrations of Hsp90α, sE-selectin, MMP-2, TIMP-1 and TIMP-2 were assessed by ELISA.

Results: The median values of Hsp90α, sE-selectin, MMP-2, TIMP-1 and TIMP-2 were significantly elevated in CKD patients vs. controls. In the case of sE-selectin and MMP-2 the concentrations kept growing together with the progressing renal failure and were significantly higher in CKD II group than in CKD I. When TIMP-1 and TIMP-2 levels were analyzed, there was no difference between CKD I and CKD II values. The Hsp90α concentrations decreased in the course of CKD and became significantly lower in CKD II than in the CKD I group. Hsp90α and sE-selectin correlated with each other and with all examined metalloproteinases. There was also a significant relation between GFR and MMP-2, Hsp90α and sE-selectin.

Conclusions: The increased concentrations of examined parameters indicate enhanced cell damage, inflammation and aggravation of proteolytic processes, responsible for progression of renal fibrosis in CKD children. Differences in behavior of selected parameters in the course of renal failure progression suggest the diversity of their engagement in various stages of CKD. Observed correlations point at the complexity of interrelations between different elements responsible for the fibrosis puzzle.

MO039 ALLOIMMUNE MEMBRANEOUS NEPHROPATHY WITH ANTI-NEUTRAL ENDOPEPTIDASE ANTIBODIES: GENETIC HOMOGENEITY BUT IGG SUBCLASS-DEPENDENT CLINICAL VARIABILITY

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Introduction and Aims: Alloimmune antenatal membranous nephropathy (MN) results from maternal antibodies that cross the placenta, bind to fetal glomerular podocytes and mediate renal disease. The infant’s mother is deficient in neutral endopeptidase (NEP) and thus she becomes immunized during pregnancy against NEP expressed by placental cells. In postnatal life, renal function is improved in all infants; however, the immunologically mediated antenatal nephron loss may lead to chronic renal failure detected during adolescence. Until now five mothers from three families with the same mechanism of disease have been identified. We report here two recent cases which illuminate the pathophysiology and provide clues to the severity of renal disease.

Methods: Circulating maternal anti-NEP antibodies were assessed by indirect immunofluorescence (IF) and Western blotting (WB). IgG subclasses with anti-NEP activity were determined by an ELISA. Mutations in the MME gene were detected by direct sequencing of genomic PCR products.

Results: The mothers of the two children born with MN had circulating antibodies against NEP showing the characteristic species-dependent pattern by IF of human, rabbit and rat kidneys. Mothers’ sera reacted also with recombinant human NEP by ELISA.

Conclusions: We have identified two additional families with alloimmune antenatal MN. Severity of renal disease was dependent on distribution of NEP-specific IgG subclasses in the mothers’ sera. The 466delC mutation previously identified in the first 3 families suggests a founder effect. Because of the potential severity of alloimmune antenatal MN, it is essential to identify families at risk by IF detection of anti-NEP and WB of NEP antigen in urine.

MO040 RISK FACTORS FOR PROGRESSION IN CHILDREN WITH IGA NEPHROPATHY: DATA FROM A EUROPEAN COHORT

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¹On behalf of VALIGA Study Group Italy

Introduction and Aims: The results of the European validation study of the Oxford classification of IgA nephropathy (VALIGA), which enrolled 1147 patients, are about to be published.

Methods: We hereby analyze data concerning the pediatric population included in VALIGA: 174 children with primary IgA nephropathy (IgAN), reported by 20 Nephrology centers from 11 European countries. Proteinuria was adjusted for body surface area and MAP - mean arterial pressure (1/3 of diastolic pressure + pulse pressure)- for gender and age. Time-average (TA) proteinuria and MAP were calculated on the follow-up (f-up). eGFR was estimated using Schwartz formula; decline in renal function was defined as the slope of eGFR over the f-up.

Results: 72% of children were males, with a mean age at renal biopsy of 12.7 ± 3.7 y and a median f-up of 4.7 y [IQ range 2.4-7.8 y]; more than 80% presented with normal renal function (eGFR > 90 ml/min/1.73m²). End-stage renal disease (ESRD) was reached by 4% of patients, 50% loss of initial eGFR by 5%; 7% of children reached the combined end point (ESRD or 50% loss of initial eGFR). At renal biopsy 57% of children presented with mesangial proliferation (M1), 24% with endocapillary proliferation (E1), 35% with segmental glomerulosclerosis (S1) and 9% with tubular atrophy/interstitial fibrosis (TA/IF). Patients with segmental sclerosis and TA/IF showed a significantly worse eGFR slope over the f-up (80 vs 51 p=0.04; T8 vs T1/2 p<0.003). At univariate linear regression, clinical data at renal biopsy (eGFR, proteinuria and MAP) were not associated with renal function decline, while data at 6-12 and 12-24 months and TA-proteinuria and MAP significantly predicted eGFR slope. A multivariate linear regression model (including proteinuria and MAP at 12-24 months together with the difference of eGFR at renal biopsy and at 12-24 months as independent variables) performed well in predicting eGFR slope (R²=0.39). This model was used to derive a formula able to estimate eGFR slope, which performs well in the VALIGA pediatric population (mean bias between estimated and really observed eGFR slope of 0.05 ± 6.6 ml/min/1.73m²).

Conclusions: The Oxford classification of IgAN was well applicable to this pediatric population, with segmental glomerulosclerosis and tubular atrophy/interstitial fibrosis being more significantly associated with renal outcome. A formula was developed that precisely estimates renal function decline over the f-up based on proteinuria, MAP and eGFR loss after 1-2 years of observation, which will need a validation on other cohorts.
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**MO041 NEW K/DIGO GUIDELINES AND KIDNEY TRANSPLANTATION: IS THE CYSTATIN-C BASED RECOMMENDATION RELEVANT?**

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**Introduction and Aims:** In 2013, K/DIGO guidelines published new recommendations for evaluation and management of chronic kidney disease (CKD). These guidelines propose a new framework for the evaluation and classification of CKD, especially in patients with glomerular filtration rate (GFR) <60mL/min/1.73m². We cite hereafter the recommendation 1.4.3.5: “We suggest measuring cystatin C in adults with GFR estimated by the CKD-EPI creatinine-based equation (eGFRcreat) ≥ 59 mL/min/1.73 m² who do not have markers of kidney damage if confirmation of CKD is required. If GFR estimated by the combined equation based on both creatinine and cystatin C (eGFRcreat-cys) is also <60 mL/min/1.73 mL, the diagnosis of CKD is confirmed. If eGFRcreat-cys is ≥ 60 mL/min/1.73 m², the diagnosis of CKD is not confirmed.” Although derived from studies unrelated to kidney transplantation, the K/DIGO guidelines aim to target the transplant population as well. Herein, we sought to determine whether the new K/DIGO strategy to detect decreased GFR might be applicable in renal transplant recipients.

**Methods:** In 670 kidney transplant recipients (KTR), we analyzed the performance of the eGFRcreat-cys to reclassify KTR in comparison with inulin clearances (mGFR) by using the analytical methodology developed in these guidelines. Serum creatinine was measured by an isotope-dilution mass spectrometry traceable enzymatic method, cystatin C by IFCC-traceable nephelometric method.

**Results:** In the whole cohort, 192 patients had eGFRcreat 45-59 mL/min/1.73m² but mGFR was above 60 mL/min/1.73m² in 39 of them (20%). When using eGFRcreat-cys in these 192 patients, 181 (94%) had also eGFR below 60 mL/min/1.73 m² (with 11 discordant results). In the 39 patients with eGFRcreat <60 but mGFR >60 mL/min/1.73 m³, 31 were also falsely classified as CKD by the eGFRcreat-cys equation. Moreover, in the 11 patients with eGFRcreat <60 and eGFRcreat-cys<60, three patients had effectively mGFR<60. Estimating GFR by eGFR creat led to 20% (39/192) of errors in CKD classification. Following the strategy suggested by the guidelines, errors in classification were actually marginally corrected (18%, 34/192).

**Conclusions:** The K/DIGO guidelines recommend the use of the eGFRcreat-cys to improve the detection of CKD in patients whom eGFRcreat 45-59mL/min/1.73m². In the present study, we show that this recommendation cannot be extended to transplant recipients. The same conclusion was reached when patients with proteinuria were excluded from the analysis.

**MO042 DE NOVO ANTI HLA ANTIBODIES AFTER KIDNEY TRANSPLANTATION: TRIGGERING FACTORS AND LONG TERM OUTCOME IN RENAL TRANSPLANT RECIPIENTS**

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**Introduction and Aims:** The aim of the study is to identify triggering factors for the development of de novo anti HLA antibodies in kidney transplant recipients (KTR) and to define their role in long term graft survival.

**Methods:** Sets of 87 KTR transplanted between 1999 and 2010 were screened for HLA antibodies (Donor Specific Antibodies [DSA] and non Donor Specific Antibodies [NDSA]) on the day of transplantation and at 1y by Luminex beads coated with a single HLA antigen (Gen-Probe Transplant Diagnostics). We included only patients free of HLA Abs on day 0 (N=660; 75%). We first compared de novo HLA+ patients with HLA neg patients for demographic parameters as well as for the events that occurred up to 1y in order to identify triggering factors for “de novo” HLA Abs. We next compared graft survival after 1y between de novo HLA+ patients and HLA neg patients. Death-censored graft survival(DCGS) curves were calculated using Kaplan Meyer method and compared by Log Rank test.

**Results:** Ninety-three patients (14.1%) developed de novo HLA antibodies (both DSA and NDSA) at 1y. Multivariate logistic regression analysis showed that peak PRA >5% (OR: 3.5; P=0.001) and episodes of biopsy-proven acute rejection (OR: 2; P=0.04) were associated with HLA Ab development. Twenty-five patients (4%) developed DSA at 1y. The N° of HLA mismatches (A+B+Dr) (OR: 1.44; P=0.03) as well as previous transplants (OR: 3.9; P=0.04) were significantly associated with DSA by multivariate logistic regression analysis. De novo HLA + patients had lower 1y DCFS than HLA neg patients (80% vs 60%; P=0.04). Anti-Class II Abs were associated with lower survival (79% vs 62%; P=0.08) whereas de novo HLA Class I Abs had no impact.

**Conclusions:** Peak PRA, previous grafts, HLA MM, and acute rejection episodes are associated with “de novo” HLA Abs. Post-transplant monitoring of HLA Abs, and particularly Class II Abs, may help to identify patients at higher risk of later graft loss.

**MO043 ABO INCOMPATIBLE LIVING DONOR KIDNEY TRANSPLANTATION WITH MINIMAL DOSE OF RITUXIMAB**

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**Introduction and Aims:** ABO KT is now an established procedure with outcome equivalent to ABO compatible KT. Lower dose of rituximab may reduce the infectious risk associated with rituximab as well as the cost.

**Methods:** Conventional dose(375mg/m²) of rituximab was used initially, the dose halved subsequently, and recently 100mg/body dose was used. Pretransplant plasmapheresis aimed anti-ABO titer at ≤8 on transplant day, but patients with higher(≥16) titer whose antibody could not be lowered to target on transplant day were also allowed to transplant. Posttransplant preemptive plasmapheresis during 2 weeks was not done routinely but as needed in patients with higher antibody titer or increase in creatinine while awaiting biopsy result. The immunosuppressive regimen other than rituximab was not different between ABO compatible and incompatible patients.

**Results:** A total of 58 ABO and 191 ABO compatible KT was done since Feb. 2007. Median follow up was 23(2-57) months. Minimal dose (100mg/body) of rituximab was used in 35 patients. There was 3 clinical acute AMR (2 in minimal dose and 1 in high dose group) in ABO compatible and 7 in ABO compatible KT patients. The duration of the depletion of peripheral CD19+ cells and the incidence of serious infection among patients with different dose of rituximab was comparable. In ABO KT patients, 2 grafts were lost due to incompatibility and interstitial nephritis. Patient and graft survival of ABO patients at 3 years is 100% and 94%, respectively. Patient and graft survival of ABO compatible patients was 96.5% and 96.4%, respectively (p=NS).

**Conclusions:** ABO KT with minimal dose of rituximab can be performed with excellent outcome, safety and reduced cost.

**MO044 VITAMIN D STATUS PREDICTS REJECTION EPISODES AND CHANGE IN ALLOGRAFT KIDNEY FUNCTION OVER TIME IN KIDNEY TRANSPLANT RECIPIENTS**

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**Introduction and Aims:** Vitamin D has potential immunomodulatory effects, but is often inadequate or deficient in kidney transplant recipients. Therefore, we evaluated whether vitamin D status affects the allograft outcomes.

**Methods:** We examined 271 renal allograft recipients in a prospective cohort followed up from August 2007 to June 2011. Outcomes of interest were time to rescue treatment for rejection episodes, annual eGFR change, and the composite event of death, 50% increase in serum creatinine, and end-stage renal disease. Multivariate and propensity score-based Cox proportional hazard models and robust linear regressions were used to estimate the effect of vitamin D status on the outcomes.

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**Results:** Mean age was 48.7 (SD, 12.3) years, 60.4% were male, and median 25-hydroxyvitamin D (25D) level was 15.8 (interquartile range, 12.4 to 20.8) ng/mL. Compared with vitamin D deficiency (<12 ng/mL), vitamin D inadequacy (≥12 and <20 ng/mL) and sufficiency (≥20 ng/mL) showed a dose-dependent association both with lower risk of rescue treatment (P for trend=0.004) and with the composite event (P for trend = 0.012). Serum 25D level showed an almost linear relationship with annual eGFR change in a multivariate regression with cubic spline functions. Propensity score matching analyses confirmed the associations of vitamin D status with these outcomes, independent of other potential confounders. Furthermore, vitamin D status showed more pronounced relationships in patients with less than 10 years since kidney transplantation (P for interaction <0.10), and serum 25D level was associated with more preserved eGFR over time (1.57 mL/min/1.73 m²/year per 10 ng/mL).

**Conclusions:** Vitamin D status predicts the kidney allograft outcomes. Sufficient vitamin D status may potentially improve the outcome of allograft kidneys through immunomodulatory effects.

**MO045 THE DISCREPANCY BETWEEN BIOLOGICAL AGE AND CALENDAR AGE: A LARGE HISTOLOGY STUDY IN IMPLANTATION BIOPSIES**

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**Introduction and Aims:** The histology and function of the kidney deteriorates with age. Replicative senescence caused by telomere shortening plays an important roll in this aging process (biological aging). The relationship between donor demographics, calendar age, telomere length and renal histology is currently unknown.

**Methods:** DNA was extracted from a blood sample in 160 deceased kidney donors who also had a baseline kidney allograft biopsy at time of transplantation. Telomere length was measured by real-time PCR in peripheral blood from donors, and the telomere-to-single copy gene (T/S) ratio was determined (T/S ratio is the proportional to the average telomere length in a cell). All baseline biopsies were rescored according to the current updated Banff classification. Donor demographics were recorded prospectively. The relationship between the individual histological lesions, donor demographics and telomere length was evaluated using SAS 9.3.

**Results:** Mean T/S ratio of telomere length was 1.1±0.53. Mean donor calendar age was 47.6±14.0. 35.6% of donors died from stroke, and 32.1% were extended criteria donors. Telomere length in peripheral blood correlated highly significantly with donor calendar age (r=-0.3; p=0.0002), which is concordant with previous literature data. Older donor calendar age was highly significantly associated with baseline histology of interstitial fibrosis, tubular atrophy and glomerulosclerosis (all p<0.01). Although there was a significant correlation between donor calendar age and telomere length T/S ratio, there was no association between the histological appearance of the baseline biopsy and telomere length. None of the other donor demographic variables (i.e. donor gender, cause of death, hypertension, smoking) correlated with telomere length in donor peripheral blood. Donor cardiovascular risk factors associated significantly with arteriolar hyalinosis and vascular intimal thickening, but did neither associate with donor calendar age nor with telomere length T/S ratio. This dichotomy between calendar-age associated renal histological lesions and cardiovascular risk-associated lesions was confirmed by principal component analysis.

**Conclusions:** Calendar age and cardiovascular risk determine renal histological damage, but biological aging and telomere shortening do not associate with histological damage of renal tissue. The current study suggests that biological aging in itself does not lead to alterations in renal histology. Additional studies that evaluate the senescent phenotype (micro-array gene expression and immunohistochemistry) of baseline biopsies before kidney transplantation are underway, to investigate this unexpected finding.
CKD PATHOPHYSIOLOGY AND COMPLICATIONS

MO050

THE ENDO THEIAL GL YOCAL YX AND NA+ AND FLUID OVERLOAD IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Dialysis patients have loss of glycocalyx barrier properties and increased levels of its constituents in blood. The endothelial glycocalyx is a negatively charged mesh of glycoproteins, proteoglycans and glycosaminoglycans lining the luminal side of blood vessels. It is able to reversibly bind positively charged sodium ions from circulation and might act as a sodium buffer. As a consequence, a reduction in the negatively charged components of the glycocalyx might result in an alteration in its sodium buffering capacity. Our aim was to investigate the role of the endothelial glycocalyx in sodium and fluid overload in hemodialysis patients.

Methods: Investigations were performed in 23 stable hemodialysis patients. We performed Sidestream darkfield (SDF) imaging of the sublingual blood vessels using a videomicroscope. The status of endothelial glycocalyx in individual blood vessels was assessed using specific ELISA’s. The following parameters were recorded: the amount of ultrafiltration, the difference in weight and blood pressure before and after the dialysis session, sodium levels in blood and dialysate. Hemodynamic stability was defined as a drop in systolic blood pressure of less than 20 mmHg after a dialysis session.

Results: The perfused boundary region and perfused diameter, as measured by SDF imaging, were 3.5 (3.3-3.9) m and 17.8 (17.4-18.9) m. Serum levels of hyaluronan and syndecan-1 were 36.8 (18.2-70.1) ng/ml and 111.0 (75.2-145.0) ng/ml. Serum levels of syndecan-1 positively correlated with the amount of ultrafiltration (p=0.03, r=0.43). In anuric patients, hyaluronan levels inversely correlated with the amount of ultrafiltration (p=0.01, r=-0.59), with the difference in weight before and after dialysis (p=0.01, r=-0.6), and correlated positively with the time on dialysis (p=0.02, r=0.53). The syndecan-1 levels were positively correlated with the perfused diameter (p=0.02, r=0.52). There was no significant difference with regard to any of the study parameters between hemodimetrically stable and unstable patients.

Conclusions: Our results suggest a relationship between the serum levels of glycocalyx constituents and the amount of ultrafiltration. Some of the negatively charged glycosaminoglycans might maintain their ability to bind sodium even when shed from the vascular wall into circulation.

MO051

HEMODIALYSIS REDUCES THE CALCIFICATION PROPENSITY OF SERUM

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Introduction and Aims: Vascular and soft tissue calcification is a major cause of death in hemodialysis (HD) patients. We have developed an in vitro test, which measures serum calcification propensity by detecting the spontaneous transformation of colloidal primary calciprotein particles (CPPs) to crystalline secondary CPPs. The effect of hemodialysis on serum calcification propensity has not been determined yet.

Methods: The intrinsic calcification propensity of pre- and post-HD sera obtained from 98 prevalent HD patients were analyzed with our novel nephelometry test. Calcium, phosphate, magnesium, fetuin-A, albumin, and total protein concentrations were related to the test results and integrated into a multivariate model with stepwise selection.

Results: HD treatment reduced serum calcification propensity by delaying transformation time (T50: pre-HD 244 ± 112 min, post-HD 340 ± 114 min, p < 0.0001) and reducing precipitate intensity (relative nephelometric units, RNU50: pre-HD 6892 ± 2404, post-HD 5234 ± 1789, p < 0.0001). A multivariate model showed, that the T50 of pre-HD sera depended mainly on magnesium (transformation
Results: In conclusion, cholecalciferol treatment improves ventricular diastolic and left atrial function in chronic dialysis patients. The effect on ventricular function was not related to changes in blood pressure since response in 24-h BP and cBP were not different between groups.

Conclusions: HD vastly improves the intrinsic calcification propensity of patient sera, with phosphate, magnesium and fetaun-A as major influencing factors. Monitoring serum-inherent calcification propensity may help improve morbidity and mortality of HD patients in the future.

**MO054** SODIUM GRADIENT AND MORTALITY IN HEMODIALYSIS PATIENTS: 5 YEAR FOLLOW-UP ANALYSIS

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Introduction and Aims: Sodium gradient (diolysate sodium minus predialysis plasma sodium) is a potentially important factor to improve clinical outcomes in chronic hemodialysis (HD) patients: However, its role is not well studied. The aim of this study was to elucidate the association between sodium gradient and mortality in HD patients treated in our department.

Methods: We studied a cohort of 261 prevalent HD patients (mean age at beginning of HD 49.69±15.59 years, mean HD vintage 99.54±72.15 months, diabetes 17.2%) receiving thrice-weekly HD treatment. We examined biochemical parameters, echocardiography measures and details of the dialysis prescription. The number of serum sodium measurements available per patient was a minimum 12. All the patients were dialyzed with a standard dialysate sodium of 140mEq/L. The patients were stratified by sodium gradient in three groups (sodium gradient > 2mEq/L, between 2mEq/L to - 2mEq/L and > -2mEq/L). We found a negative correlation between sodium gradient and age and pulse pressure, and positive correlation with treatment time, ultrafiltration and interdialytic weight gain. Patients with sodium gradient > 2mEq/L, between 2mEq/L to -2mEq/L and > -2mEq/L are significantly different with age (49.74 ± 14.92 years; 42.05 ± 18.71; 52.35 ± 12.86; P<0.02), treatment time (3.99 ± 0.18 hours; 4.05 ± 0.10; 3.91 ± 0.25; P<0.004), ultrafiltration (3.49 ± 0.92 l; 3.09 ± 0.78; 2.96 ± 0.83; P=0.028), interdialytic weight gain (5.56 ± 1.37 %; 4.96 ± 1.21; 4.46 ± 1.25; P<0.000), predialysis sodium levels (136.63 ± 0.86 mmol/L; 140.26 ± 1.01; 142.94 ± 0.95; P=0.000) and left atrial function in chronic dialysis patients. The effect on ventricular function was not related to changes in blood pressure since response in 24-h BP and cBP were not different between groups.

Conclusions: This study showed that a sodium gradient between 2 mEq/L to -2mEq/L was associated with lower all-cause mortality in HD patients. Prospective studies investigating sodium gradient on clinical endpoints are therefore indicated.
**LUPUS NEPHRITIS**

**MO055** THE INFLAMMASOME-RELATED MOLECULES NLRP3 AND ASC SUPPRESS LUPUS NEPHRITIS OF C57BL/6lpr/lpr MICE

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**Introduction and Aims:** NLRP3/ASC inflammasome signaling translates infectious and sterile dangers into the secretion of mature IL-1β and IL-18 and subsequently into IL-1R8-dependent secretion of multiple pro-inflammatory cytokines. We hypothesized that the NLRP3/ASC inflammasome would contribute in a similar manner to autoimmune tissue inflammation, e.g. to immune complex glomerulonephritis in systemic lupus erythematosus, i.e. lupus nephritis.

**Methods:** To address this question we generated Nlpr3- or Asc-deficient C57BL/6-lpr/lpr mice, the latter being a model of spontaneous SLE-like autoimmunity.

**Results:** Surprisingly, Nlpr3- and Asc-deficient C57BL/6-lpr/lpr mice displayed an aggravated autoimmune phenotype with massive lymphoproliferation, severe crescentic immune complex glomerulonephritis, and autoimmune lung disease, which are usually absent in C57BL/6-lpr/lpr mice. Immune phenotyping revealed that both Nlpr3- and Asc-deficiency both shifted lymphocyte apoptosis to lymphocyte necrosis, which induced multiple pro-inflammatory elements and suppressed negative regulators of innate immunity such as NLRP1a, NLRP2, NLRP6 and NLRP12. Lymphocyte necrosis and innate immune activation were associated with the expansion and activation of spleen dendritic cells, macrophages, T cells, and B cells.

**Conclusions:** Together, Nlpr3- or Asc-deficiency both aggravate autoimmunity and autoimmune tissue injury in lupus-prone C57BL/6-lpr/lpr mice. This reveals an unexpected immunosuppressive role of NLRP3 and ASC in this context, which may to relate to a previously unknown role of NLRP3 and ASC for preventing lymphocyte necrosis, which exposes additional lupus autoantigens and drives the autoimmune process. These data identify both Asc and Nlpr3 as previously unknown SLE susceptibility genes in mice.

**MO056** TREATMENT WITH HUMAN LEUKOCYTE ANTIGEN (HLA-G) ATTENUATES PROGRESSION OF LUPUS NEPHRITIS IN MRL-lpr/lpr MICE

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**Introduction and Aims:** Human leukocyte antigen (HLA)-G is a nonclassical HLA class I molecule that has tolerogenic functions and acts on cells of both innate and adaptive immunity. HLA-G interacts with PIR-B expressed on mouse leukocytes especially on B cells, dendritic cells (DCs) and macrophages. Administration of microbeads coated with HLA-G-β2m absorbed on microbeads will improve renal inflammation by inhibiting DCs maturation and B1 cells activation in MRL/lpr mice.

**Methods:** We injected microbeads coated with HLA-G-β2m (2microgram/week/mouse) for 10 wks starting from week 12 of age. Microbeads without HLA-G-β2m were injected as vehicle control. Plasma samples were drawn two weeks after initiation of treatment and at the end of the study. Urine samples, tissue samples were collected at the end of the treatment period. Kidney tissues were processed for histological analysis. Various lymphocyte subsets were analyzed by FACS from spleen and kidney. Part of the isolated tissue was used for the expression analysis of RT-PCR.

**Results:** HLA-G treatment attenuated lupus nephritis, determined by the activity and chronicity index of histomorphological damage. HLA-G treatment improved renal function as demonstrated by serum BUN levels in the plasma. HLA-G treatment reduced the intra-renal accumulation of CXCR3 positive T cells. IL-17 and IFN-γ-producing T cells were also reduced in the kidney significantly in the HLA-G treated group. Infiltration and activation of dendritic cells (CD11c+MHCII+) and macrophages (F4/80+MHCII+) (analyzed by FACS) as well as expression of pro-inflammatory mediators in the kidney was significantly reduced by HLA-G treatment. Plasma levels of rheumatoid factor, IL-12p40, TNF-α and IL-17 were significantly reduced by the treatment. HLA-G treatment did not have any significant effect on the leukocytes subsets in the spleen and on the autoantibody production. HLA-G suppress the production of IL-12p40 by bone marrow derived dendritic cells stimulated with TLR ligands.

**Conclusions:** HLA-G treatment inhibited accumulation and activation of dendritic cells in the kidney and significantly attenuated the progression of lupus nephritis in MRL/lpr mice.

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**MO057** DETERMINATION OF URINARY TWEAK/FN14 mRNA AS A BIOMARKER OF LUPUS NEPHRITIS ACTIVITY

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**Introduction and Aims:** Lupus nephritis (LN) is a major cause of morbidity and mortality of systemic lupus erythematosus (SLE). Recent studies suggested that TWEAK/Fn14 pathway is involved in the pathogenic processes of LN. Quantification of TWEAK mRNA (mRNA) and Fn14 mRNA in urine is emerging as a noninvasive method of screening LN-associated biomarkers. This study was designed to observe the urinary mRNA profile of TWEAK/Fn14 in patients with lupus nephritis (LN) and to identify new biomarker of lupus nephritis activity.

**Methods:** Thirty one lupus patients with active lupus nephritis or without renal lesion were included in this study. Ten healthy volunteers were served as control. Lupus activity was assessed by the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). Urinary mRNA expression of TWEAK and Fn14 and monocyte chemotactic protein-1 (MCP-1) was studied by real-time quantitative polymerase chain reaction.

**Results:** The urinary mRNA levels of all genes studied were significantly higher in the LN group compared with non-LN group and controls (p<0.05). Urinary mRNA levels of all target genes positively correlated with 24h urinary proteins. SLE disease activity index (SLEDAI) and serum anti-double stranded DNA (anti-dsDNA) antibodies. The expression of TWEAK, Fn14, and MCP-1 mRNA correlated with 24h urinary proteins (r = 0.622, p = 0.001; r = 0.5289, p = 0.002; r = 0.442, p = 0.013, respectively). The expression of TWEAK, Fn14, and MCP-1 mRNA correlated with SLEDAI (r = 0.719, p = 0.001; r = 0.612, p = 0.001; r = 0.568, p = 0.001, respectively). The expression of TWEAK, Fn14, and MCP-1 mRNA correlated with anti-dsDNA (r = 0.651, p = 0.001; r = 0.651, p = 0.001; r = 0.417, p = 0.02, respectively). Furthermore, TWEAK mRNA was found to positively correlate with Fn14 and MCP-1 mRNA (r = 0.871, p < 0.0001; r = 0.561, p<0.001).

**Conclusions:** The urinary mRNA profiles of TWEAK, Fn14, and MCP-1 may served as novel biomarkers of active lupus nephritis.

**MO058** ANTIBODIES AGAINST MONOMERIC CRP - A PROMISING BIOMARKER OF LUPUS NEPHRITIS?

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**Introduction and Aims:** Autoantibodies against monomeric CRP (anti-mCRP Abs) have been recently found in patients with systemic lupus erythematosus (SLE), especially with renal involvement. The goal of the study was to verify the presence of these Abs in correlation with clinical activity of the disease and manifestation of active lupus nephritis (LN).

**Methods:** The study included 104 patients (pts) diagnosed with SLE (75 with LN and 29 with non-renal flare), 31 pts with primary glomerulonephritis and 31 healthy volunteers. The total of 290 blood samples from 166 people aged 19 to 86 years (mean 40.76±14.06) were analyzed. Immunological and clinical disease activity indicators such as complement haemolytic activity, antinuclear (ANA) and anti-dsDNA Abs, serum creatinine, daily proteinuria, white blood cells (WBC) count were measured using commercially available tests. Disease activity was estimated by SLE Disease Activity Index (SLEDAI). The presence of anti-mCRP Abs was tested with the use of in-house ELISA. Each sample was measured in quadruplicate, the specific absorbency value was normalized with 100% assigned to reference high anti-mCRP SLE serum value and the results were averaged.

**Results:** LN class II was diagnosed in 4 pts, III in 9 pts, IV in 33 pts, IV/O in 7 pts and V in 8 pts. Positive anti-mCRP Abs were observed in 160 blood samples (55.17%) with a significant association with renal involvement (p <0.0001). 66.4% of blood samples from patients with LN were anti-mCRP positive, in contrast to 45%, 19% and 35% of samples
from pts with non-renal lupus, primary glomerulonephritis and healthy volunteers, respectively. The highest titers of anti-mCRP Abs occurred among patients with LN, but there was no correlation with the severity of nephropathy measured by the size of daily proteinuria. Regression analysis showed that the diagnosis of LN class V significantly (p = 0.0089) increased the likelihood of positive anti-mCRP Abs (87% positive in LN class V vs 71%, 59%, 64%, 57% in class II, III, IV, IV/V, respectively). The levels of anti-mCRP Abs were significantly higher in class V LN compared to the other groups (p <0.0001). Anti-mCRP Abs were positively correlated with SLEDIAI index (p=0.023), antinuclear Abs (p<0.0001) and anti-dsDNA Abs (p<0.0001) and negatively with WBC count (p= 0.005) and complement haemolytic activity (p<0.0001).

Conclusions: The study confirmed that anti-mCRP Abs may be a potential biomarker of renal involvement in SLE patients. Although Abs levels correlate with classical activity indicators, there was no correlation with the severity of nephropathy measured by the size of daily proteinuria. However the highest prevalence in membranous lupus nephritis highlights the promising role of anti-mCRP Abs as a biomarker of histopathological changes in the glomeruli.

MO059 IMMUNOADSORPTION IN LUPUS NEPHRITIS: THREE DIFFERENT HIGH AFFINITY COLUMNS ARE EQUALLY EFFECTIVE IN INDUCING REMISSION

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Introduction and Aims: Pathogenic autoantibodies and immune complexes are a hallmark of SLE. They can effectively be removed by extracorporeal procedures such as immunoadsorption (IAS). We previously reported that IAS performed with columns using sheep IgG as ligand (Ig-Therasorb®) reduces proteinuria, global disease activity and pre-treatment dsDNA levels in highly active lupus nephritis (Stummvoll 2005). Meanwhile, three different high-affinity IAS columns using different adsorbing ligands are in use for lupus patients. We now attempted to answer the question which column should be preferred in the treatment of (a) active, refractory lupus nephritis and for (b) maintenance therapy once disease activity has been reduced.

Methods: We analyzed all patients with histologically proven lupus nephritis (n=26) and analyzed the effects of 3 months of IAS on global disease activity and renal outcome. All patients presented with contraindications or refractoriness to standard cyclophosphamide and/or mycophenolic acid therapy. Patients were grouped according to the column used: (i) IgG-group (Ig-Therasorb®, n=16), (ii) ProtA-group (Immunosorba®, n=5), and (iii) Gam-group (Globaffin®, n=5). When low/moderate disease activity was achieved, 8 patients were switched from IgG to either ProtA (n=6) or Gam (n=2) while the rest of the therapy and the IAS protocol was kept constant.

Results: All columns significantly lowered serum levels of IgG, IgM, and anti-dsDNA. Serum-creatinine decreased from 1.7, 2.1 and 1.9 mg/dl respectively to near-normal range after three months of treatment. Proteinuria significantly decreased in all groups to 48% 60% and 64% respectively, while serum-albumin increased accordingly. All groups presented with comparably high disease activity scores (SIS, SLEDAI) at the start of IAS and achieved a significant reduction of overall disease activity and a steady increase in serum complement levels. No severe adverse event (allergic reaction, critical hypotension) occurred. In stable, low/moderately active patients a column-switch from IgG to either ProtA or Gam did not affect parameters of renal function or global disease activity.

Conclusions: Immunoadsorption reduces serum-creatinine, proteinuria and disease activity in highly active, refractory lupus nephritis, leading to improved renal function. In our retrospective analysis, no column offered clear advantages, neither during induction nor for maintenance therapy. Thus, it is primarily not the type of the ligand, but the successful removal of autoantibodies that is pivotal for reducing SLE activity. Our findings may facilitate future attempts for randomized controlled trials on IAS in lupus nephritis.
Introduction and Aims: Aberrant calcium signaling has been implicated in many scenarios of kidney disease and glomerular damage. Gain of function mutations in TRPC6 calcium channels can lead to alterations in proper podocyte morphology and the loss of integrity in the glomerular filter leading to proteinuria. Additionally, increases in intracellular calcium in the podocyte occur under other non-genetic insults such as blood pressure elevation, bacterial infection, and trauma. The protein phosphatase calcineurin is activated when cytoplasmic calcium levels rise, and our group has previously demonstrated that constitutive activation of calcineurin leads to a rearrangement of the podocyte actin cytoskeleton and subsequent proteinuria in mice. However, to date, calcineurin's canonical downstream target, the transcription factor nuclear factor of activated T-cells (NFAT), has not been well characterized for its role in podocytes.

Methods: We have generated a transgenic mouse model for the podocyte-specific, doxycyclin (Dox)- inducible expression of a constitutively active NFAT mutant form (NFATc1nuc).

Results: Mice develop profound proteinuria within four days of Dox exposure and partial podocyte foot process (FP) effacement. Prolonged NFATc1nuc expression for up to four months produced sustained proteinuria accompanied by an increase in the effaced FP area, but in the absence of any other histological changes within the glomerulus or the tubulointerstitium. This phenotype is reminiscent of the pathology seen in patients with Minimal Change Disease (MCD). Animals that are left on constant Dox treatment for 12 months develop histological changes consistent with Focal Segmental Glomerulosclerosis (FSGS) accompanied by impaired renal function.

Conclusions: Furthermore, our preliminary data show that proteinuria in mice with short-term NFATc1 activation in podocytes is reversible, whereas mice with NFATc1nuc expression for two months are unable to revert to normal podocyte morphology and glomerular filter function once Dox is removed and normal Chow is re-introduced. These findings indicate that NFATc1nuc mice have a two-phase renal phenotype, first with MCD-like alterations that are reversible, followed by a later irreversible period that resembles FSGS-like changes. Future experiments aim to determine the precise "point of no return", and to study, if the phenotypic switch from a MCD-like to an FSGS-like phenotype occurs in concert with podocyte proteinuria. We postulate that direct NFAT target genes are responsible for early phenotypic changes, whereas later irreversible alterations are induced by epigenetic mechanisms including differences in histone modifications.

MO060

TIME DEPENDENT PODOCYTE SPECIFIC NFAT ACTIVATION MEDIATES BETWEEN MCD LIKE AND FSGS LIKE PHENOTYPES

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MO062

PAN-GENOMIC BINDING OF HYPOXIA-INDUCIBLE TRANSCRIPTION FACTORS IN RENAL CANCER CELLS

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Introduction and Aims: Renal cell cancer (RCC) accounts for more than 100,000 deaths per year worldwide. The great majority of cases are clear cell (ccRCC) and are associated with inactivation of the von Hippel-Lindau (VHL) tumor suppressor in renal tubular cells and consequent activation of the HIF transcriptional cascade, raising fundamental questions as to how the HIF pathway contributes to ccRCC. Gene transfer and knock-down studies point to a role for HIF-2, but not HIF-1, in the progression of ccRCC xenografts. However, so far, there has been little knowledge of direct transcriptional targets of the HIFs in renal cancer cells.

Methods: To define the genomic environment of HIF-binding and genes directly under control of HIF-2 in renal cancer cells, we have undertaken genome-wide analyses of HIF-DNA-binding in VHL-defective RCC cells using chromatin immunoprecipitation coupled to high throughput sequencing. Using gene set enrichment analysis high stringency HIF-binding sites were correlated with the transcriptional response to HIF-2 knock down in VHL-defective 786-O renal cancer cells and to hypoxia in 786-O cells re-expressing functional VHL. Furthermore, HIF-binding sites were intersected with the transcription levels of genes in matched samples of renal cancer and control tissue.

Results: We could identify 608 high stringency HIF-2-binding sites in 786-O renal cancer cells. HIF-2 binding was observed frequently at promoter distant sites. HIF-2 binding strongly correlated with upregulation of gene expression induced by HIF or hypoxia. Importantly, the association was independent of the distance of the HIF-binding site to the regulated gene. This implies that promoter distant HIF-binding is functional and occurs most likely at enhancers of gene transcription. Furthermore, HIF-binding sites in 786-O cells were strongly associated with genes deregulated in renal cancer tissue providing further evidence for a direct role of HIF-2 in renal cancer. In addition, this analysis has identified a HIF-2 binding site which is in high linkage disequilibrium with a RCC associated polymorphism on chromosome 11 recently identified by GWAS. This site physically associates with the promoter of CCND1, an established oncogene, and is unique to VHL-deficient ccRCC cells indicating that it acts as a renal cancer-specific long range enhancer of cyclin D1 transcription.

Conclusions: This work defines genome-wide HIF-binding in renal cancer cells and identifies HIF as an activator of gene transcription. Specific analysis of a HIF-binding site at the CCND1 locus exemplifies the importance of the HIF-system in renal cancer development. Further analysis of HIF-binding in normal renal tissue versus renal cancer provides a promising approach to identify key regulators of the physiologic HIF response and factors involved in tumour development.

MO063

THE ANTI-AGING GENE KLOTHO ACTS AS A TUMOR SUPPRESSOR IN RENAL CELL CARCINOMA (RCC) AND REPRESENTS A POTENTIAL PREDICTIVE MARKER OF METASTASIS

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Introduction and Aims: RCC accounts for about 3% of adult malignancies, with clear cell RCC (ccRCC) representing the most common histological subtype and having a high metastatic index. The identification of new biomarkers in ccRCC is important to stratify patients (pts) into prognostic risk groups and guide future therapy decisions. The renoprotective antiaging gene Klotho has been recently found to work as a tumor suppressor in different human cancers but no data are reported in RCC. Aim of our study was to evaluate Klotho expression in tissue and serum of RCC pts and correlate it with disease progression.
Abstracts

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MO064 DEREGULATED MiRNAs IN RENAL CELL CARCINOMA: DIAGNOSTIC POTENTIAL, CHROMOSOMAL DISTRIBUTION, PUTATIVE GENE TARGETS AND MOLECULAR PATHWAYS IN WHICH THEY ARE IMPLICATED

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Introduction and Aims: Renal cell carcinoma (RCC) is composed of various distinct subtypes, the most prevalent of which are clear cell (ccRCC), papillary (papRCC) and chromophobe (chRCC). MicroRNAs (miRNAs) are small non-coding RNAs of approximately 22 nt size, and modulate differentiation, growth, apoptosis and proliferation of cells. More than 50% of miRNA genes are located in cancer-associated genomic regions or in fragile sites, frequently amplified or deleted in human cancer. Recognition of miRNAs that are differentially expressed (DE) between RCC and normal tissue may help to identify those miRNAs that are involved in this human malignancy.

Methods: MiRNA profiling was performed on 28 FFPE tissues of ccRCC, chRCC, papRCC and 20 normal cases. Results of DE miRNAs were validated using qRT-PCR and in-situ hybridization (ISH). The ability to discriminate between RCC subtypes and normal samples was characterized by ROC curves. The chromosomal distribution of the DE miRNAs was detected and compared with reported genomic alterations in each subtype. The miRNA targets were predicted using miRWalk. Enriched gene sets were grouped in functional categories by IPA and GO analysis.

Results: We identified 434 DE miRNAs in all kidney tumours and built a molecular signature that accurately classified RCC subtypes among them. Ten miRNAs (miR-10b-5p, miR-1257, miR-1303, miR-23c, miR-3171, miR-4270, miR-514b-3p, miR-515-5p, miR-620 and miR-98) were co-deregulated among RCC subtypes, whereas 270 miRNAs were identified uniquely in ccRCC, 33 in papRCC and 5 in chRCC, respectively. The expression of the most DE miRNAs was validated using qRT-PCR. The miRNAs exhibited deregulation patterns that agreed with previously reported chromosomal gains and losses, in each subtype. mRNA for miR-25-5p revealed that its differential expression is cancer-cell associated. The top Canonical pathways of the putative gene targets of the deregulated miRNAs, included Molecular Mechanisms of Cancer (p=1.72E-04); PPARα/RXRα Activation (p=2.15E-03); Bladder Cancer Signaling (p=3.57E-03); Cell Cycle: G1/S Checkpoint Regulation (p=5.37E-03) and Estrogen-mediated S-phase Entry (p=6.25E-03). The major gene networks and their associated functions included Tissue Development, Cancer; Tumor Morphology, Cellular Movement; Cell Cycle, Cellular Growth and Proliferation, Cellular Development; and Cell Death and Survival, Tumor Morphology, Cell Morphology, VHL, HIF1A, EPAS1, SMARCB1, TP53 and PAWR constituted the most central nodes in these networks.

Conclusions: Our comprehensive study highlights the dynamic role of miRNAs in the three most common renal cell carcinoma subtypes.

Methods: We used a genome wide screening of the human exons expressed in 11 ccRCC vs paired adjacent non-tumoral renal tissue by microarray. Genes with an FDR<5% and f.c.≥2 were considered to be differently expressed. Klotho expression in tumor tissue of RCC pts, including primitive and metastatic pts, was studied using quantitative RT-PCR and immunohistochemistry. The soluble serum Klotho levels were titrated in 35 primitive RCC, 25 metastatic RCC and 40 samples including non urogenital cancers and healthy donors, by a sandwich ELISA. Comparisons of variables among different groups were performed by Student’s t-test and Mann-Whitney U-test. Frequencies were compared by chi-squared test. Kaplan-Meier estimates were used to generate overall patient survival curves and differences were assessed by log-rank test.

Results: Ingenuity pathway analysis revealed a set of genes modulated in ccRCC, associated with inflammatory response, cancer and renal disorders. Among them, Klotho was strongly down-regulated in all ccRCC (f.c.: -41.9, p=0.0007) respect to paired normal renal tissue (NT), Klotho mRNA reduction in RCC when compared to NT was also confirmed by RT-PCR (p=0.04). Also at protein level, Klotho significantly decreased in metastatic RCC respect to primitive RCC sera (p<0.001). This trend was also observed in serum samples, where circulating Klotho significantly decreased in RCC metastatic RCC than primitive RCC (44.3±15 domestic 77.3±9.2, p<0.03). This trend was also confirmed by RT-PCR (p=0.04). Also at protein level, Klotho significantly decreased in metastatic RCC than primitive RCC (44.3±15 vs 77.3±9.2, p<0.03). This trend was also observed in serum samples, where circulating Klotho significantly decreased in RCC metastatic RCC than primitive RCC (44.3±15 vs 77.3±9.2, p<0.03). This trend was also observed in serum samples, where circulating Klotho significantly decreased in RCC metastatic RCC than primitive RCC (44.3±15 vs 77.3±9.2, p<0.03). This trend was also observed in serum samples, where circulating Klotho significantly decreased in RCC metastatic RCC than primitive RCC (44.3±15 vs 77.3±9.2, p<0.03). This trend was also observed in serum samples, where circulating Klotho significantly decreased in RCC metastatic RCC than primitive RCC (44.3±15 vs 77.3±9.2, p<0.03). This trend was also observed in serum samples, where circulating Klotho significantly decreased in RCC metastatic RCC than primitive RCC (44.3±15 vs 77.3±9.2, p<0.03). This trend was also observed in serum samples, where circulating Klotho significantly decreased in RCC metastatic RCC than primitive RCC (44.3±15 vs 77.3±9.2, p<0.03). This trend was also observed in serum samples, where circulating Klotho significantly decreased in RCC metastatic RCC than primitive RCC (44.3±15 vs 77.3±9.2, p<0.03). This trend was also observed in serum samples, where circulating Klotho significantly decreased in RCC metastatic RCC than primitive RCC (44.3±15 vs 77.3±9.2, p<0.03). This trend was also observed in serum samples, where circulating Klotho significantly decreased in RCC metastatic RCC than primitive RCC (44.3±15 vs 77.3±9.2, p<0.03). This trend was also observed in serum samples, where circulating Klotho significantly decreased in RCC metastatic RCC than primitive RCC (44.3±15 vs 77.3±9.2, p<0.03). This trend was also observed in serum samples, where circulating Klotho significantly decreased in RCC metastatic RCC than primitive RCC (44.3±15 vs 77.3±9.2, p<0.03). This trend was also observed in serum samples, where circulating Klotho significantly decreased in RCC metastatic RCC than primitive RCC (44.3±15 vs 77.3±9.2, p<0.03). This trend was also observed in serum samples, where circulating Klotho significantly decreased in RCC metastatic RCC than primitive RCC (44.3±15 vs 77.3±9.2, p<0.03). This trend was also observed in serum samples, where circulating Klotho significantly decreased in RCC metastatic RCC than primitive RCC (44.3±15 vs 77.3±9.2, p<0.03). This trend was also observed in serum samples, where circulating Klotho significantly decreased in RCC metastatic RCC than primitive RCC (44.3±15 vs 77.3±9.2, p<0.03). This trend was also observed in serum samples, where circulating Klotho significantly decreased in RCC metastatic RCC than primitive RCC (44.3±15 vs 77.3±9.2, p<0.03). This trend was also observed in serum samples, where circulating Klotho significantly decreased in RCC metastatic RCC than primitive RCC (44.3±15 vs 77.3±9.2, p<0.03). This trend was also observed in serum samples, where circulating Klotho significantly decreased in RCC metastatic RCC than primitive RCC (44.3±15 vs 77.3±9.2, p<0.03). This trend was also observed in serum samples, where circulating Klotho significantly decreased in RCC metastatic RCC than primitive RCC (44.3±15 vs 77.3±9.2, p<0.03).
**GLOMERULAR INJURY**

**TOC007** **MACROPHAGE MIGRATION INHIBITORY FACTOR (MIF) - A NOVEL ENDORGANOUS FIBROSIS LIMITING FACTOR**

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Introduction and Aims: Macrophage migration inhibitory factor (MIF) is a pleiotherapy cytokine with chemokin-like functions, e.g. for macrophages. Experimental studies have almost unequivocally shown that MIF is pro-inflammatory and disease-aggravating in inflammatory diseases including experimental glomerulonephritis. Inhibition of MIF was envisaged as a novel therapeutic approach in these diseases. Surprisingly, we recently showed that MIF was antifibrotic in models of liver fibrosis, in particular via its receptor CD74. This finding prompted us to analyze the role of MIF in renal fibrosis.

Methods: We manipulated MIF using genetic deletion (Mif−/−mice), neutralization via MIF antibody (MIF-Ab) or a small molecule MIF inhibitor (ISO-1) and by application of murine recombinant MIF (mrMIF) in three different murine models of renal fibrosis: unilateral ureteral obstruction (UUO), unilateral ischemia/reperfusion induced fibrosis (I/R) and Alport mice. In addition, we investigated the consequences of genetic deletion of the MIF receptor CD74 (CD74−/−mice) in UUO induced fibrosis.

Results: In comparison to wild-type mice (WT), Mif−/−mice had more interstitial fibrosis and macrophage infiltrates in UUO (both day 5 and 10). Confirmatory, compared to isotype matched IgG, MIF-Ab treatment led to aggravated fibrosis and macrophage influx in UUO (day 5). On day 7 of UUO, compared to vehicle treated mice, ISO-1 increased renal fibrosis whereas application of mrMIF reduced fibrosis (even though both treatments were initiated on day 3 after UUO). Treatment with MIF-Ab significantly reduced mortality in Alport mice compared to IgG treated animals. Compared to WT mice, mice lacking the MIF receptor CD74 showed an increased interstitial fibrosis and macrophage influx in both UUO (day 5) and I/R (day 21), resembling the results of Mif−/−mice.

Conclusions: We show that MIF inhibition and CD74 deficiency aggravated whereas MIF application ameliorated renal fibrosis. We thus identified a hitherto unappreciated dual role of MIF in renal disease, which is pro-inflammatory in glomerular disease but antifibrotic in the interstitium.

**TOC008** **EXTRACELLULAR VESICLES DERIVED FROM ENDOTHELIAL PROGENITOR CELLS INHIBIT PROGRESSION TOWARD CHRONIC KIDNEY DISEASE AND FIBROSIS BY A RNA-DEPENDENT MECHANISM**

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Introduction and Aims: Endothelial progenitor cells (EPCs) are bone marrow-derived precursors with pro-angiogenic properties. A decrease of circulating EPCs in patients with chronic kidney disease (CKD) is associated with progression to end stage renal failure. EPCs exert their protective effect by the release of paracrine mediators including extracellular vesicles (EVs), small particles involved in cell-to-cell communication through the transfer of proteins and genetic material. The aim of this study was to evaluate the role of EPC-derived EVs in lowering progression toward CKD and fibrosis in the 5/6 nephrectomy rat model.

Methods: EPCs were isolated from peripheral blood and EVs were characterized for protein and RNA content. Wistar rats were subjected to 5/6 nephrectomy and treated at week 4 and 8 with infusion of 30 μg EPC-derived EVs treated with vehicle or 1U/ml RNase. Proteinuria, creatinine clearance and histology were evaluated at 14 weeks. In vitro, we studied the effects of EPC-EVs on human kidney-derived endothelial and tubular epithelial cells cultured with uremic toxins (p-cresyl-sulphate, indoxyl-sulphate, ADMA).

Results: EPC-EVs carried different mRNAs and microRNAs involved in angiogenesis, inhibition of apoptosis and fibrogenesis. Administration of EPC-derived EVs in rats subjected to 5/6 nephrectomy reduced proteinuria and preserved renal function with a limitation of histological signs of tubulo-interstitial fibrosis and glomerulosclerosis (decrease of α-SMA and ADMA-positive areas). Moreover, ETV-treated nephrectomized rats showed a preserved expression of podocyte (nephrin, synaptopodin) and tubular epithelial (E-cadherin, aquaporin-2) markers and a decrease of capillary rarefaction (RECA-1 staining). These protective effects were not observed when EVs were treated with RNase, suggesting the key role of RNAs shuttled by EVs. In addition, fibroblast-derived EVs did not exert renoprotection. In vitro, EVs induced proliferation, resistance to apoptosis and angiogenesis of kidney-derived endothelial cells incubated with uremic toxins. On tubular cells, EVs decreased de-differentiation, apoptosis and TGF-β secretion induced by uremic toxins. These effects were not observed when EVs were treated with RNase.

Conclusions: EPC-EVs demonstrated decreased proteinuria and lowered progression toward CKD in the 5/6 nephrectomy rat model. The mRNA and microRNA cargo shuttled by EVs to kidney endothelial and tubular epithelial cells protected from capillary rarefaction and progression toward renal fibrosis by inhibiting epithelial-to-mesenchymal transition.

**TOC009** **PARIENTAL PODOCYTES - TRANSDIFFERENTIATION FROM PARIETAL EPITHELIAL CELLS OR MIGRATION OF PODOCYTES?**

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Introduction and Aims: In adults, it is still unresolved whether parietal epithelial cells (PECs) can potentially act as progenitor cells by differentiating into podocytes. “Parietal podocytes”, i.e. fully differentiated podocytes residing on the inner aspect of Bowman’s capsule, are an interesting model in this context. Parietal podocytes have been observed in multiple human kidney diseases, in particular in atubular glomeruli.

Methods: First, a mouse model to generate atubular glomeruli by electrocoagulation was established and characterized in different genetic backgrounds. In addition, glomerular cysts were formed particularly in young mice of the Svi129 genetic background. Next, PECs or podocytes were traced in the above-described model for detubularization by irreversible genetic tagging in triple transgenic mice (PECF- or Pod-tTA/LCI/L26R). Our results showed conclusively that PECs undergo apoptosis after detubularisation and that visceral podocytes migrate onto Bowman’s capsule. No direct transdifferentiation from PECs towards podocytes was observed. This finding was confirmed in the unilateral ureter obstruction (UUO) model. Immunohistochemical stainings of human kidney biopsies always showed a sharpedged border between PECs and podocytes on Bowman’s capsule of atubular glomeruli. No gradual differentiation of PECs into podocytes could be observed, supporting that no transdifferentiation of PECs into podocytes occurred also in humans.

Conclusions: In summary, there are two surprising findings of this study: 1. Detubularisation leads to acute ablation of PECs and 2. visceral podocytes migrate onto Bowman’s capsule in atubular glomeruli. Transdifferentiation from PECs to parietal podocytes did not occur in this model.

**TOC010** **NECROTIC GLOMERULAR CELLS RELEASE HISTONES THAT TRIGGER GLOMERULAR INFLAMMATION AND CRESCENT FORMATION IN GLOMERULONEPHRITIS**

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Introduction and Aims: Extracellular histones, released from dying cells have the potential to kill endothelial cells and to activate Toll like receptor (TLR-2) and -4, which was shown to drives tubulointerstitial inflammation in septic or postischemic acute kidney injury. However, their contribution to glomerulonephritis is yet unknown. We speculated that extracellular histones elicited similar pathogenic effects also in glomerulonephritis.

Methods: C57BL/6 male mice were procured from Jackson Laboratories (Bar Harbour, MA). All experimental procedures were approved by the local government authorities. Glomerulonephritis was induced in mice with single intravenous injection of 100 μl of a sheep anti-GBM antiserum. Groups of mice were treated i.p. with either with 20 mg/kg of control IgG or anti-histone antibody (BWA3) that has the potential to neutralize the
effects of extracellular histones in vitro and in vivo. After 7 days animals were sacrificed and kidneys were collected for further data analysis by immunostaining, flow cytometry, ELISA and RT-PCR. Proteinuria was assessed as albumin to creatinine ratio in spot urine samples.

Results: Intravenous injection of antisera in control mice induced proteinuria, increased urinary albumin/creatinine ratio, plasma creatinine and BUN levels. This was associated with reduced number of podocytes, crescentic glomerulonephritis, and with infiltration of neutrophils and macrophages into the kidney. Anti-histone antibody treatment significantly reduced proteinuria and increased the numbers of WT-1/nephrin positive podocytes. This was associated with less glomerulosclerosis, crescents, and tubular atrophy.

Conclusions: We conclude that the release of histones from dying cells contribute to renal immunopathology and dysfunction during crescentic glomerulonephritis. This may either relate to their direct toxic effects on endothelial and epithelial cells or to their potential to activate innate immunity via TLR2 and TLR4.
LIPIDS AND OTHER RISK FACTORS

TO012 DYSFUNCTIONAL HIGH-DENSITY LIPOPROTEIN (HDL) IN CHRONIC KIDNEY DISEASE (CKD): A PROSPECTIVE OBSERVATIONAL TRIAL OF 3,306 PATIENTS

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Introduction and Aims: In healthy subjects, HDL-cholesterol (HDL) serum levels are inversely correlated with the rate of cardiovascular events. Recent studies revealed that under uremic conditions the vasoprotective properties of HDL may be altered by incorporation of serum amyloid A (SAA) in the HDL particle, resulting in reduced endothelial nitric oxide (NO) and an enhanced superoxide production. However, the clinical relevance of these findings remains unclear. We assessed the relationship between HDL levels and all-cause or cardiovascular mortality in a large cohort of patients undergoing coronary angiography.

Methods: The LURC study enrolled 3,306 patients between 1997 and 2000 undergoing coronary angiography. Patients were followed for median of 9.9 years. HDL and SAA levels were measured at inclusion. To assess the effect of HDL and SAA on all-cause and cardiovascular mortality, Cox regression analyses were performed. Patients were divided for SAA or HDL quartiles, respectively. Additionally, we determined the effect of increasing HDL concentrations on endothelial NO and superoxide production in presence of SAA by using electron-spin resonance spectroscopy.

Results: Patients with CKD (cystatin C eGFR ≤ 60 ml/min, n=474) exhibited significantly reduced HDL levels, while SAA levels were increased as compared to patients without CKD (n=2,832). In the whole study population, we identified increasing SAA levels as strong predictor for all-cause and cardiovascular mortality during follow-up. Interestingly, high HDL levels compensated for the adverse effect of SAA on mortality. Indeed, we confirmed that HDL ameliorated the effect of SAA on endothelial NO and superoxide production in vitro. However, this compensatory effect of HDL was dramatically reduced in CKD patients, indicating a loss of the vasoprotective effects of HDL. Therefore, we determined the effect of high HDL levels per se on mortality. High HDL levels significantly reduced the risk for all-cause (HR 0.743, p=0.012) and cardiovascular (HR 0.683, p=0.013) mortality in patients without CKD. In marked contrast, higher levels of HDL did not significantly reduce the risk for all-cause and cardiovascular mortality during follow-up in patients with eGFR ≤ 60 ml/min (HR 1.003, p=0.986 and HR 0.925, p=0.705).

Conclusions: These results show for the first time that HDL loses its vasoprotective properties in patients with CKD compared to those without CKD. Moreover, we were able to demonstrate that higher HDL levels do not reduce the risk for all-cause and cardiovascular mortality in CKD patients. These findings underscore the relevance of HDL as an important factor in pathogenesis of atherosclerotic disease in patients with CKD.

TO013 FEBOXOSTAT IMPROVES GFR AND BP IN NON-DIABETIC ADULTS WITH CKD 2-3

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1Nephrology and RRT Dept. National Medical Academy of Postgraduate Education named P. Shupyk Kiev Ukraine, 2Pathology Dept. National Medical University named by O. Bogomolets Kiev Ukraine

Introduction and Aims: Asymptomatic elevated uric acid levels are frequent in CKD. Lowering uric acid with allopurinol improves GFR, BP, and might decrease cardiovascular events in CKD patients. The aim of the study was to investigate the influence of febuxostat on GFR and BP in non-diabetic patients with CKD 2-3 with mild hypertension and no history of gout.

Methods: 56 patients with asymptomatic hyperuricemia and CKD 2-3 (GFR 54±3 ml/min) were enrolled in a 14-month randomized prospective open-label study in parallel groups: 20 on allopurinol 300 mg, 16 on febuxostat 80 mg and 20 free of treatment as control group. GFR by GFR-EPI, ambulatory BP monitoring, urine microalbumin-creatinine ratio, and C-reactive protein, fasting blood glucose were measured at baseline, 6 and at 14 months. A multiple regression model incorporating variables expected to influence GFR (gender, age, CRP level and systolic/diastolic BP), as well as serum uric acid was performed both before and after treatment.

Results: Age, gender, GFR, level of microalbuminuria and ACE/ARB regime were similar in all groups at baseline. Allopurinol treatment as well as febuxostat resulted in a decrease in serum uric acid, a decrease in systolic BP, and an increase in GFR compared with baseline. Febuxostat treatment led to the most beneficial decrease in the level of uric acid (−312±49 µmol/l, P≤0.01 with control and P≤0.05 with allopurinol group), increased GFR (+12±3 ml/min, P≤0.05 with control and P=0.92 with allopurinol group), blood pressure decrease (−8.3±3.1 mm Hg, P≤0.05 with control and P=0.90 with allopurinol group), microalbuminuria (−128±34 mg, P≤0.01 with control and P≤0.05 with allopurinol group), better CRP level and left ventricular hypertrophy control. The effects were mild but significant so that a larger number of patients and longer follow-up will be necessary to determine whether such a strategy may provide long-term survival benefits and progression of renal disease. Potential benefits of febuxostat were body mass control comparing with control group and better tolerability compared with allopurinol group.

Conclusions: At least 1-year treatment with febuxostat (better than allopurinol) improves GFR and BP in patients with asymptomatic hyperuricemia in non-diabetic CKD 2-3. More studies with febuxostat are necessary to assess the risk/benefit of lowering uric acid in non-diabetic adults with CKD and asymptomatic hyperuricemia.

TO014 HYPERTENSIVE URGENCIES WITH HYPOVOLEMIA IN CKD PATIENTS

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Introduction and Aims: Although hypervolemia is considered the main cause of hypertension in CKD patients, there are frequently encountered normo- or hypovolemic cases, in clinical practice. The aim of our study was to determine if there are CKD patients (stage 3 and 4) with hypovolemia presenting hypertensive emergencies.

Methods: Between January 2010 - December 2011 all individuals <65 years with CKD stage 3 and 4 (MDDR formula), who were admitted for hypertensive emergencies, performed a test to appreciate volemia by measuring vascular transthoracic bioimpedance. Simultaneously; an emergency lab test was used to measure natremia.

Results: From the 498 CKD stage 3 or 4 patients presenting hypertensive crises at the emergency room, 44 were excluded because of a concomitant acute cardiac event (unstable angina, myocardial infarction or arrhythmia). Consequently, the volemic status was evaluated in the remaining 454 patients: - 319 (70.26%) had hypervolemia; - 95 (20.92%) had hypovolemia; - 40 (8.81%) had normovolemia. In the hypovolemic group, 57 patients presented hyper- or normonatremia (12.55% from all cases) and respectively 38 associated hyponatremia (8.37% from all cases). In the hypovolemic group, tubulointerstitial nephropathies and cystic renal diseases were the most frequent primary renal diseases (50.52%, p<0.001). Hypovolemia was significantly more frequent in patients with CKD stage 3 (38.86% from all patients with CKD stage 3) than in those with CKD stage 4 (11.30% from all patients with CKD stage 4) - χ2 = 24.183, p<0.001.

Conclusions: In our study, association between hypovolemia and hypertension was significantly more frequent in patients with CKD stage 3 secondary to a tubulointerstitial nephropathy. Restoring volemic status is mandatory for controlling arterial pressure and, in case of associated hyponatremia, sodium supplements may be paradoxically necessary even when arterial pressure is elevated.

TO015 RENAL ARTERY STENOSIS IS PREDICTIVE OF CARDIOVASCULAR EVENTS IN PATIENTS AFFECTED BY ISCHEMIC HEART DISEASE

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Introduction and Aims: The presence of atherosclerotic renal artery stenosis (RAS), even when incidentally discovered, is independently associated with a higher risk of cardiovascular (CV) mortality and mortality in caucasian patients (pts) with ischemic heart disease.
Methods: A cohort of 1298 pts affected by ischemic heart disease, consecutively enrolled from 2006 for one year, undergoing screening renal arteriography at the time of cardiac catheterization, were studied at baseline and followed up for 5 years. Major CV events (MACCE), defined as myocardial infarction, stroke, death from CV causes, coronary artery revascularization, pulmonary oedema, were collected. Cox regression analysis was used to investigate the effect of several risk factors on time to the first MACCE.

Results: The mean age of the cohort was 64±10 yrs; M 70%, F 30%; diabetes was present in 36% of pts, hypertension in 87%, dyslipidemia in 75%; eGFR was 81±23 ml/min/1.73 m2. A total of 973 pts out of 1298 (75%) had at least one coronary vessel involved (1vessel in 278 pts; 2vessel in 241; 3vessel in 158; Left main coronary artery in 69). RAS ≥50% was found in 70 out of 1298 patients (5.4%). Follow up data at 5 yrs were available in 1196 pts (RAS ≥50% in 64 pts), and in 887 pts when including echocardiographic data at baseline. The follow up population was representative of the original cohort. At least one MACCE was present in 23% of pts with RAS<50%, and in 57% of pts with RAS ≥50%. In a multivariate Cox regression model only age, the presence of RAS, the severity of coronary artery disease and left ventricular mass significantly predicted the time to the first CV event. The impact of RAS on time to the first CV event is shown in Fig1

Conclusions: Our data showed that the prevalence of RAS≥50% is quite low in a cohort of caucasian pts affected by coronary artery disease. The presence of RAS is significantly related to the risk of MACCE, thus suggesting that the early diagnosis is useful to better characterize the CV risk profile of pts affected by ischemic heart disease for aggressive CV preventive therapy.

Introduction and Aims: Structural and functional brain white matter (WM) abnormalities are poorly characterised in Haemodialysis (HD) patients despite the observed deterioration in functional status after initiating HD. We aim to examine the brain WM microstructure using Diffusion Tensor Magnetic Resonance Imaging (DTI) and its correlation with cognitive impairment.

Methods: DTI was done in 74 subjects, 49 incident HD patients and 25 age-matched normal controls (NC). Images were analysed using FSL software package (http://www.fmrib.ox.ac.uk/fsl/). Fractional Anisotropy (FA) and Mean Diffusivity (MD) maps were first computed for each subject then a voxelwise statistical analysis of the FA data was done using TBSS (Tract-Based Spatial Statistic). Cognitive assessment was done using the Montreal Cognitive Assessment (MoCA) and Trail making tests (TMT) A & B. Pulse wave velocity (PWV) and other haemodynamic measures were also performed.

Results: Measures of WM damage in HD patients compared to NC were evident by lower FA peak intensity values and higher MD ones (FA 0.471±0.031 vs 0.486±0.022 P=0.023, MD 0.00194±0.000363 vs 0.00167±0.0003 P=0.002). TBSS demonstrated a diffuse pattern of WM damage in HD patients with statistical significance (P<0.05, corrected) (Figure1). MoCA scores were lower in HD patients (25 IQR 22-28 vs 28 IQR 26-30, P=0.004). TMT A & B times were higher in HD patients (TMT A 35s IQR 26-49 vs 22s 21-30, P=0.001) (TMT B 80s IQR 57-121 vs 56s IQR 43-87). Higher FA values correlated with better cognitive performance (MoCA r=0.416 P=0.001, Trail B -0.315 P=0.031). PWV was a determinant of WM damage predicting lower FA and high MD values, FA (R^2 = 0.173, β = -0.416, P= 0.004), MD (R^2 = 0.101, β = -0.033, P= 0.003).

Conclusions: HD patients have significant WM structural abnormalities which manifests as cognitive impairment and reduced attention and mental flexibility compared to aged-matched normal controls. PWV and other structural and functional haemodynamic parameters continue to be major contributors and end organ damage in the high risk group.

### Table

<table>
<thead>
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<th>Variables</th>
<th>HR</th>
<th>CI</th>
<th>P</th>
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<td>1.4-3.2</td>
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<td>1.4-3.2</td>
<td>&lt;0.001</td>
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<td>0.9-2.3</td>
<td>0.08</td>
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<td>1.5-3.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
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<td>2.2-5.5</td>
<td>&lt;0.001</td>
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<tr>
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<td>1.002-1.082</td>
<td>0.04</td>
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Introduction and Aims: Accumulating evidence indicates that inflammatory mechanisms play a significant role in initiation and progression of diabetic nephropathy. Besides its important function as a regulator of inflammatory processes, we have recently reported that oncostatin M (OSM) also exerts potent antifibrotic effects in human proximal tubular HK-2 cells. In this study we investigated OSM’s effects on the pro-inflammatory cytokines TNF-α and IL-1β in HK-2 cells, particularly with regard to their effects on mRNA expression of CC-chemokine ligand 5 (CCL5/RANTES), thrombospondin-1 (TSP-1) and tenasin C (TNC).

Methods: Cell culture, real-time PCR.

Results: 10 ng/ml of either TNF-α or IL-1β led to a time-dependent upregulation of CCL5, TSP-1 and TNC mRNA expression when compared with unstimulated HK-2 cells. Induction of CCL5 mRNA levels in the presence of TNF-α or IL-1β started after 3 h and led to a strong upregulation after 48 h of incubation, which was 137.0-fold (TNF-α) and 17.9-fold (IL-1β), respectively. While TNF-α-stimulated expression of TSP-1 mRNA started after 6 h and peaked at 24 h (27.0-fold), upregulation of TSP-1 mRNA in the presence of IL-1β was highest after 48 h (2.5-fold). TNF-α - as well as IL-1β-driven induction of TNC mRNA started after 3 h and reached a 3.1-fold maximum after 6 h. Interestingly, after 6 h of stimulation OSM showed an additive effect on TNF-α and IL-1β-stimulated TNC mRNA expression. However, when administered together for 24 h, OSM (10 ng/ml) completely blocked both TNF-α and IL-1β-induced TSP-1 mRNA expression and inhibited TNF-α and IL-1β-stimulated TNC mRNA expression in HK-2 cells. CCL5 mRNA levels following 6 h of incubation in the presence of TNF-α or IL-1β alone showed a 14.0- and 3.4-fold increase, respectively, while OSM alone hardly affected basal CCL5 mRNA expression. In contrast, co-administration of TNF-α or IL-1β together with OSM for 6 h resulted in an upregulation of CCL5 mRNA expression, which was 27.0-fold and 11.5-fold, respectively. A similar but even more impressive additive effect was detected after 24 h. While TNF-α or IL-1β alone led to a 51.7-fold and 6.0-fold increase in CCL5 mRNA expression when compared with unstimulated control cells, OSM alone did not affect CCL5 mRNA levels. However, 24 h incubation in the presence of OSM together with TNF-α or IL-1β-stimulated CCL5 mRNA expression to values of 82.6-fold and 50.0-fold, respectively.

Conclusions: In HK-2 cells, OSM exerts a strong additive effect on TNF-α and IL-1β-stimulated mRNA expression of the pro-inflammatory chemokine CCL5 after 6 h and 24 h of treatment. In contrast, this IL-6 family member inhibits TNF-α and IL-1β-induced mRNA expression of the two matricellular proteins TSP-1 and TNC after long-term incubation (24 h) albeit an initial transient additive effect on TNC (6 h). Thus, besides its long-term inhibitory effects on matricellular protein expression, OSM is able to amplify TNF-α and IL-1β-mediated CCL5 mRNA expression.

ATP-P2X SIGNALING MEDIATES NLRP3 INFLAMMASOME ACTIVATION: A NOVEL PATHWAY OF DIABETIC NEPHROPATHY

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Introduction and Aims: Tubulointerstitial inflammation plays a determinant role in the development of diabetic nephropathy (DN). Cytokines in IL-1 family are the key pro-inflammatory cytokines of tubulointerstitial inflammation. Extracellular ATP can cause P2X receptors to activate the NOD-like receptor 3 (NLRP3) inflammasome and cause IL-1β and IL-18 maturation and release. This study investigates the role of ATP-P2X signaling in NLRP3 inflammasome activation and renal interstitial inflammation characteristic of DN.

Methods: The immunohistochemistry and other molecular biological technologies were employed to investigate P2X receptors expression in type 2 diabetic patients with nephropathy. The level and location of P2X4 corresponding to the urine IL-1β, IL-1β and IL-18 expression were employed to investigate P2X4 expression in type 2 diabetic patients with nephropathy. The level and location of P2X4 corresponding to the urine IL-1β, IL-1β and IL-18 expression were characterized. The effects of ATP-P2X4 signaling on NLRP3 inflammasome activation was further assessed in vitro culture experiments in HK - 2 cells.

Results: P2X4 expression was increased in renal tubule epithelial cells with type 2 diabetic nephropathy compared to those in the control group. Linear correlation analysis shows that P2X4 expression was positively related with urine IL-1β and IL-18 levels. Moreover, P2X4 expression was co-localized with NLRP3, IL-1β, and IL-18 expression. In vitro culture experiments showed NLRP3 protein expression, and cell supernatant with levels of IL-1β, IL-1β and ATP significantly increased after high glucose stimulation. However, apyrase, which consumes extracellular ATP, completely blocked the effect caused by high glucose. Meanwhile, extracellular potassium concentration was reduced and calcium concentration was increased under high glucose conditions. Changes in potassium and calcium concentration were blocked by Apyrase and 5-BDBD. Moreover, suramin, TNP-ATP, and 5-BDBD all attenuated...
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L NLPR3, IL-1β and IL-18 expression induced by high glucose. P2X4 gene silencing significantly inhibited increased NLPR3, IL-1β and IL-18 expression induced by high glucose.

Conclusions: ATP-P2X4 signaling mediates high glucose-induced activation of the NLPR3 inflammasome, regulates IL-1 family cytokine secretion, and causes the development of renal interstitial inflammation in DN.

Conclusions: Taken together, these results suggest that PBI-4050 offers the potential as a novel therapy for the reduction of diabetic nephropathy.

**TO022 THE CCR2 ANTAGONIST CCX140 IMPROVES RENAL FUNCTION IN TWO TYPES OF DIABETIC MICE EXPRESSING HUMAN CCR2**

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1ChemoCentryx Inc. Mountain View CA United States

Introduction and Aims: Diabetic nephropathy (DN) is a major complication of uncontrolled diabetes. C-C Chemokine Receptor 2 (CCR2) has been implicated in the renal recruitment of blood monocytes in response to hypertension and hyperglycemia. It may also be involved in activation of parenchymal renal cells (e.g., podocytes, mesangial) under pathological conditions. CCX140 is a potent, selective, and orally bioavailable small molecule CCR2 antagonist that is currently being studied in two Phase 2 clinical trials in DN. Here we describe the effects of CCX140 on hyperglycemia and renal function in two types of diabetic mice.

Methods: Due to the high selectivity of CCX140 for human CCR2, the mouse CCR2 coding region was replaced with human CCR2 (hCCR2KI mice). Uni-nephrectomized hCCR2KI mice were placed on a high fat/high protein diet for 36 weeks (hCCR2KI DIO). hCCR2KI db/db mice were obtained from breeding of CCR2hCCR2KI/leprdb/db mice. CCX140 was dosed daily to hCCR2KI/db/db mice (age 12-19 weeks) for a total of 6 weeks, or to hCCR2KI DIO mice (age 4-4 weeks) for 8 weeks. Assessments included body weight, fasting plasma glucose, serum clinical chemistry, and 24 hour urinary output of albumin and creatinine.

Results: At study start, mice were highly albuminuric (hCCR2KI-DIO: ~500 mg alb/day; hCCR2KI/db/db: 1200-1500 mg alb/day) and diabetic (hCCR2KI/db/dbFPG: 300-400 mg/dl; hCCR2KI DIO FPG: ~190 mg/dl). Treatment with CCX140 for 6-8 weeks was well tolerated. CCX140 treatment significantly reduced UAER and albumin:creatinine ratio (ACR) in both mouse models. In hCCR2KI/db/db mice: Relative changes in UAER from study start to week 6 were ~14% and ~50% for vehicle and CCX140, respectively (p<0.01); changes in ACR from study start to week 6 were ~3% and ~75% for vehicle and CCX140, respectively (p<0.05). Treatment-related improvement in fasting glucose was also observed (vehicle: +45%, CCX140: -10%, p<0.01). In hCCR2KI DIO mice: Relative changes in UAER from study start to week 8 were +40% and +23% for vehicle and CCX140, respectively (p<0.001); changes in ACR from study start to week 8 were +56% and +72% for vehicle and CCX140, respectively (p<0.01). Treatment-related improvement in fasting glucose was also observed (vehicle: 190 mg/dL; CCX140: 150 mg/dL; p<0.01). These effects were apparent as early as 1 week after start of treatment. Also observed at the end of the study were increased podocyte density and reduced interstitial macrophage infiltration in connection with CCX140 treatment (p<0.01 and 0.05, respectively).

Conclusions: Rapid and significant improvements in albuminuria and hyperglycemia were seen with CCX140 in 2 mouse models of DN. These data are highly supportive of the clinical evaluation of CCX140 in DN. Results from the two ongoing Phase 2 DN trials are expected in 2013.
TO027
LONGITUDINAL PREDICTORS OF C-REACTIVE PROTEIN IN HEMODIALYSIS PATIENTS: RESULTS FROM THE MONDO INITIATIVE

Rakesh Malhotra1, Yuedong Wang3, Peter Kotanko2, Daniele Marcelli4, Aileen Grassmann5, Cristina Marelli5, Michael Etter6, Lenn Usyov7 and Mondo Consortium

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Introduction and Aims: C-reactive protein (CRP) is a marker of systemic inflammation in hemodialysis (HD) patients and is associated with poor outcomes. We have previously examined the cross-sectional relationship between neutrophil-to-lymphocyte ratio (NLR) and albumin levels with CRP. The aim of the present study was to evaluate the demographic, clinical and biochemical determinants of longitudinal CRP measurement in HD patients.

Methods: Our cohort includes HD patients, who were enrolled as part of the MONDO (MONitoring Dialysis Outcomes) research initiative. We extracted data for only those patients in whom concurrent measurements of NLR, albumin, and CRP were available. Of the total 20407 patients included in the analysis, 13605 (66.7%) were randomly selected for the derivation cohort and the remaining 6802 (33.3%) were assigned to the validation cohort. The derivation and validation sets have a total of 91,924 and 45,654 observations, respectively. We constructed a linear mixed-effect model to analyze the relationship of NLR and albumin with Log CRP, as measured on a continuous scale. The linear mixed model was further tested in the validation cohort.

Results: The median age was 62 yrs, 57% of the patients were men. The median dialysis vintage was 6.2 months (IQR 0-40 months). The median (IQR) NLR, albumin and CRP were 3.1(1.9-3.6), 3.95(3.7 to 4.2) and 11.9(2.0 to 12.2), respectively. Low albumin level (albumin <3.5g/dL) and high NLR (NLR ≥5) were associated with poor outcomes. We developed a long-functional linear regression model using the plasma levels of inflammatory cytokines in subjects enrolled in the multi-ethnic Chronic Renal Insufficiency Cohort study. We measured the plasma levels of IL-1β, IL-6, IL-10, TNF-α, TGF-β, hs-CRP, fibrinogen, and serum albumin in 3,939 subjects using ELISAs. An inflammation score was computed based on plasma levels of pro-inflammatory cytokines and acute phase proteins. Bioelectric impedance analysis was used to determine the fat mass and fat free mass.

Results: As compared to subjects with no evidence of inflammation, those with inflammation score ≥4 had a significantly higher BMI (28.5±5.4 vs. 34.2±7.9 kg/m², p<0.001), fat mass (24.8±9.8 vs. 33.5±16.2 kg, p<0.001), and fat free mass (59.6±15.5 vs. 63.0±16.1 kg, p=0.015). In multivariable analysis, each unit increase in inflammation score was associated with an increase of 1.80 (CI 1.57-2.03), 3.29 (CI 2.87-3.70), and 1.74 (CI 1.37-2.12) unit increase in BMI, fat mass, and fat free mass respectively (p<0.001). After adjusting for potential confounding variables, each unit increase in inflammation score was associated with 3.49 (CI 2.91-4.08), 2.99 (CI 2.30-3.68), and 1.33 (CI 2.01-2.45) units increase in fat mass in Caucasians, African Americans, and Hispanics respectively (p<0.001).

Conclusions: Adiposity is associated with a higher inflammatory response in Caucasians compared to African Americans and Hispanics. The abundant energy depot with decreased burden of inflammation may explain the survival advantage observed in overweight African Americans with kidney disease.

TO028
THE INFLUENCE OF RACE AND ETHNICITY ON THE ASSOCIATION BETWEEN BODY COMPOSITION AND INFLAMMATION IN PATIENTS WITH CHRONIC KIDNEY DISEASE: FINDINGS FROM THE CRIC STUDY

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1Renal Disease and Hypertension The George Washington University Washington DC United States, 2University of Pennsylvania Philadelphia PA United States, 3Nephrology and Hypertension Cleveland Clinic Cleveland OH United States, 4Non-surgical Medicine University of Michigan Ann Arbor MI United States, 5Medicine University of Illinois Chicago IL United States, 6Epidemiology Tulane University New Orleans LA United States, 7DKUHD NIDDK Bethesda MD United States

Introduction and Aims: African Americans with large body mass index (BMI) have better survival compared to their Caucasian counterparts with CKD. In order to test the hypothesis that the inflammatory response to adiposity varies by race, we measured the plasma levels of inflammatory cytokines in subjects enrolled in the multi-ethnic Chronic Renal Insufficiency Cohort study.

Methods: We measured the plasma levels of IL-1β, IL-6, IL-10, TNF-α, TGF-β, hs-CRP, fibrinogen, and serum albumin in 3,939 subjects using ELISAs. An inflammation score was computed based on plasma levels of pro-inflammatory cytokines and acute phase proteins. Bioelectric impedance analysis was used to determine the fat mass and fat free mass.

Results: As compared to subjects with no evidence of inflammation, those with inflammation score ≥4 had a significantly higher BMI (28.5±5.4 vs. 34.2±7.9 kg/m², p<0.001), fat mass (24.8±9.8 vs. 33.5±16.2 kg, p<0.001), and fat free mass (59.6±15.5 vs. 63.0±16.1 kg, p=0.015). In multivariable analysis, each unit increase in inflammation score was associated with an increase of 1.80 (CI 1.57-2.03), 3.29 (CI 2.87-3.70), and 1.74 (CI 1.37-2.12) unit increase in BMI, fat mass, and fat free mass respectively (p<0.001). After adjusting for potential confounding variables, each unit increase in inflammation score was associated with 3.49 (CI 2.91-4.08), 2.99 (CI 2.30-3.68), and 1.33 (CI 2.01-2.45) units increase in fat mass in Caucasians, African Americans, and Hispanics respectively (p<0.001).

Conclusions: Adiposity is associated with a higher inflammatory response in Caucasians compared to African Americans and Hispanics. The abundant energy depot with decreased burden of inflammation may explain the survival advantage observed in overweight African Americans with kidney disease.

TO029
EFFECTS OF WEIGHT LOSS IN OBESE PATIENTS WITH IMPAIRED RENAL FUNCTION: A SYSTEMATIC REVIEW

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Introduction and Aims: Obesity is an independent risk factor for development and progression of chronic kidney disease (CKD). We conducted a systematic review to assess the benefits of intentional weight loss, either achieved by surgical and non-surgical interventions, in obese subjects with altered GFR, proteinuria or albuminuria.

Methods: MEDLINE, EMBASE and CENTRAL databases were searched for English-language articles without time restriction up to December 28, 2012. We included any randomized or non-randomized trial, single-arm, prospective or retrospective observational study providing longitudinal data on the effect of weight loss on renal parameters in obese patients (BMI>30 kg/m²) with altered kidney function (GFR <90 or >125 mL/min/m²; creatinine >1.3 mg/dL; pathological proteinuria or albuminuria), without follow-up restrictions.

Results: From a pool of 1469 articles retrieved, 1460 citations were excluded as irrelevant and 9 studies were excluded after full text evaluation. 30 studies (2013 subjects) were reviewed, including 17 prospective studies, 16 retrospective reports and one RCT. Follow up duration ranged from 4 weeks to 5 years. In the 13 studies (562 patients) where weight loss was achieved by bariatric surgery, BMI significantly decreased in all studies (Δ ranging from -4.5 to -8.8 kg/m²); GFR decreased in 6 studies on hyperfiltering patients (Δ ranging from -13.0 to -35 mL/min/m²) and increased in one study on patients with CKD stage 3-4; Albuminuria decreased in 6 studies (Δ ranging from -6 to -53 mg/24h) and proteinuria decreased in 5 studies (Δ...
Abstracts

Innsbruck Austria, 5Mosaiques Diagnostics & Therapeutics Hannover Germany, development of ESRD.

Conclusions:
- 2.5 g/24h).
- longest-term studies are needed to assess the impact of this intervention on renal outcomes, such as CKD progression and the development of ESRD.

Conclusions: In obese patients with altered renal function, weight loss, particularly if achieved by surgical interventions, improves proteinuria, albuminuria and normalizes GFR. Larger, longer-term studies are needed to assess the durability of this improvement and the effects on renal outcomes, such as CKD progression and the development of ESRD.

Introduction and Aims: Given the involvement of kidneys in amino acid and protein metabolism, chronic kidney disease severity is likely to progressively influence amino acid plasma concentrations and urinary excretion. The timing and the characteristics of appearance of these alterations in plasma and urinary amino acid profiles remain to be established.

Methods: We studied 77 CKD patients which were grouped by disease severity: CKD stage 2-3 (24 patients), CKD stage 4-5 non dialysed (28 patients) and haemodialysis (HD) patients (25 patients). Plasma samples (all patients) and urine samples (non-dialysed patients) were taken and analysed by LC-MS/MS after PITC-derivatization for amino acid and amine determinations. Plasma and urine routine laboratory tests were also available.

Results: Compared to patients at CKD stage 2-3, patients with CKD stage 4-5 had significantly higher plasma citrulline (p<0.001), ornithine (p<0.01) and ADMA levels (p<0.001), as well as increased citrullinuria and prolinuria (both p<0.001). They also had significant reductions in plasma tryptophan and urinary ADMA excretion (both p<0.001). Multiple linear regressions including eGFR reproduced these results and highlighted additional associations. Plasma citrulline was significantly increased in diabetic patients (p=0.02). Heavy proteinuria was associated with significantly higher urinary excretion of 10 AA (p<0.05). Urinary lysine decreased with serum albumine and CRP levels (both p=0.01). Plasma phenylalanine was directly associated with CRP and inversely with bicarbonates (respectively, p=0.04, p=0.35). Finally, plasma ADMA and urinary valine respectively increased and decreased with serum Na levels (respectively, p<0.05, p=0.04). Compared to non-dialysed patients, HD patients had lower total AA and EAA plasma levels, and 18 of the 23 plasma determinations were significantly changed (78%). Using analyses of variance, we found that as CKD progressed to HD, several plasma AA ratios were significantly increased (Orn/Arg (p=0.01), Cit/Orn and ADMA/SDMA (both p<0.001)) or decreased (EAA/NEAA (p<0.01), Tyr/Phe, Arg/Cit and Arg/ADMA (all three p<0.001)).

Conclusions: Major alterations in the plasma amino acid profiles are observed in dialysis patients, which may be already visible at early stages of chronic kidney disease, in keeping with previous reports. We further characterised for the first time the associations between CKD stages and urinary excretion of AA, and established etiology-related modifications of plasma and urinary AA profiles that may be relevant when caring CKD patients and defining nutritional therapies.

**TO029** PLASMA AND URINARY AMINO ACID PROFILES IN CKD PATIENTS STAGE 2 TO HEMODIALYSED

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Introduction and Aims: Given the involvement of kidneys in amino acid and protein metabolism, chronic kidney disease severity is likely to progressively influence amino acid plasma concentrations and urinary excretion. The timing and the characteristics of appearance of these alterations in plasma and urinary amino acid profiles remain to be established.

Methods: We studied 77 CKD patients which were grouped by disease severity: CKD stage 2-3 (24 patients), CKD stage 4-5 non dialysed (28 patients) and haemodialysis (HD) patients (25 patients). Plasma samples (all patients) and urine samples (non-dialysed patients) were taken and analysed by LC-MS/MS after PITC-derivatization for amino acid and amine determinations. Plasma and urine routine laboratory tests were also available.

Results: Compared to patients at CKD stage 2-3, patients with CKD stage 4-5 had significantly higher plasma citrulline (p<0.001), ornithine (p<0.01) and ADMA levels (p<0.001), as well as increased citrullinuria and prolinuria (both p<0.001). They also had significant reductions in plasma tryptophan and urinary ADMA excretion (both p<0.001). Multiple linear regressions including eGFR reproduced these results and highlighted additional associations. Plasma citrulline was significantly increased in diabetic patients (p=0.02). Heavy proteinuria was associated with significantly higher urinary excretion of 10 AA (p<0.05). Urinary lysine decreased with serum albumine and CRP levels (both p=0.01). Plasma phenylalanine was directly associated with CRP and inversely with bicarbonates (respectively, p=0.04, p=0.35). Finally, plasma ADMA and urinary valine respectively increased and decreased with serum Na levels (respectively, p<0.05, p=0.04). Compared to non-dialysed patients, HD patients had lower total AA and EAA plasma levels, and 18 of the 23 plasma determinations were significantly changed (78%). Using analyses of variance, we found that as CKD progressed to HD, several plasma AA ratios were significantly increased (Orn/Arg (p=0.01), Cit/Orn and ADMA/SDMA (both p<0.001)) or decreased (EAA/NEAA (p<0.01), Tyr/Phe, Arg/Cit and Arg/ADMA (all three p<0.001)).

Conclusions: Major alterations in the plasma amino acid profiles are observed in dialysis patients, which may be already visible at early stages of chronic kidney disease, in keeping with previous reports. We further characterised for the first time the associations between CKD stages and urinary excretion of AA, and established etiology-related modifications of plasma and urinary AA profiles that may be relevant when caring CKD patients and defining nutritional therapies.

**TO031** PLASMA LEVELS OF THE PROTEIN-BOUND UREMIC RETENTION MOLECULES P-CRESYL SULFATE AND INDOXYL SULFATE INVERSELY RELATE TO SOLUBLE KLOTHO LEVELS IN CKD PATIENTS

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Introduction and Aims: Klotho is an anti-aging protein predominantly expressed in the kidney, parathyroid gland and choroid plexus of the brain. Membrane Klotho functions as an obligate cofactor for FGF23, whereas soluble Klotho functions as a humoral factor that regulate several ion channels, Na-dependent Pi cotransporters and type II TGF-b receptors. Little is known about the plasma levels of soluble Klotho and their contributing factors in patients with chronic kidney disease (CKD). Recent in vitro and animal data suggest that the protein-bound uremic retention molecules indoxyl sulfate (IndS) and p-cresyl sulfate (PCS) suppress Klotho expression. The present study aimed to elucidate the relationship between IndS, PCS and soluble Klotho in CKD patients.

Methods: Parameters of mineral metabolism including soluble Klotho (ELISA, IBL), FGF23 (ELISA Kainos), bi-PTH (IRMA), and calcitriol (RIA) as well as IndS and PCS (HPLC) were measured in 115 CKD patients (57 men, 59±15 years) (NCT00441623).

Results: Median plasma Klotho levels were 835 (263-4520) pg/ml. The evolution of soluble Klotho, FGF23, bi-PTH, calcitriol, phosphate and fractional excretion of phosphate (FEPhos) across CKD stages is summarized in [Figure 1]. In univariate regression analysis, diabetes, low eGFR (CKD-EPI) and high age, CRP, phosphate, IndS, PCS, FGF23, bi-PTH were all significantly associated with low soluble Klotho levels. In multivariate, PCS remained significantly correlated with soluble Klotho levels, independent of age and eGFR (R²=0.13, p=0.0002).

Conclusions: Together with experimental data, our data suggest that the protein-bound uremic toxins may contribute to the suppression of Klotho in CKD patients. Suppressed Klotho expression may be in the causal pathway between high levels of these toxins and adverse outcomes.

**[Figure 1]**
RENAL PHYSIOLOGY AND KIDNEY STONES

TO032 KIDNEY STONES AND CARDIOVASCULAR EVENTS: A COHORT STUDY

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Introduction and Aims: Kidney stone formers share some common risk factors associated with the development of atherosclerosis including diabetes and hypertension. However, whether having a kidney stone is associated with increased risk of cardiovascular events is uncertain.

Methods: We studied 3,897,684 people aged ≥18 years and living in Alberta Canada between 1997 and 2009, excluding those on dialysis or with a kidney transplant at baseline. Individuals who developed one or more kidney stone were identified from claims and facility utilization data. We compared the risk of incident acute myocardial infarction (AMI), death due to coronary heart disease (CHD), percutaneous transluminal coronary angioplasty (PTCA)/coronary bypass surgery (CABG) or stroke between stone formers and non-stone formers.

Results: During median follow-up of 11y, 25,532 (0.8%) participants had at least one kidney stone, 28,455 (0.9%) had an AMI, 34,643 (1.1%) died of CHD, 28,539 (0.9%) underwent PTCA or CABG, and 16,697 (0.5%) had a stroke. In total, 87,262 (3%) individuals had at least one cardiovascular event during follow-up. Compared to people without kidney stones, people who had at least one kidney stone during follow-up had an increased risk of subsequent AMI (adjusted HR 1.54, 95% CI 1.38, 1.72), PTCA/CABG (HR 1.62, 95% CI 1.46, 1.81) and an increased risk of subsequent AMI (adjusted HR 1.62, 95% CI 1.46, 1.81). The magnitude of the excess risk associated with a kidney stone appeared more pronounced for younger people (i.e., old people, p=0.001) and women (vs men, p=0.01).

Conclusions: The occurrence of a kidney stone is associated with an increased risk of cardiovascular events including AMI, death due to CHD, percutaneous transluminal coronary angioplasty/coronary bypass surgery or stroke.

TO033 CALCIUM SENSING RECEPTOR INFLUENCES THE EXPRESSION OF CLAUDIN 14 IN LOOP OF HENLE THICK ASCENDING TRACT

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Introduction and Aims: The calcium-sensing receptor (CaSR) is a membrane protein activated by extracellular calcium and expressed throughout the renal tubule. In the thick ascending limb of Henle tract (Talh) the CaSR inhibits the reabsorption of calcium through its regulatory action on claudin 14 (CLDN14) that blocks the channel for the transport of calcium into the intercellular junctions (tight junctions), favoring the excretion of calcium and hypercalciuria. It was observed that mice with reduced expression of CaSR showed a downregulation of CLDN14. To demonstrate in humans the relationship between the two molecules, we evaluated the expression of CaSR and CLDN14 in 104 human renal medullary tissue samples.

Methods: The sample was obtained from normal non-neoplastic tissue immediately after the nephrectomy. The expression of CaSR and CLDN14 was measured as mRNA and was normalized to the mRNA of glyceraldehyde-3-phosphate dehydrogenase (GAPDH). The total mRNA was extracted from 10-30 mg of renal tissue. The mRNA of CaSR, CLDN14 and GAPDH were measured using SYBR-Green Real-Time PCR of 100 ng of cDNA using specific primers. It was also made genotyping of DNA extracted from the samples for the polymorphism rs6776158 A> G of the CaSR gene 1 promoter by the specific genotyping assay.

Results: The transcriptional activity of the promoter 1 CaSR gene in the presence of allelic variants of the polymorphism rs6776158 A> G has been previously tested in HEK293 cells transfected with a plasmid containing the promoter 1 and the luciferase gene. The results in this in-vitro system have shown that the minor G allele of rs6776158 causes a decrease of the promoter transcriptional efficiency and a reduced expression of CaSR. In renal medulla tissue, the expression (mRNA) of CaSR was higher in patients carrying the A allele (n = 92) compared to homozygotes for the minor G allele (n = 12; 1.1 ± 1.2 vs 1.0 ± 0.58 ± 0.74 vs. vs. mm ± SD, p = 0.048). The expression of CLDN14 was higher in patients carrying the A allele compared to homozygotes for the minor G allele (2.21 ± 0.22 vs 1.69 ± 1.17, p = 0.018). The expression of CLDN14 was positively correlated with that of the CaSR in renal medullary tissue (r = 0.40, p = 0.001).

Conclusions: The reduction of CaSR expression is associated with a reduced expression of CLDN14 in the Talh, favoring the renal reabsorption of calcium in Talh. The CaSR seems then to adjust the expression of calcium through the control of the expression of CLDN14 in Talh. Inactivating the promoter polymorphisms of the CaSR can protect from hypercalciuria through activation of paracellular reabsorption in Talh.

TO034 POSSIBLE CORRELATION OF DOWN-REGULATED CLAUDIN-16, TIGHT JUNCTION MOLECULE IN TAL, WITH LOWERED MAGNESIUM REABSORPTION ASSOCIATED WITH TUBULO-INTERSTITIAL NEPHROPATHY

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Introduction and Aims: Hypermagnesiuria has been considered as a characteristic pathological setting in tubulo-interstitial nephropathy (TIN) although its underlying mechanisms has not been understood. The aim of this work was to elucidate the molecular profile of Mg transporting molecules in TIN by use of unilateral ureter obstruction (UUO) model which showed glomerular injury-independent TIN.

Methods: Left kidney was sampled at day-0, 1 and 7 after ligation of left ureter of male SD rats. For the assessment of TIN and changes in the expressions of Mg transporting molecules, histological observations, immunohistochemical analysis, RT-PCR and Western blotting were applied to the study.

Results: Fractional excretion of Mg was increased at day-7 but not at day-1 (3.1±0.8% at day-0, 4.6±2.05% at day-1, 10.7±0.8% at day-7). Gene expression of claudin-16, tight junctional pathway of Mg at mTAL, was also decreased at day-7 but not at day-1 (100.3

TO032 Figure 1:

TO032 Figure 2:

TO034 Figure 1:

TO034 Figure 2:

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±3.6% at day-0, 89.3±10.7% at day-1, 59.4±2.3% at day-7) while expression of TRPM6/7, Mg channel at DCT, was not changed even at day-7. Time-differential pattern of immunohistochemistry of claudin-16 was agreed with that of gene expression, which was also confirmed by Western blot analysis (densitometry analysis: 100.0±30.3 at day-0, 42.6±5.7 at day-1, 11.7±3.0 at day-7). Significant development of TIN, assessed by time-differential increase in the ratio of interstitial area (1.19±0.01 at day-0, 0.19±0.01 at day-1, 0.32±0.03 at day-7) and gene expression of MCP-1 (105.1±14.8% at day-0, 132.9±25.7% at day-1, 302.7±31.7% at day-0) and TGF-β (101.1±7.6% at day-0, 99.4±3.8% at day-0, 259.3±52.0% at day-0), was apparent at day-7 but not at day-1. Finally, appearance of peritubular capillaries (PTC), assessed by immunohistochemistry of JG-12 antibody, was diminished at day-7 but not at day-1.

**Conclusions:** Present results might suggest that the hypermagnesuria associated with TIN would be caused by dysfunction of Mg reabsorption at TAL resulted from the significant decrease of claudin-16 expression. Interstitial ischemia by the decreased number of PTC might possibly affect on the expression of claudin-16.
TUBULAR ISCHEMIA AND TOXICITY

TO035 ENDOTHELIAL PROGENITOR CELL-DERIVED EXTRAVASCULAR EXCELLENCES INHIBIT KIDNEY ISCHEMIA-REPERFUSION INJURY THROUGH THE TRANSFER OF mRNAs CODING FOR COMPLEMENT INHIBITORS TO INJURED TUBULAR EPITHELIAL AND ENDOTHELIAL CELLS

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Introduction and Aims: Endothelial progenitor cells (EPCs) are bone marrow-derived precursors known to reverse acute kidney injury (AKI) by paracrine mechanisms including the release of extracellular vesicles (EVs), small particles playing a role in intercellular communication through the transfer of proteins and mRNAs. Activation of the complement cascade in tubular epithelial and endothelial cells mediates kidney ischemia-reperfusion injury (IRI). The aim of this study was to evaluate whether the protective role of EPC-derived EVs in kidney IRI may be associated with complement inhibition.

Methods: EPCs were isolated from peripheral blood and EVs characterized for size, protein and RNA content. We evaluated the effects of EVs in a rat model of kidney IRI and in vitro in human tubular epithelial and endothelial cells cultured in hypoxia.

Results: EPC-derived EVs size 60-130 nm and carried different subsets of mRNAs and microRNAs able to modulate cell proliferation and apoptosis. By RT-PCR, we found within EVs mRNAs coding for the complement inhibitors factor H, DAF and CD59. After i.v. infusion, EVs localized within peritubular capillaries and tubular cells exerting morphologic and functional protection from AKI by reducing tubular cell apoptosis and leukocyte infiltration. EV administration reduced C5b9 deposition and enhanced the expression of factor H, DAF and CD59 in the ischemic kidney. The renoprotective effect of EVs was reduced after their treatment with RNase to decrease mRNA expression of all complement inhibitors. In vitro, EVs reduced hypoxia-induced apoptosis of tubular epithelial and endothelial cells by decreasing the deleterious effect of C5b9 activation and by up-regulating the expression of factor H, DAF and CD59, thus confirming the in vitro data. The role of factor H, DAF and CD59 mRNA transfer to injured renal cells was inferred by experiments using RNase-treated EVs or EVs released from EPCs engineered to knock-down all complement inhibitors by specific siRNA.

Conclusions: EPC-derived EVs protect the kidney from ischemic AKI by delivering mRNAs coding for factor H, DAF and CD59 to injured tubular epithelial and endothelial cells. These results confirmed previous data on the relevance of complement inhibition after kidney IRI and suggest the potential use of EPC-derived EVs as therapeutic option to avoid delayed graft function after kidney transplantation.

TO037 CD40 GENE SILENCING PREVENTS WARM RENAL ISCHEMIA-REPERFUSION INJURY

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Introduction and Aims: Ischemia-reperfusion injury has been associated with the incidence of both acute and chronic rejection. Together with the alloimmunization responses it is one of the most important causes of graft loss. Here, we test whether an anti-CD40 siRNA reduces kidney ischemia injury in a model of rat warm renal ischemia.

Methods: In the present study male Wistar rats were divided in 5 groups. SCR, group treated with scrambled siRNA (n=11); CD40-15, group treated with 500ug of siRNA (n=6); CD40-50, group treated with 150ug of siRNA (n=8); CD40-150, group treated with 500ug of siRNA (n=7) and CD40-500, group treated with 500ug of siRNA (n=6). The siRNA anti CD40 was administered 1hour before the ischemia. Ischemia was induced by clamping both renal pedicles for 40minutes, followed by reperfusion. Animals were followed up during 48hours.

Results: Compared to scrambled controls, serum urea and creatinine levels were lower in treated groups. The histopathological analysis illustrates a renoprotective effect in those groups treated with higher doses of siRNA. Note that the highest dose of siRNA was the most effective reducing kidney interstitial infiltrate and tubular lesions. Analysis of kidney gene expression showed that there was no activation of innate immunity (TLR3) due to the siRNA molecule itself, and that the siRNA reduced CD40 and, also, proinflammatory cytokines such as IL-4, IL-2 and NFKB in treatment groups. Interstitial monocyte infiltrate (CD68+) showed a reduction in those kidneys with higher doses of siRNA treatment. An additional study with 1CR mice using only the 50ug dose showed similar functional and structural protection.

Conclusions: Systemic administration of a siRNA anti CD40 in models of ischemia-reperfusion injury was highly effective diminishing the molecular and cellular inflammatory response, improving serum urea and creatinine levels, and reducing tubular and interstitial lesions. Thus, the blockade of costimulatory signal CD40 becomes a potential therapeutic tool to modulate ischemia-reperfusion injury.

TO038 THE ROLE OF MICRORNAS IN RENAL ISCHEMIA-REPERFUSION INJURY

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Introduction and Aims: Ischemia induced acute tubular necrosis (ATN) is one of the main causes of acute kidney injury (AKI). Reperfusion paradoxically increases the injury due to apoptotic processes. The modulation of pro-apoptotic genes is currently under investigation. MicroRNAs are posttranscriptional regulators of gene-expression. Our aim was to investigate the miRNA expression profile and to elucidate their role in ischemia reperfusion (IR) induced ATN.

Methods: After unilateral renal ischemia of C57Bl6 mice, renal function (urea/nitrogen) and morphology (PAS stain, NGAL) were assessed in different phases of acute kidney injury. The miRNA expression profile was evaluated at 24 hours post-ischemia (Luminex multiplex assay). miRNA expression time-course was also analyzed during the reperfusion phases (real-time PCR).

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Results: Three miRNAs (miR-21, miR-17-5p and miR-106a) were significantly elevated in IR injury after 24 hours of reperfusion (3.0, 1.5 and 1.4 fold, respectively, p<0.05). Real-time PCR analysis demonstrated, that these miRNAs started to elevate after 24 hours of reperfusion, in the maintenance phase, further increasing at 48 hours (miR-21: 2.3 fold, p<0.01; miR-17: 2.2 fold, p<0.01; miR-106a, 1.9 fold, p<0.01). After sublethal ischemia miRNA levels normalized together with kidney damage markers in the recovery phase.

Conclusions: We identified three miRNAs with altered expression in the maintenance phase of IR injury. Validated targets of the identified miRNAs have mostly pro-apoptotic effects. Therefore our results suggest that these miRNAs may be involved in the regeneration processes and could represent possible therapeutic tools in the treatment of ATN.


TO039 THE ROLE OF THE SIGMA-1 RECEPTOR – AKT - ENOS PATHWAY IN RENAL ISCHEMIA/REPERFUSION INJURY

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Introduction and Aims: The protective role of a novel pathway, the Sigma-1 receptor (S1R)-Akt-endothelial nitrogen monoxide synthase (eNOS) axis has been recently described in heart ischemia/reperfusion (IR) injury. In renal IR we previously showed that S1R agonists are protective, however the exact mechanism is still unknown. Here in renal IR we studied the effect of S1R agonist fluvoxamine (FLU) and antagonist NE-100 on the S1R-Akt-eNOS signaling pathway.

Methods: Male Wistar rats were treated i.p. with FLU (20 mg/bwkg; FLU), FLU and NE-100 (20 mg/bwkg and 1 mg/bwkg; FN) or vehicle (VEH). 30 minutes after the treatment animals were harvested (T30') or subjected to renal ischemia for 50 minutes followed by 2 (T2) or 24 (T24) hours of reperfusion. Sham-operated, untreated animals served as controls (C) (n=10/group). The renal S1R-Akt-eNOS proteins were analyzed by Western blot and immunofluorescence microscopy.

Results: 30 min after FLU treatment renal Akt and eNOS expression were elevated compared to C. After IR both proteins continually increased with time (C vs. T2 vs. T24). While at T2 there was no difference among the groups, at T24 renal Akt and eNOS protein levels were higher in the VEH group compared to FLU. NE-100 diminished all effects of FLU. S1R expression remained unchanged in the different groups. S1R-Akt-eNOS were co-localized in renal tubular cells. In C and after FLU treatment a nucleus-associated staining was observed, while in VEH and FN groups S1R-Akt-eNOS showed a more cytoplasmic localization.

Conclusions: The S1R-Akt-eNOS axis could be a novel pathway in the pathophysiology of renal IR injury. The S1R agonist FLU might exert its renoprotective effect by altering these proteins. This work was supported by LP2011-008/2012 Lendulet Research Grant; NIH grant R01 DK56843 and a. It was also supported by grants of OTKA PD83431, ETT 06-066/2009 and TÁMOP 4.2.4.A/1-11-1-2012-0001.
TO041 INHIBITION OF RENIN-ANGIOTENSIN SYSTEM WAS ASSOCIATED WITH LOWER HOSPITALIZATION RATE DUE TO BONE FRACTURE IN HAEMODIALYSIS PATIENTS WITH SECONDARY HYPERPARATHYROIDISM

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Introduction and Aims: Chronic kidney disease (CKD) requiring haemodialysis (HD) treatment, have a high risk for bone fracture mainly due to secondary hyperparathyroidism (SHPT). Renin-angiotensin system (RAS) associates the activation of osteoclasts in vitro. Thus, use of angiotensin converting enzyme inhibitor (ACEI)/angiotensin II receptor blocker (ARB) may inhibit bone resorption. We examined whether or not inhibition of RAS reduces incidence of bone fracture in HD patients with SHPT.

Methods: The Mineral and Bone Disorder Outcomes Study for Japanese CKD Stage 5D Patients (MBD-3D) was a 3-year prospective case-cohort study which analyzed 8229 HD patients with SHPT in 86 facilities in Japan. All patients had either an iPTH of at least 180 pg/ml or were receiving intravenous active vitamin D steroids or the oral active vitamin D analogue. Data were prospectively collected every 3 months between 2008 and 2011 from subjects in a sub-cohort consisting of a randomly selected (n = 3276) of the whole cohort. We examined the association between use of ACEI/ARB at baseline and hospitalization rate due to bone fracture during the study period of 3 years in the sub-cohort. Cox proportional hazard model was used to adjust for confounders (age, gender, duration of HD treatment, primary cause of kidney disease, body mass index, Kt/V, previous histories of cardiovascular disease or diabetes mellitus, smoking, serum albumin, hemoglobin, serum calcium, serum phosphate, alkaline phosphatase, and iPTH) at baseline. Further, we conducted a subgroup analysis according to iPTH levels to examine whether the association between use of ACEI/ARB and hospitalization rate due to bone fracture differed by SHPT severity.

Results: Incidences of hospitalization due to bone fracture were 4.6% in ACEI/ARB users and 6.5% in non-ACEI/ARB users, respectively (log-rank test p=0.02). Use of ACEI/ARB was associated with lower hospitalization rate due to bone fracture (adjusted hazard ratio [AHR] 0.65, 95% confidence interval [CI] 0.47-0.91). The AHRs (adjusted hazard ratio [AHR] 0.65, 95% confidence interval [CI] 0.47-0.91) of at least 180 pg/ml or were receiving intravenous active vitamin D steroids or the oral active vitamin D analogue. Data were prospectively collected every 3 months between 2008 and 2011 from subjects in a sub-cohort consisting of a randomly selected (n = 3276) of the whole cohort. We examined the association between use of ACEI/ARB at baseline and hospitalization rate due to bone fracture during the study period of 3 years in the sub-cohort. Cox proportional hazard model was used to adjust for confounders (age, gender, duration of HD treatment, primary cause of kidney disease, body mass index, Kt/V, previous histories of cardiovascular disease or diabetes mellitus, smoking, serum albumin, hemoglobin, serum calcium, serum phosphate, alkaline phosphatase, and iPTH) at baseline. Further, we conducted a subgroup analysis according to iPTH levels to examine whether the association between use of ACEI/ARB and hospitalization rate due to bone fracture differed by SHPT severity.

Conclusions: Inhibition of RAS was associated with lower hospitalization rate due to bone fracture in HD patients with SHPT.

TO042 BONE DISEASE THERAPY IN CKD CAN INFLUENCE LEVELS VITAMIN K DEPENDENT PROTEINS (VIKI STUDY)

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Introduction and Aims: Vitamin K is involved in the production of Bone and Matrix Gla Proteins (BGP and MGP respectively), regulating bone and vascular health. We carried out an observational study to evaluate an association between current bone disease therapy and SHPT and SHPT-BGP levels in 387 patients. We assessed SHPT-BGP levels for ≥1 year.

Methods: Cross-sectional study in hemodialysis patients, 18 dialysis centers in Northern Italy. We included 387 hemodialysis patients. We determined of serum concentrations of BGP (CLIA, DiaSorin Inc. – Stillwater, MN – USA), MGP (ELISA, Biomedica Medizinprodukte GmbH & Co KG – Wien – A) and routine biochemistry. We evaluated vertebral fractures (VF, reduction in vertebral body height by ≥20%).

Results: Of the 502 prevalent patients, 26.7% were prescribed a calcium-containing PB (CCPB) only, 33.9% a non-calcium-containing PB (NCCPB) only, 7.8% both a CCPB and NCCPB, and 31.7% no PB. Patients prescribed CCPB were older than those receiving NCCPB and had slightly lower pre-dialysis serum phosphate and parathyroid hormone levels (PTH) (table 1). No significant difference in mortality was observed when the following groups were compared: any PB vs no PB (HR 1.02, 95% CI 0.97-1.03, p=0.09); CCPB vs no PB (HR 0.97, 95% CI 0.87-0.99, p=0.01); and CCPB vs NCCPB (HR 1.11, 95% CI 0.99-1.25, p=0.12). However, a significant increase in mortality was observed for those patients on a CCPB compared with NCCPB (HR 1.57, 95% CI 1.12-2.11, p=0.01) (figure 1). 5-year mortality in the group prescribed CCPB at baseline was 62.7%, compared with 47.6% in the group on NCCPB.

Conclusions: In this large, well-defined HD cohort, there was an association between prescription of CCPB and increased 5-year mortality when compared to NCCPB, independent of achieved baseline phosphate and other factors that might influence survival.

TO043 PHOSPHATE BINDERS AND FIVE-YEAR MORTALITY IN PREVALENT HAEMODIALYSIS PATIENTS

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Introduction and Aims: Hyperphosphataemia is associated with increased morbidity and mortality in haemodialysis (HD) patients. Though phosphate binders (PB) are used to help achieve recommended serum phosphate targets, there is no convincing evidence suggesting significant superiority of one class of PB over another. We aimed to investigate the impact of choice of PB on 5-year mortality in a cohort of HD patients.

Methods: We studied all prevalent patients attending 6 HD units receiving HD for >90 days on 06/04/2007. Laboratory data averaged over 3-months were extracted from a prospectively maintained electronic patient record, as were baseline demographics and outcomes. A Cox regression model was used to examine the impact of PB on mortality, taking into account co-variates listed in table 1, as well as primary renal diagnosis.

Results: Of the 502 prevalent patients, 26.7% were prescribed a calcium-containing PB (CCPB) only, 33.9% a non-calcium-containing PB (NCCPB) only, 7.8% both a CCPB and NCCPB, and 31.7% no PB. Patients prescribed CCPB were older than those receiving NCCPB and had slightly lower pre-dialysis serum phosphate and parathyroid hormone levels (PTH) (table 1). No significant difference in mortality was observed when the following groups were compared: any PB vs no PB (HR 1.02, 95% CI 0.97-1.03, p=0.09); CCPB vs no PB (HR 0.97, 95% CI 0.87-0.99, p=0.01); and CCPB vs NCCPB (HR 1.11, 95% CI 0.99-1.25, p=0.12). However, a significant increase in mortality was observed for those patients on a CCPB compared with NCCPB (HR 1.57, 95% CI 1.12-2.11, p=0.01) (figure 1). 5-year mortality in the group prescribed CCPB at baseline was 62.7%, compared with 47.6% in the group on NCCPB.

Conclusions: In this large, well-defined HD cohort, there was an association between prescription of CCPB and increased 5-year mortality when compared to NCCPB, independent of achieved baseline phosphate and other factors that might influence survival.
A CASE-CONTROL STUDY OF CALCIPHYLAXIS IN END-STAGE RENAL DISEASE PATIENTS IN FRANCE

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Introduction and Aims: Calciphylaxis, or calcific uremic arteriolopathy (CUA), is a skin disease characterized by painful skin ulcerations and necrosis due to medial calcification and intimal proliferation in small arteries. It usually occurs in end-stage renal disease patients, with a reported incidence of 1 to 4%. In the last years, the number of cases reported increased remarkably in our region (Normandy, North West of France). Thus, we decided to conduct a retrospective case-control study involving all the dialysis centers of our region to evaluate incidence, risk factors, therapeutic attitudes and outcomes in patients with CUA.

Methods: CUA diagnosis was based on characteristic clinical features. All the cases of CUA diagnosed between January 1st 2005 and December 31st 2010 in the 17 dialysis centers of Normandy were included. Prospective data were systematically collected. In addition, for each CUA case, 2 control patients matched for age and duration of dialysis (haemodialysis or peritoneal dialysis) were identified in the case-patient’s center. Statistical analysis was performed to determine significance of the differences observed and calculate odds ratios.

Results: A total of 21 cases were reported from 7 centers. Five cases were excluded because of missing data or uncertain diagnosis. All the patients presented with painful lesions, and 13 patients (81%) were prescribed morphin. Skin biopsy was performed in 10 cases (63%). Univariate analysis comparing the 16 cases with the 32 matched controls identified that the cases had higher body mass index (32.4 ± 6.2 vs 26.2 ± 5.9 kg/m², p<0.001), and were more diabetic (81% vs 28%, p<0.001) and tended to be younger (63.3 ± 10.9 vs 68.7 ± 15.2 years, p=0.058). Warfarin therapy was more frequent in cases (75%) than in controls (22%, p<0.001). Calcium, phosphoremia, and calcium-phosphorus product were higher in cases than in controls (p<0.05). Albuminemia and pre-albuminemia were lower in cases than in controls (p<0.05).

Under treatment, the skin lesions resolved in 8 patients (50%). Sodium thiosulfate was prescribed in 8 patients (50%). As of July 2011, 8 patients were deceased (50%).

Conclusions: The results of this study show that warfarin therapy and lower serum albumin levels are significant and strong risk factors for the development of calciphylaxis in chronic dialysis patients in France. Although mortality is high in CUA, this study suggests a reduction over the last years, possibly explained by the use of sodium thiosulfate or the better identification of this disease.
PROGERIA SYNDROME IN CKD/ESRD

SO001 RENAL IMPAIRMENT ASSOCIATES WITH LESS FUNCTIONAL IMPROVEMENT AFTER ACUTE STROKE

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Introduction and Aims: Despite a progressively higher incidence of stroke in patients with chronic kidney disease (CKD) there is very little data on the presentation and access to acute stroke services in these populations as well as their clinical outcome. We therefore examined the association between renal function and clinical outcome measures within the UK Stroke Improvement National Audit Programme (SINAP).

Methods: This retrospective cohort study examined patients presenting to acute stroke services at our centre [1st Jan 2011 – 1st March 2012]. Patient demographics, laboratory data [inc. full blood count, renal & liver function tests, C-reactive protein and coagulation profile] as well as clinical variables that were recorded as part of SINAP were examined. eGFR was calculated using the CKD-EPI equation with CKD defined by an eGFR<60ml/min. The primary outcome measure was an improvement in the modified Rankin Score [mRS] at discharge and secondary outcome measures included inpatient mortality.

Results: Overall 1805 cases were studied [mean age 69.4±16.6yrs], 1122 [62%] were acute strokes [87% ischaemic, 13% haemorrhagic], 9% transient ischaemic attacks and the remainder stroke mimics. Overall 27% stroke patients had CKD [28% ischaemic vs. 21% haemorrhagic strokes, p=0.09]. 11% patients with ischaemic stroke received thrombolysis however CKD was associated with less thrombolytic use [19% vs. 29%, p=0.03] despite similar times to presentation compared to non-CKD cohorts [p=0.2] and more disability at presentation [median mRS 4 vs. 3, p=0.0001]. Higher eGFR independently associated with a greater chance of improvement in mRS by discharge on multivariate analysis [11% per 10ml/min eGFR, p<0.001]. Older age [p<0.001], lower haemoglobin [p=0.01] and higher white cell count [p=0.003] associated with a higher risk of death but CKD was not [p=0.2].

Conclusions: Renal impairment independently associates with worse functional outcomes despite modern stroke care. Nonetheless these patients are also less likely to be thrombolysed for acute ischaemic stroke, which suggests a possible inequity in access to healthcare that requires urgent study.

SO002 HYPERPHOSPHATEMIA INDUCES INTEGRIN LINKED KINASE EXPRESSION AND LEADS TO CELLULAR SENESCEENCE AND AGING: STUDIES IN VIVO AND IN VITRO

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Introduction and Aims: Hyperphosphatemia has been related to premature aging in the Klotho deficient mice and in the FGF23 KO mice. Serum phosphate levels inversely correlated with species lifespan. Senescence is a cell cycle arrest promoted by the replicative life of the cells or by stressful stimuli. Mechanisms involved in aging induced by hyperphosphatemia are actually unknown. Integrin linked kinase (ILK) is a protein involved in the relationship between cells and surrounding extracellular matrix regulating cellular proliferation and survival. It has been previously described that ILK was increased in old animals. Aims: To explore the role of hyperphosphatemia in renal and vascular aging. We propose that serum phosphate levels increases with aging in mice and promote the upregulation of the ILK expression leading to cellular senescence.

Methods: We compare 3 months old C57Bl 6 mice with 15 months old mice. We analyze serum phosphate by a colorimetric method and the mRNA expression of Klotho, NaPi2a transporter, 1a-hydroxylase and 24-hydroxylase and ILK by real time RT-PCR in kidney. We analyzed the expression of senescent genes, p53 and p16 by western blot in kidney from these animals. To analyze whether hyperphosphatemia induces ILK expression leading to cellular senescence we used human vascular smooth muscle cells (HVSAC) treated with 10 mM beta-glycerophosphate (BGP) during 24, 48 or 72 hours.

Results: We found that 15 month old mice show higher serum phosphate, decreased Klotho expression, increased NaPi2a and 1a-hydroxylase expressions and decreased 24-hydroxylase expression than young animals. Old animals also have a higher αKlotho expression, increased NaPi2a and 1a-hydroxylase and ILK by real time RT-PCR in kidney. We analyzed the expression of senescent genes, p53 and p16 by western blot in kidney from these animals. To analyze whether hyperphosphatemia induces ILK expression leading to cellular senescence we used human vascular smooth muscle cells (HVSAC) treated with 10 mM beta-glycerophosphate (BGP) during 24, 48 or 72 hours.

Conclusion: We conclude that old animals show a decreased expression of Klotho protein disturbing the phosphate homeostasis and leading to the increase in serum phosphate levels. The resulting hyperphosphatemia seem to induce senescence in kidney and vascular cells through the increment of ILK expression.
**NOVEL EPITHELIAL CELL MODELS**

**SO003**
**DIVERSE ROLES OF mTOR COMPLEXES IN TUBULAR FUNCTION**

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**Introduction and Aims:** The serin/threonine kinase mTOR plays a pivotal role in orchestrating cellular homeostasis and stress response and occurs in two distinct multiprotein complexes (mTOR-complex 1 and 2). In mTOR-complex 1, mTOR associates with raptor (regulatory-associated protein of mTOR) whereas in mTOR-complex 2 mTOR associates with rictor (rapamycin-insensitive companion of mTOR). Despite the widespread use of mTOR inhibitors in renal transplantation and renal cell carcinoma only little is known on physiology and pathophysiology of these kinases in tubular epithelial cells.

**Methods:** We studied mice lacking mTOR-complex 1 or mTOR-complex 2 in the renal tubular epithelium. Cell specific deletion of raptor or rictor alleles was achieved by using constitutive Ksp or doxycycline inducible Pax8-rtTA promoter driven Cre lines, respectively. After crossing, these mice were analysed using functional assays, light and electron microscopy, immunfluorescence (IF) and western blotting.

**Results:** All mice were viable. Embryonal deletion of mTORC1 (Raptor fl/fl*KspCre) caused a urinary concentration defect in the thick ascending loop (TAL) resembling Bartter syndrome that was not seen after deletion during adulthood (Raptor fl/fl*Pax8-rtTA). Kidney histology showed impaired mitochondrial biogenesis in Raptor fl/fl*KspCre mice resulting in loss of tubular cells and reduced expression of TAL transport proteins. Deletion of mTORC2 did not result in any obvious phenotype under control nor under low salt conditions in Rictor fl/fl*KspCre mice. However, when challenged with a low salt/high potassium diet or the diuretic triamterene Rictor fl/fl*KspCre in contrast to wt mice rapidly developed salt wasting, hyperkalemia and renal failure despite excessive aldosterone levels. IF revealed absent phosphorylation of SGK1 at Ser422 in Rictor fl/fl*KspCre mice which seems to be critical to allow K+ secretion under reduced cellular Na+ uptake. Rictor fl/fl*Pax8-rtTA similarly developed weight loss upon a low salt/high potassium diet or triamterene treatment.

**Conclusions:** mTORC1 and mTORC2 fulfill distinct roles in renal tubular homeostasis. mTORC2 is essential for the aldosterone mediated renal tubular Na+/K+ handling.

**SO004**
**WHAT IS THE ROLE OF ENaC IN THE Na+ RETENTION OBSERVED DURING DECOMPENSATE CIRRHOSIS?**

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**Introduction and Aims:** Cirrhosis is a frequent and severe disease complicated by abnormal renal Na+ retention, promoting edema and ascites formation. Although many aspects of the abnormal renal Na+ retention in cirrhotic patients are understood, the mechanisms that initiate and maintain renal Na+ retention remain a matter of debate. Which ion transporters are deregulated?

**Methods:** In order to shed some light on the topic, we compared the renal transcriptomes of control mice and mice with decompensate cirrhosis (bile duct ligated) and we investigated the role of amiloride sensitive Na+ Channel (ENaC) in the cortical collecting duct (CCD), portion of the nephron known as responsible for the final regulation of Na+ and water homeostasis. To this purpose we used the CCD specific aENaKO mice and measured physiological parameters as ascites formation, plasma aldosterone levels, hematocrit, Na+ and K+ excretion and the Na,K-ATPase activity in the CCD.

**Results:** The transcriptome analysis revealed a significant up-regulation of 121 transcripts and a down-regulation of 162 transcripts. Surprisingly, we observed no alteration regarding the mRNA abundance of Na+ or water transporters between control and ascitic mice. Moreover, despite increased aldosterone plasma levels in ascitic mice, there was no alteration in mRNA levels known as aldosterone or vasopressin induced/repressed genes. Physiological studies revealed increased plasma aldosterone levels and a decrease in hematocrit after bile duct ligation for both genotypes. The development of ascites occurred in about 30% of the cirrhotic mice genotypes. The development of ascites occurred in about 30% of the cirrhotic mice independently of their genotype. The plasma aldosterone levels increased after bile duct ligation and were higher in mice with ascites.

**Conclusions:** Data from the microarray analysis revealed that the mRNA levels coding for the Na+ and water transporters are not significantly modified suggesting that the regulation takes place at the protein level. The physiological measurements showed that Na+ reabsorption in the CCD through ENaC is not the cause of the inadequate Na+ retention leading to ascites accumulation in decompensate cirrhosis. This raises the question concerning the role of ENaC in the previous segments and about the existence of another mechanism of Na+ reabsorption independent of ENaC.
CONGENITAL ANOMALIES OF KIDNEY AND URINARY TRACT

SO005 LOW BIRTHWEIGHT AND LATER RENAL FUNCTION - THE ROLE OF ADULTHOOD OBESITY. RESULTS FROM THE 1946 BRITISH BIRTH COHORT STUDY

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Introduction and Aims: Low birth weight has been shown to be associated with later renal function, but it is unclear to what extent this is explained by other established kidney disease risk factors. We investigated the roles of diabetes, hypertension and obesity.

Methods: The Medical Research Council National Survey of Health and Development is a socially stratified sample of 5362 singleton children born in one week in March 1946 in England, Scotland and Wales, and followed up since. At age 60-64 years 2192 study members with complete data were analysed. A multiple imputation analysis expanded the analysis sample to 4584. Birth weight was related to three markers of renal function at age 60-64 (estimated glomerular filtration rate (eGFR) calculated using cystatin C, eGFR calculated using creatinine and cystatin C, and urine album-creatinine ratio (uACR)) using linear regression.

Results: Each 1 kg lower birth weight was associated with 2.11 (95% confidence interval (CI) 0.67, 3.55) ml/min/1.73m² lower cystatin C-based eGFR, 2.18 (95% CI 0.85, 3.51) ml/min/1.73m² lower creatinine and cystatin C-based eGFR, and 0.064 (95% CI -0.009, 0.137) log-mg/mmol higher log-uACR. These associations were not confounded by socioeconomic position and were not explained by diabetes or hypertension. There was some evidence that the birth weight-eGFR association was stronger in study members who were overweight in adulthood.

Conclusions: Our findings highlight the role of lower birth weight in renal disease and suggest that in those born with lower birth weight particular emphasis should be placed on avoiding the deleterious effects of becoming overweight in adulthood.

SO006 RENAL ABNORMALITIES IN FAMILY MEMBERS OF INDIVIDUALS WITH CAKUT

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Introduction and Aims: Congenital abnormalities of the kidney and urinary tract anatomy (CAKUT) are common in children and occur in 1 out of 500 newborns. Most cases of CAKUT are sporadic and limited to the urinary tract, but some of them are associated with positive family history. The genetic causes for the nonsyndromic forms of CAKUT are unknown. The objectives of this study are to determine whether CAKUT occur in familial patterns and to identify if phenotypical variability of renal malformations exists in affected families.

Methods: The medical files of CAKUT patients were retrospectively reviewed, and renal and urinary tract abnormalities were recorded for all affected relatives.

Results: We reviewed 1166 patients with CAKUT. Out of these patients, 103 (47 males, 56 females) (8.8 %) patients with the mean age of 3.1±3.7 years had relatives with kidney or urinary tract abnormalities of whom 54 (52.4 %) were the first degree relatives. The most common abnormalities were vesicoureteral reflux in 46 (44.7 %) patients followed by ureteropelvic junction stenosis in 20 (19.4 %), ectopic kidney in 18 (17.5 %), unilateral renal agenesis/hypoplasia-dysplasia in 6 (5.8 %) and multicystic dysplastic kidneys in 5 (4.9 %). Thirteen patients were diagnosed prenatally. Consanguinity was present in 26 (25.2 %) families. The most common abnormalities in relatives were vesicoureteral reflux in 30 (29.1 %), unilateral renal agenesis in 25 (24.3 %) and ureteropelvic junction stenosis in 15 (14.6 %). Same urological abnormality was observed in 32 patients and relatives of which the most common was vesicoureteral reflux.

Conclusions: Some forms of congenital abnormalities of the kidney and urinary tract abnormalities have a familial pattern, involving incomplete and variable penetrance. Molecular genetic studies will give important details of urinary tract morphogenesis in the near future. Family members of CAKUT should be informed and followed carefully for the possible urinary tract abnormalities.
NEW INSIGHTS INTO THE LOOP OF HENLE

PROFOUND AND SYNERGISTIC SALT WASTING BY ACETAZOLAMIDE AND HYDROCHLOROTHIAZIDE: MOLECULAR BASIS AND IMPLICATIONS AS A DIURETIC REGIMEN IN PATIENTS WITH FLUID OVERLOAD

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Introduction and Aims: The carbonic anhydrase inhibitor acetazolamide (ACTZ) is a mild diuretic, hence not widely used in fluid overloaded states. It is however the treatment of choice for certain non kidney conditions such as idiopathic intracranial hypertension, also known as pseudotumor cerebri, glaucoma and acute mountain sickness. Hydrochlothiazide (HCTZ), a specific inhibitor of Na-Cl cotransport, is a mild agent but the most widely used diuretic in the world for control of mild hypertension.

Methods: Sprague Dawley rats (150-200 gm) were placed in metabolic cages and after acclimation were divided into four different groups: 1) Control, 2) HCTZ treatment (4mg/100g BW) for 4 days, 3) ACTZ treatment (100mg/kg BW) for 10 days, and 4) ACTZ treatment for 6 days followed by ACTZ plus HCTZ for 4 more days (a total of 10 days of ACTZ and 4 days of HCTZ). Balanced studies (water intake, urine output, food intake, body weight and urine osmolality) were measured daily, and at the end of the experiments animals were euthanized and their blood and kidneys were collected.

Results: Daily treatment with ACTZ for 6 days caused mild diuresis in rats, with urine output increasing from 11.5 to 24 ml/day, along with ~80% reduction in pendrin expression and ~70% increase in NCC expression in the kidney. Daily injection with HCTZ alone for 4 days caused a very mild diuresis, with urine output increasing from a baseline of 11.5 to 13.7 ml/day. However, treatment of rats that were on ACTZ (above) with daily HCTZ injection increased the urine output from 24 to 59 ml/day on day 4 of HCTZ injection (p<0.01, n=5). Sodium excretion increased by 80% in ACTZ plus HCTZ group and animals developed significant volume depletion, metabolic alkalosis and prerenal failure.

Conclusions:
1. Acetazolamide downregulates pendrin and leaves the thiazide sensitive Na-Cl cotransporter as the major salt absorbing transporter in the distal nephron in the setting of increased delivery of salt from the proximal tubule.
2. Despite being considered mild agents individually, we propose that the combination of Acetazolamide and Hydrochlorothiazide is a powerful diuretic regimen for patients with fluid overload such as those with congestive heart failure or nephrotic syndrome.
3. Patients that are treated with Acetazolamide for its non diuretic effects should avoid taking Hydrochlorothiazide for hypertension due to profound diuretic effect of the combination therapy.
HYPERTENSION IN CKD

**SO049**

**COMPARISON OF THE EFFECTS OF PRE-HD AND HOME BLOOD PRESSURE ON DEATH AND CARDIOVASCULAR OUTCOMES AMONG CHRONIC HEMODIALYSIS PATIENTS: A SUB-ANALYSIS OF OCTOPUS**

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**Introduction and Aims:** There has been reported to be U-shape phenomenon between pre-hemodialysis (HD) blood pressure and the risks of death or cardiovascular disease among chronic HD patients. However, there remains significant uncertainty surrounding the effects of home blood pressure. In the present analysis, we compared the effects of pre-HD and home blood pressure on the risks of death and cardiovascular outcomes among HD patients who participated in OCTOPUS (NDT 2013 in press).

**Methods:** OCTOPUS was a randomised controlled trial which investigated the effects of angiotensin receptor blockade olmesartan among HD patients. The present analysis included 251 patients (54% out of 469 randomised) with morning home blood pressure measurements. At each HD session, pre-HD blood pressure was measured using a standard sphygmomanometer with the patient in supine position after 5 minutes rest. Home blood pressure was measured in sitting position after 5 minutes rest using an automatic device (HITACHI 9700) based on the cuff oscillometric method on the morning of non-HD days. Data on pre-HD and home blood pressure was collected for 6 days (3 measurements for each) every 6 months and the mean value was used in the present analysis. Outcome was composite of death, nonfatal stroke, nonfatal myocardial infarction, and coronary revascularization. The effects of achieved follow-up pre-HD and home blood pressure on the outcome were evaluated using a time-dependent Cox proportional hazards model.

**Results:** At baseline, there were normal blood pressure in 4 (2%), white coat hypertension in 28 (13%), masked hypertension in 6 (3%), and persistent hypertension in 172 (82%). Home systolic blood pressure was 8.3 mmHg lower than pre-HD blood pressure, while home diastolic blood pressure was 2.9 mmHg higher. Although there was trend towards an inverse association between pre-HD systolic blood pressure and the composite outcome (hazard ratio 0.92, 95% CI 0.80-1.06), home systolic blood pressure was tended to be associated with increased risks of the outcome (hazard ratio 1.08, 95% CI 0.96-1.23).

**Conclusions:** Compared to pre-HD blood pressure, home blood pressure seemed to be better in predicting mortality and cardiovascular outcomes.

**SO050**

**INCREASED PULSE PRESSURE IS ASSOCIATED WITH DEPRESSED LOW FREQUENCY POWER OF HEART RATE VARIABILITY IN HAEMODIALYSIS PATIENTS**

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**Introduction and Aims:** Elevated Pulse Pressure (PP) has been associated with adverse outcomes in HD patients and with reduced baroreflex sensitivity in healthy subjects. The aim of the study was to investigate the relationship between PP and autonomic activity evaluated by heart rate variability (HRV) in dialysis patients.

**Methods:** In 42 stable haemodialysis patients continuous 5-hour Holter recordings were obtained during dialysis and repeated five times at 2-weeks intervals. The high-frequency (HF) and low-frequency components (LF) of HRV were calculated every 5 minutes and were averaged during the first and after the third hours of recordings denoted as HF1, LF1 and HF2 respectively. PP was calculated from routine pre and post dialysis blood pressure (BP) measurements.

**Results:** Age was 59±14, females 18 (42.9%), diabetics 18 (42.9%), presence of coronary artery disease(CAD) 10 (23.8%), 183 intradialytic recordings were analysed. BP measurements and HRV parameters in normalised units are shown in table 1.

<table>
<thead>
<tr>
<th></th>
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<th>CAD</th>
<th>P value</th>
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<th>CAD</th>
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<td>PP mmHg (post dialysis)</td>
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<tr>
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**SO050 Figure 1:**

**SO050 Figure 2:**
Repeated measures ANOVA in the 27 subjects who completed five analysable recordings showed reproducibility of all BP and HRV indices ($p>0.05$). Diabetics and patients with CAD exhibited higher PP, decreased LF and increased HF. All BP parameters decreased through dialysis ($p<0.05$) but mean HRV parameters did not. After adjustment for ultrafiltration post-dialysis PP correlated positively with HF (Pearson cor. HF1 0.337 $p$ 0.000 and HF2 0.283 $p$ 0.000) [Figure 1] and inversely with LF (Pearson cor. LF1 -0.346 $p$ 0.000 and LF2 -0.294 $p$ 0.000) [Figure 2].

**Conclusions:** This is the first study to demonstrate inverse correlation between pulse pressure and LF power in dialysis patients. Research is warranted to clarify this association.
**PHOSPHATE: A NOVEL RISK FACTOR FOR CARDIOVASCULAR DISEASE AND CKD PROGRESSION**

SO051

**DELETERIOUS EFFECTS OF PHOSPHATE ON VASCULAR FUNCTION**

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**Introduction and Aims:** Elevated serum phosphate is an independent risk factor for cardiovascular disease. Whether this is a direct effect of elevated phosphate or dependent on changes in intracellular calcium or calcium/phosphate product is unknown. We examined the direct effects of phosphate concentration in human resistance vessels and human umbilical vein endothelial cells (HUVECs).

**Methods:** Surplus adipose tissue was removed from patients with chronic kidney disease (CKD) stage 5 undergoing live donor transplantation and their normal donors. Resistance vessels were dissected and incubated in a physiological saline solution (PSS) with normal (1.18mM) or high phosphate concentration (2.5mM) for 16 hours, then mounted on a myograph. Vasoconstrictor responses to phenylephrine (PE) and vasorelaxation responses to carbachol and sodium nitroprusside (SNP) were measured.

**Gene expression** was studied with PCR. **Results:** Vessels from patients with and without CKD incubated in high phosphate relax less well to carbachol (p<0.05). Vessels from patients without CKD relaxed less well to SNP (p<0.05), this difference is not seen in vessels from patients with CKD.

**Conclusions:** Elevated phosphate decreases endothelium dependent vasodilatation in patients with and without CKD. This may be a marker of endothelial dysfunction, supported by the reduced eNOS protein expression and increased nitrotyrosine expression seen in HUVECs. Elevated phosphate also impairs endothelial independent relaxation in vessels from healthy patients without CKD. In vessels from healthy patients, elevated phosphate may alter cyclic GMP production and guanylate cyclase expression. These experiments indicate direct effects of elevated phosphate on the NO system, and on vascular function, and support the notion that phosphate has direct effects in uremia.

**MAGNESIUM SUPPLEMENTATION PREVENTS PHOSPHATE-INDUCED CALCIFICATION IN HUMAN AORTIC VASCULAR SMOOTH MUSCLE CELLS**

SO052

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**Introduction and Aims:** Patients with chronic kidney disease (CKD) have a high prevalence of vascular calcification as a result of elevated blood phosphate (P_i) levels. Consequently, cardiovascular disease is the leading cause of death in this population. The pathogenesis of vascular calcification is not well understood, but it appears to be a cell-mediated, dynamic and actively regulated process that resembles bone formation. Increasing evidence from in vitro, animal and clinical studies point to an inhibitory effect of magnesium (Mg^{2+}) on this calcification process. The aim of the present study was to delineate the molecular mechanism responsible for the inhibitory effect of Mg^{2+}-supplementation on P_i-induced calcification in human aortic vascular smooth muscle cells.

**Methods:** Human aortic vascular smooth muscle cells (HaSMC) were cultured in DMEM containing 5% v/v fetal calf serum supplemented with MgCl_2 and/or H_2PO_4 reaching a final concentration of 2 and 3 mM, respectively. HaSMC were harvested after 3 and 14 days and calcium (Ca^{2+}) and P_i depositions were determined. Additionally, total RNA was extracted at day 14 using Trizol and used for Real-Time PCR analysis to screen for changes in mRNA expression of genes involved in calcification (RUNX2) and Mg^{2+} homeostasis (TRPM7 and MagT1).

**Results:** Treatment of HaSMC using H_2PO_4 resulted in Ca^{2+} (Fig 1a) and P_i depositions (not shown) after 14 days, which were prevented by Mg^{2+}-supplementation. Additionally, upregulation of RUNX2 a marker of calcification in high-phosphate conditions was prevented by Mg^{2+} -supplementation whereas the expression levels of TRPM7 and MagT1, two genes involved in Mg^{2+} homeostasis, remained unaltered (Fig 1b).

**Conclusions:** Our results demonstrate the potential of Mg^{2+}-supplementation in the prevention of HaSMC calcification that warrants further investigation of genes involved in Mg^{2+}-homeostasis (e.g. TRPM6 and CNNM2).
POLYCYSTIC KIDNEY DISEASE (ARPKD/ADPKD) GETS COMPLEX: GENETIC NETWORK AND MUTATIONS IN MULTIPLE CILIA-RELATED GENES

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Introduction and Aims: Polycystic kidneys paved the way for elucidation of cilia-related disorders and notably most ciliopathies have a renal cystogenic component. Autosomal dominant polycystic kidney disease (ADPKD) is one of the most common Mendelian disorders with a prevalence of 1:500-1000 and typically a late-onset disease caused by mutations in PKD1 or PKD2. About 2% of ADPKD patients show an early and severe phenotype with considerable perinatal morbidity and mortality that can be clinically indistinguishable from the recessive form of polycystic kidney disease (ARPKD) caused by PKHD1 mutations. In addition, other clinically and genetically heterogeneous disease entities may also mimic polycystic kidney disease and have to be taken into consideration.

Methods: We developed a customized NGS (next-generation sequencing) panel that targets all genes for cystic and polycystic kidney disease as well as a bunch of other cilia-related disorders. Overall, our NGS panel allows the parallel investigation of 258 genes with in total 4637 exons.

Results: We demonstrate severely affected PKD patients who carry, in addition to their expected familial germline defect, further mutations that are likely to aggravate the phenotype. We also show that polycystic kidney disease may also be mimicked by mutations in other genes typically causing other ciliopathies, such as nephronophthisis and Meckel syndrome. Finally, we were able to identify mutations in novel genes for cystic and polycystic kidney disease.

Conclusions: Cystic and polycystic kidney diseases get increasingly complex and there is evidence for a genetic and proteomic network with mutations in multiple cilia-related genes. Due to these aspects, we established a novel genetic testing approach based on Next-Generation Sequencing (NGS) that allows simultaneous investigation of 258 genes in a very time- and cost-efficient manner.

AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD); PKD1 AND PKD2 MUTATIONAL SCREENING IN 100 ITALIAN PATIENTS

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Introduction and Aims: Autosomal dominant polycystic kidney disease (ADPKD), the most common inherited kidney disorder with an incidence of 1 in 400 to 1 in 1000 individuals, is characterized by the development and progressive enlargement of renal cysts leading to end-stage renal failure. ADPKD is typically diagnosed by imaging such as ultrasonography, computed tomography, or magnetic nuclear resonance. However, a diagnosis by imaging may be uncertain, especially in young individuals (<30 years) and in individuals with a negative family history. ADPKD is caused by mutations in PKD1 or PKD2 genes. The molecular diagnosis of ADPKD is complicated by extensive allelic heterogeneity and particularly by the presence of six highly homologous sequences of PKD1/exons 1–33. Although, clinical studies and case reports describing one or few families have been reported in Italian population, to date a comprehensive molecular study of ADPKD is still lacking. Here, we report our comprehensive mutation analysis of PKD1 And PKD2 genes in 100 Italian ADPKD patients.

Methods: PKD1 and PKD2 genes were analyzed in 100 ADPKD Italian patients - the largest Italian cohort analyzed to date - by direct sequencing, Multiplex Ligation-dependent Probe Amplification (MLPA) and RNA analysis. The potential pathogenicity of the newly identified missense variants was evaluated by combining different methods: PolyPhen, Sorting Intolerant from Tolerant (SIFT) and Mutation Taster.

Results: We identified the largest number of pathogenic mutations (n= 50) reported in a single study in Italian population. The mutations are of all different type (17 missense, 10 nonsense, 8 splice site, 15 small deletions and insertions) and are spread over the exons of the PKD1 gene. Twenty PKD1 mutations have not been previously described, expanding the spectrum of known ADPKD pathogenic mutations, and 10 were de novo, described in sporadic ADPKD patients, providing in such cases a definitive diagnosis of ADPKD. Of the 20 different novel PKD1/mutations 3 were found in ≥2 unrelated patients in our cohort. Notably, all of these recurrent mutations were found in patients from Southern Italy, a sign of founder mutations.

Conclusions: In summary, we performed a comprehensive mutation screening of PKD1 and PKD2 genes in Italian population. Our study represents a significant advance in the molecular diagnosis of ADPKD Italian patients because (1) analyze the largest Italian cohort to date and report the largest number of new mutations in a single Italian study; (2) describe for the first time new potential founder mutations in ADPKD patients from Southern Italy and (3) emphasize the important role of molecular genetic screening in ADPKD young individuals and sporadic patients for the definitive diagnosis.
NOVEL RISK MARKERS/FACORS FOR PROGRESSION IN CKD

MO001

META-ANALYSIS OF 50 GENOME-WIDE ASSOCIATION STUDIES IDENTIFIES MULTIPLE NOVEL LOCI FOR RENAL FUNCTION AND KIDNEY DAMAGE: THE CKDGEN CONSORTIUM

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Introduction and Aims: Chronic kidney disease (CKD) is a major health issue associated with end stage renal disease and cardiovascular mortality and morbidity. To expand the knowledge of its biological basis, we conducted large-scale meta-analyses of genome-wide association studies (GWAS) of renal function and kidney damage phenotypes.

Methods: Creatinine-based GFR estimated with the 4-parameter MDRD study equation (eGFRcrea), CKD (eGFRcrea < 60 ml/min/1.73m²), urinary albumin-to-creatinine ratio (UACR), and microalbuminuria (MA) were analyzed in 50 population-based studies on European-ancestry subjects. The total sample size was of 133,728 subjects for eGFRcrea/CKD and 52,716 for UACR/MA. Each participating study performed sex- and age-adjusted GWAS of the renal phenotypes on 2.5 million single nucleotide polymorphisms. The results were pooled through inverse-variance weighted, fixed-effects meta-analyses. Genome-wide significance threshold was set to 5x10^-8.

Results: The new analyses confirmed 30 genomic loci previously identified as associated with eGFRcrea and the CUBN locus previously associated with MA, and identified 18 new independent loci for eGFRcrea (P-values from 6.0x10^-13 to 4.7x10^-8). All of them had homogeneous effects between studies (median I² = 2%, range: 0-29%), significant signals were located in the 1,25-dihydroxyvitamin D3 and thereby involved in calcium homeostasis. Other metabolism. The strongest novel signal was located at 20q13 near the = 33,144), which suggests a role in renal function rather than merely in creatinine

Conclusions: The increased sample size of the new GWAS meta-analyses allowed us to uncover a high number of novel loci, most of which are likely involved in renal function regulation. While a detailed characterization of these loci is ongoing, including confirmation through independent replication, the new findings advance our understanding of the biologic mechanisms underlying kidney function and renal damage.

MO002

FUNCTIONAL VARIANTS IN NEPH3 (FILTRIN) AND NPHS2 (PODOCIN) CAN PREDICT PROGRESSION IN PRIMARY HEMATURIC GLOMERULOPATHIES. FURTHER EVIDENCE SHOWS THAT NEPH3 CAN BE A CAUSE OF MICROALBUMINURIA IN THE GENERAL POPULATION

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Introduction and Aims: The wide spectrum of phenotypic expression, ranging from benign isolated hematuria to severe proteinuria and renal failure, is a critical issue in primary hematric diseases, such as Thin Basement Membrane Nephropathy (TBMN) and IgA nephropathy. Main aim of this study is to identify genetic modifiers that are responsible for this heterogeneity and use them as predictive markers of progressive renal impairment. Additionally, we investigate their potential role in the general population.

Methods: We looked in silico for potential functional SNPs in genes expressed in the slit diaphragm (SD). Six variants were genotyped in a cohort of well-studied adult TBMN patients from 19 families, with a homogeneous genetic background. Additionally, we re-sequenced the whole coding region of NPHS2 (podocin). Patients were categorized as "Severe" and "Mild", based on the existence or not of proteinuria, CRF and ESKD. Four more hematric cohorts were used for validation, including IgA nephropathy patients. 6351 DNA samples from the Framingham Heart Study (FHS) cohort were used to investigate if the NEPH3-V353M variant has any renal effect in the general population.

Results: V353M in NEPH3 (filtrin) gave suggestive association (p=0.036), where 353V is highly conserved. The same significance came out for R229Q and E238Q variants from NEPH32 variants together. A pooled hematric cohort of 524 patients (including the IgA nephropathy patients) confirmed theV353M association, under the dominant model (p=0.0017, OR=5.95 adjusting for genotype; allelic association p=5.1x10^-6 adjusting for kinships). R229Q and E238Q variants in NPHS2 gave a borderline significant result for TBMN and CFHR5 familial hematuria cohorts. Genotyping 6531 subjects of the FHS for NEPH3-V353M revealed an association of the homozygous 353M/M genotype with microalbuminuria (p=1.0x10^-6, OR=12.8 adjusting for gender/ age). Co-immunoprecipitation assays showed that 353M disturbs Nephe3 homodimerization and Nephe3-Nephrin heterodimerization.

Conclusions: We showed that variants in SD specific genes may promote the long-term degeneration of the SD integrity healthy subjects or most significantly on the background of another primary glomerular disease. The most significant result concerned the NEPH3 gene, where three independent sample groups and functional studies support a "rare variant-large effect" phenomenon for V353M in renal disease.
FINE-TUNING OF SODIUM TRANSPORT IN THE DISTAL NEPHRON

MO003  EFFECT OF ISOTONIC AND HYPERTONIC SALINE AND ISOTONIC GLUCOSE ON URINARY EXCRETION OF PROTEIN FROM THE AQUAPORIN2 WATER CHANNELS AND EPITHELIAL SODIUM CHANNELS IN HEALTHY HUMANS

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Introduction and Aims: The renal distal nephron plays an important role in the maintenance of sodium balance, extra cellular volume and blood pressure. Urinary excretion of aquaporin2 (u-AQP2) and the γ-fraction of epithelial sodium channels (u-ENaCγ) are currently used to evaluate the water transport via aquaporin-2 water channels and sodium transport via epithelial sodium channels in the principal cells in the distal nephron. In humans, u-AQP2 varies with sodium intake, but the effect of an acute intravenous volume load with isotonic saline, hypertonic saline and glucose on u-AQP2 and u-ENaCγ has never been studied in a randomized, controlled trial in healthy humans.

Methods: We studied the effect of isotonic saline 0.9% (23 ml/kg), hypertonic saline 3.0% (7 ml/kg) and isotonic glucose 5% (23 ml/kg) at the end of three periods each of 5 days duration with wash out periods of two weeks between interventions, in a randomized, placebo-controlled crossover study. The study comprised of 23 healthy subjects, who consumed a standardized diet, regarding calories, sodium and fluid for 4 days before each examination day. GFR was measured as 51Cr-EDTA renal clearance using continuous infusion technique. We measured urinary concentrations of AQP2 and ENaC corrected for creatinine, renal function and sodium handling, vasoactive hormones and systemic blood pressure at baseline and after infusion.

Results: After isotonic saline infusion u-AQP2CR increased (123%), whereas FE Na increased (123%). After hypertonic saline infusion there was an increase in u-AQP2CR (25%), u-ENaCCr(19%) and FE Na (96%), whereas CH2O decreased (-16%), ENaCγ decreased (-153%). After isotonic glucose infusion there was a decrease in u-AQP2CR (-10%) and FE Na (-44%) whereas CH2O increased (164%). Systolic BP, pulse rate and GFR increased slightly and to the same extend during all three infusions. AVP remained unchanged after isotonic saline and glucose, but increased after hypertonic saline (139%). PRC, AngII and p-Aldo decreased after isotonic and hypertonic saline infusion, but not after glucose infusion.

Conclusions: The study documented that u-AQP2 and u-ENaCγ reflects changes in water- and sodium channel activity in the kidney distal tubule during changes in body fluid volumes in healthy subjects.

MO004  STE20-LIKE KINASE SPAK DIFFERENTIALLY REGULATES Na-(K)-Cl cotransporters along the distal nephron under the endocrine control of AVP

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Introduction and Aims: The Na+-K+-2Cl--cotransporter (NKCC2) of the thick ascending limb (TAL) and the Na+-Cl-cotransporter (NCC) of the distal convoluted tubule (DCT) are critical for renal salt handling. Activation of these transporters by vasopressin (AVP) increases their phosphorylation at defined, conserved N-terminal threonine and serine residues. Little is currently known, however, about the kinase pathways that mediate this action of AVP. Two homologous Ste20-like kinases, SPAK and OR1, have been recognized as key enzymes that can phosphorylate the cotransporters directly. In this process, full-length SPAK variant (FL-SPAK) and OR1 interact with a truncated isoform, KS-SPAK, which has inhibitory effects. Our study tested the hypothesis that SPAK is an essential component of the AVP stimulatory pathway.

Methods: To this end, short- and long-term effects of desmopressin (dDAVP), a V2 receptor-specific agonist, on the kinases and transporters were evaluated in wild type and SPAK-deficient mice and in AVP-deficient rats. Western blot, Immunohistochemistry, ultrastructural analysis and co-immunoprecipitation were performed.

Results: SPAK variants displayed prominent regulatory changes along TAL and DCT along with activation of the cotransporters, whereas OR1 was less involved. The KS- and FL-SPAK variants were modulated by AVP for their selective interaction with NKCC2 in control of its activation, whereas the phosphorylation of NCC was essentially governed by FL-SPAK alone.

Conclusions: In sum, our data specify how SPAK may serve as a hallmark kinase in modulating Na+ reabsorption along the distal nephron under the endocrine control of AVP.
ANTIBODY MEDIATED GRAFT DAMAGE

**MO005**

**DIAGNOSIS OF ANTIBODY-MEDIATED REJECTION THROUGH EARLY PROTOCOL BIOPSIES IN SENSITIZED PATIENTS**

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**Introduction and Aims:** HLA sensitized patients are at risk for antibody-mediated rejection (ABMR). This data reinforce the need for surveillance in order to early diagnose and treat humoral processes. Our purpose was to evaluate the importance of early protocol biopsies to diagnosis ABMR in sensitized patients.

**Methods:** From Jul/2010 to Jun/2012, 101 sensitized patients defined as PRA>10% (class I and/or II by Flow-PRA) were transplanted at our institution. Out of them, 60 performed donor-specific antibodies test (DSA) at transplant and a protocol-bx at a median time of 7 days (4-11) and were included in this study. A second for cause biopsy (IB) was done at the physicians’ discretion in 18 patients without previous acute rejection (AR) diagnosis. DSA were analyzed by single antigen bead assays at the time of biopsies which were classified according to Banff’09 criteria.

**Results:** Patients (pts) mean age was 48±12 years, 48 were female (80%), 45 first transplant (75%) and 42 (70%) received a kidney from deceased donor. Thirty four pts never presented AR episodes while 26 did. AR were diagnosed in the first 5 weeks after transplantation (median 13 days) in 20/26 (77%). Day 7 protocol biopsies (PB) showed AR in 12/26 (46%): 10 (85%) ABMR and 2 (15%) T-cell mediated rejection (TCMR). The IB (n=18) done at a median of 11 days from the PB (range 3-112), showed AR in another 14 pts (56%): 10 (71%) ABMR and 4 (29%) TCMR. Pre-Tx mean MFI in ABMR pts did not differ between PB: 6091 (1596-11181) vs IB 2304 (840-14600) (p=NS). It also did not differ at the time of biopsy (2823 vs. 2277 in PB vs IB, respectively; p=NS). ABMR was more severe at the IB (type II; n=7) than in PB (type II; n=3). Patients with early ABMR diagnosis at PB had a trend to higher long-term MDRD (49±12mL/min) compared to patients with ABMR at IB (41±11mL/min) and similar to the whole non-ABMR patients (50±17mL/min).

**Conclusions:** In conclusion, protocol biopsy is useful to diagnosis ABMR as early as in the first week post-Tx. Early recognition of ABMR allows earlier treatment and possibly better long-term graft function in sensitized patients.

**MO006**

**INTEGRATED MESSANGER RNA AND microRNA PROFILES SUGGEST AN INTERFERON ALPHA SIGNATURE IN CHRONIC ANTIBODY-MEDIATED REJECTION (CAMR) OF KIDNEY TRANSPLANTATION**

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**Introduction and Aims:** CAMR is the main causes of chronic graft injury and subsequent graft loss, but its pathogenesis is still largely unclear. The aim of the study was to investigate the molecular mechanisms underlying the pathophysiology of CAMR, integrating microRNAs (miRNAs) and gene expression profiles of peripheral blood mononuclear cells (PBMCs) isolated from CAMR patients and controls.

**Methods:** We enrolled 6 patients with biopsy-proven CAMR and 6 stable transplant recipients with normal graft histology and function (control group). miRNAs and gene expression profiles of peripheral lympho-monocytes isolated from both groups were assessed using Agilent microarrays (60K microarray slides). Our results were evaluated by statistical analysis (unpaired t tests, Benjamini-Hochberg multiple testing correction) and functional pathway analysis (Ingenuity Pathway Analysis) and then validated by real-time PCR in an independent set of patients.

**Results:** The comparison between CAMR and control patients, using a FDR<5% and a fold-change ≥2, revealed that 18 miRNAs were differentially expressed between the two groups. All of them resulted down-regulated in the CAMR group. The principal component analysis showed the ability of these miRNAs to clearly distinguish the two groups. When matching miRNA data with mRNA expression profiles of the two groups, we identified 6 out of 18 differentially expressed miRNAs as being predicted modulators of 14 mRNAs as being predicted modulated by 14 miRNAs resulting as differentially expressed in our gene expression experiments. All 6 miRNAs resulted down-regulated (FC<−2) and, accordingly, their 14 predicted target mRNAs resulted up-regulated in our gene expression microarray results. Ingenuity Pathway Analysis (IPA) performed on all 18 miRNAs demonstrated that 13 of them were connected in the interferon-alfa network (IPA score=38). In addition, IPA assessed on the 14 target mRNAs further confirmed the involvement of the interferon-alpha pathway (IPA score=26). Quantitative real time PCR performed in an independent set of patients (6 CAMR and 6 control patients) of these miRNAs confirmed the microarray data.

**Conclusions:** Our data suggest a key role of interferon-alpha pathway during CAMR and open new perspectives for identification of therapeutic targets.
SODIUM IN KIDNEY FAILURE PATIENTS: NEW OPEN QUESTIONS

Introduction and Aims: Blood pressure (BP) is controlled primarily by Na and water balance because of the infinite gain property of the kidneys to rapidly eliminate excess fluid and salt. Up to fifty percent of patients with essential hypertension are salt-sensitive, as manifested by a rise in BP with salt loading.

Methods: 626 naïve hypertensive patients underwent an acute Na load (310 mEq NaCl in 2 h ev) to monitor the simultaneous changes in BP and renal Na excretion. Genotyping was performed by using novel technique that uses arrays with fluorescent probes and ability to allelic discrimination of 124 SNPs in candidate genes for multiple mid-throughput genotyping (OpenArray, OA). Associations with genetic markers were performed with GLM and chi-squared; logistic regression analysis for salt resistant/sensitive (SR/SS) comparison was also used.

Results: OA genotype association study detected a strong association with variation in MYO32, SIK1 and UMOD. In combined analyses, we found significant epistatic interactions between these SNPs. A genetic profile is a specific combination of variants (ADD1, NCX1, NEDD4L, PRKG1, MYO, MYO32, SIK1 and UMOD). In combined analyses, we found significant epistatic interactions between these SNPs. A genetic profile is a specific combination of variants in terms of SNPs or SNP interactions. Furthermore, we built a genetic profile able to identify the SS and SR hypertensive: those carrying the SS profile display changes in pressure-natriuresis relationship was obtained for each patient by plotting urinary Na excretion in Y axis and mean BP in the X axis. Patients carrying the SS genetic profile resulted in a right shift along X axis, while was vertically steep in SR profile (GLM p<0.0001).

Conclusions: Our finding suggests a clear relationship between Na intake, genetic pathways regulating the contractile state of muscular vascular cells, renal Na excretion and intracellular activity underline pressure natriuresis and salt sensitive phenotype.

HIGH SALT DIET MODULATES DISTRIBUTION OF RENAL VEGF-A AND ITS EXCRETION IN RATS

Introduction and Aims: High sodium intake, a risk factor in hypertension is also considered to affect kidney function and structure. VEGF-A (Vascular Endothelial Growth Factor A), established renal protective factor could be involved in renal response to increased concentration of Nain body fluids and/or to elevated blood pressure.

Methods: Male Wistar rats and SHR (Spontaneously Hypertensive Rats) were maintained on standard (STD, 0.25% Na w/w) or high sodium (HS, 4% Na) diet. After 21-days’ exposure to the diets, rats were anaesthetized and kidneys and urine were collected. PFA-fixed paraffin-embedded slices were used for hematoxylin-eosin (HE) staining or labeling with anti-PCNA (Proliferating Cell Nuclear Antigen) or anti-VEGF-A antibodies. HE slices were used to calculate glomerular injury index (GII). 50 randomly selected glomeruli from each kidney were assessed by a semi-quantitative injury scale: grade 0, entire glomerulus normal; grade 1, injured area up to 25% (minimal injury); grade 2, injured area 25-50% (moderate injury); grade 3, injured area 50-75% (moderate-to-severe injury); grade 4, injured area 75-100% (severe injury). GII was calculated using the formula: GII= [(1 x n1) + (2 x n2) + (3 x3) + (4 x n4)] / (n0+n1+n2+n3+n4), where nx is the number of glomeruli in each stage of injury. Urine was studied to determine osmolality and VEGF-A concentration. VEGF-A concentration was standardized by urine osmolality.

Results: The exposure to high salt diet affected renal glomerular structure in both strains, but the damage was much more pronounced in SHR. Anti-PCNA labeling in the glomeruli was elevated in Wistar rats; in SHR it was independent of the diet and similar as in Wistar HS group. In Wistar rats, GII only slightly increased (0.78 ± 0.17 HS vs 0.95 ± 0.12 STD; p < 0.01). Moreover, SHR maintained on STD diet showed a damage comparable with that observed in HS Wistars. VEGF-A excretion, which was similar in both strains on STD diet, was much more distinct in HS SHR group (16.61 ± 1.77 ng/mOsm HS vs 2.08± 1.60 ng/mOsm STD; p < 0.01). Both parameters: GII and VEGF excretion were positively correlated (r = 0.67; p < 0.05). Anti-VEGF-A labeling revealed a distinct pattern in both strains: in Wistar there were no differences between outer and inner medulla on STD diet whereas after HS diet a lack of labeling in the inner medulla was observed. In SHR on both diets the labeling pattern was similar as in STD Wistars.

Conclusions: The finding that renal excretion of VEGF-A is correlated with the Glomerular Injury Index supports the notion derived from clinical investigations that VEGF may be an early marker of glomerular nephropathy. Distinct pattern of VEGF-A immunoreactivity in the inner medulla could be an index of a predisposition to hypertension.
NEW PERSPECTIVES IN TRANSPLANTATION THERAPY

MO048 MARKERS OF INFLAMMATION, TISSUE DAMAGE AND REGENERATION IN URINARY EXOSOMES FROM TRANSPLANTED PATIENTS

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Introduction and Aims: Exosomes are microvesicles secreted from various types of activated cells. Urinary exosomes are mainly derived from cells of the nephron and carry the surface protein markers of the cells of origin. In this perspective urinary exosomes can be an easily available source of information about the renal condition and the damage degree. The aim of this study was the evaluation of the expression of different markers of inflammation, tissue damage and regeneration by exosomes present in the urine of kidney transplanted patients.

Methods: Urinary exosomes were isolated from 11 control transplanted patients, 9 patients with slow graft function (SGF, defined as creatinine levels > 3 mg/dL on day 5 post transplant, but no need for dialysis) and 10 healthy subjects matched for sex and age. Urine samples were collected 1 (day 1) and 7 (day 7) days after the transplant. Exosomes were obtained from the second fresh morning urine treated with protease inhibitor, centrifuged to eliminate cell debris and Tamm-Horsfall protein and ultracentrifugated at 100000 g for 1 h. As exosomes are smaller than the lower sensitivity limit of the cytofluorimeter, cytofluorimeter analysis was performed after adsorption of isolated vesicles on 4 μm aldehyde–sulphate latex beads. Expression of CD45, CD56 and VEGF-R2 was indicated as geometric mean and values normalized on the CD24 (urine exosome marker). microRNA were isolated using mirVana kit and analysed by quantitative RT-PCR.

Results: A panel of several markers was tested on urinary exosomes. CD45 and CD56 were used as markers of inflammation, and VEGF-R2 as marker of endothelial damage. At day 1 after transplant CD45, CD56 and VEGF-R2 were higher in transplanted patients than in normal subjects. Moreover, CD45 and CD56 were higher in SGF patients in respect to controls. At day 7, CD45, CD56 and VEGF-R2 decreased in control patients and returned to basal levels. In contrast, no decrease was observed in SGF patients, who maintained higher values. Finally, at day 7, an increase in microRNA involved in renal regeneration were observed in both control and SGF patients.

Conclusions: These findings suggest that markers of inflammatory cells, of endothelial damage and of cell regeneration can be detected in the urinary exosomes of transplanted patients. Their levels are correlated with the pathophysiological condition of the graft function and its cellular/molecular causes. These data suggest an interesting diagnostic role for the urinary exosomes.

MO049 ULTRASOUND-BASED DETECTION OF MICROBUBBLES TARGETED TO T-LYMPHOCYTES AS NON-INVASIVE DIAGNOSTIC INVESTIGATION OF ACUTE REJECTION IN DIFFERENT RAT MODELS OF RENAL DISEASE

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Introduction and Aims: Despite the development of novel and powerful immunosuppressive regimen, episodes of acute allograft rejection (AR) after renal transplantation are still a major concern. Since AR is a negative prognostic factor for the development of chronic allograft failure and for long-term graft survival, the early diagnosis and detection of AR is crucial in order to maintain allograft function. Hence, in this study we present a novel ultrasound-based approach to detect and differentiate AR using antibody-coated microbubbles targeted to T-lymphocytes in a rat renal transplantation model.

Methods: 30x10⁶ human T-lymphocytes were injected into adult uni-nephrectomized, allogeneically kidney transplanted rats (Lewis-Brown Norway (LBN) to Lewis). After conjugation with a human anti-CD3 antibody microbubbles were administrated and ultrasound measurements were performed investigating the native as well as the transplanted kidney. Syngeneically (iTX) transplanted rats (LBN to LBN), rats with ischemia/reperfusion injury (IRI, 45 min warm ischemia), and rats subjected to acute cyclosporine A toxicity (CSA) (50 mg/kg for 2 days i.p.) served as controls. In vivo results were confirmed by immunohistochemical detection of T-lymphocytes after post mortem dissection.

Results: Ultrasoundography using T-cell targeted microbubbles clearly detected an increased infiltration of human T-lymphocytes into renal allografts undergoing AR on postoperative day 4 (5.41 ± 1.32 A.U., p < 0.05, n = 5-8 in all groups) when compared to native control kidneys (1.09 ± 0.18 A.U.). Moreover, no differences were found between native kidneys and iTX (0.99 ± 0.30 A.U.), CSA (0.12 ± 0.04 A.U.) and kidneys with IRI (0.46 ± 0.29 A.U.). Quantiﬁcation of ultrasound signal intensity correlated well with results obtained by immunohistochemical analysis.

Conclusions: Antibody-mediated contrast enhanced ultrasound targeting T-lymphocytes is a novel option for the non-invasive assessment of acute allograft rejection in a rat renal transplantation model. This method allows the discrimination of AR from important differential diagnosis like acute tubular necrosis and acute calcineurin inhibitor toxicity. Since it might easily be transferred into clinics it has significant potential to improve the early diagnosis of AR in patients.
AKI: SPECIFIC CAUSES AND CONDITIONS

ACUTE KIDNEY INJURY AFTER HEART- AND/OR LUNG TRANSPLANTATION: RETROSPECTIVE ANALYSIS OF INCIDENCE, RISK FACTORS AND OUTCOME OF 1400 PATIENTS

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Introduction and Aims: Acute kidney injury (AKI) is a severe complication after solid organ transplantation and contributes to increased mortality and morbidity. Long term consequences are chronic kidney disease (CKD) after non renal solid-organ transplantation. In this study we analysed retrospectively renal function of 1476 patients undergoing heart, lung or heart and lung transplantation at the Hannover Medical School between 1996 and 2010. The aim of the retrospective data analysis was to assess the incidence, morbidity and mortality due to AKI and to identify possible risk factors.

Methods: Electronic retrospective data extraction was performed for the patient’s laboratory data (biochemistry and hematology), type of surgery, length of stay on the intensive care unit (ICU), need for renal replacement therapy (RRT), episodes of hypotension, urinary output (UO), use of nephrotoxic medicaments, preoperative concomitant medication and previous medical history. AKI was defined by loss of eGFR > 25%, UO < 0.5 ml/hour for more than six hours, raise of creatinine > 50% compared to baseline (pre-OP or first creatinine at ICU) or absolute increase in serum eGFR > 25%, UO < 0.5 ml/hour for more than six hours, hypotension, urinary output (UO), use of nephrotoxic medicaments, preoperative concomitant medication and previous medical history. AKI was defined by loss of eGFR > 25%, UO < 0.5 ml/hour for more than six hours, raise of creatinine > 50% compared to baseline (pre-OP or first creatinine at ICU) or absolute increase in serum creatinine of more than or equal to 0,3 mg/dl (≥ 26.4 μmol/l). The grade of the AKI was divided into 3 different stages according to the current AKIN-criteria (Acute Kidney Injury-Network).

Results: The incidence for AKI was 40% after single lung tx, 50% after double lung tx, 76% after heart tx and 78% after combined heart and lung tx. Duration of ICU stay, of mechanical ventilation as well as length of hospitalisation correlated with the degree of AKI. 30 mortality correlated with onset of AKI. Independent risk factors were transfusion of blood products during surgery and pre-existing impaired renal function. The data were used to generate a cart analysis for risk prediction for AKI. This retrospective analysis is to our knowledge, the largest patient group of lung transplanted patients.

Conclusions: AKI occurs is an important complication after lung and heart transplantation and contributes to increased morbidity and mortality.

A NEW CLINICAL MODEL FOR POSTOPERATIVE AKI: ROLE OF ENDOGENOUS OUABAIN

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Introduction and Aims: Acute Kidney Injury is a frequent complication of cardiac surgery. A lot of models predicting AKI requiring dialysis (AKI-D) have been proposed, but only few studies focused on milder AKI not requiring dialysis (AKI-ND), which is very common and contributes to several in-hospital outcomes. Endogenous Ouabain (EO) is an adrenal stress hormone with hemodynamic and renal effects. Recently, our research group has reported that higher pre-operative EO levels are associated with a worse renal outcome after cardiac surgery. Our aim is to develop a new risk model of AKI-ND using both clinical aspects and levels of EO as biomarker.

Methods: The primary outcome was AKI according to AKIN stage II. We built predictive risk model (CLIN-AKI) considering clinical variables (age, sex, preoperative EF, basal eGFR, surgery type, hypertension, diabetes, redo-intervention). A further risk score (CLIN-EO-AKI) was developed adding preoperative EO values to the CLIN-AKI score. We selected the Northern New England Cardiovascular Disease Study Group (NNECDSG) model (the only preoperative model for AKI-ND reviewed) for comparison. CLIN-AKI and CLIN-EO-AKI risk score were calculated by rounding off to the nearest 0.5 value the odds ratio in multivariable analysis for AKI.

Results: All models were tested on more than 800 patients admitted for elective cardiac surgery. 79 pts developed AKI (9.9%). EO levels were confirmed strongly associated with incidence of AKI (respectively 2.2%, 9.8%, 17.7% according to EO tertiles; p<0.00001) and clinical complications (total ICU stay and in-hospital mortality). NNECDSG model was confirmed as a good predictor of AKI (AUC 0.73, value comparable to the reference population of NNECDSG). Our CLIN-AKI model has a better predicting power for AKI per se (AUC 0.79 - CI 95% 0.73-0.84). Adding the preoperative EO level to the clinical model AUC increased to 0.83 (CI 95% 0.79-0.87). Inclusion of EO improved the risk prediction over the clinical models alone (AUC difference respectively +0.06, p<0.03 and +0.1 (C.I. -0.14 to 0.03), p<0.01).

Conclusions: We developed a powerful and accurate risk model based on eight simple preoperative variables. This model was greatly improved by the addition of EO level as marker of kidney and vascular subclinical damage. Both these models are straightforward, useful and readily applicable at the bedside.
FOREFRONT IN HYPERTENSION

TO003
ATRASENTAN THERAPY ENHANCED RECOVERY OF RENAL FUNCTION AFTER RENAL ANGIOPLASTY IN EXPERIMENTAL RENOVASCULAR DISEASE

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Introduction and Aims: Despite of technical success, renal angioplasty (PTRA) improves renal function and/or resolves hypertension in only 1/3 of the patients with chronic renovascular disease (RVD). We have shown that chronic treatment with atrasentan, a specific endothelin-A receptor blocker, attenuates functional and structural damage in the stenotic kidney during progression of RVD. We hypothesized that concurrent PTRA and atrasentan treatment will recover renal function more effectively than each therapeutic intervention alone.

Methods: Unilateral RVD was induced in 16 pigs by renal artery stenosis. After 6 weeks, single-kidney blood flow (RBF) and filtration rate (GFR) was quantified in vivo in the stenotic kidney of all RVD pigs using multi-detector computed tomography (MDCT). Then, pigs were randomized as follows: untreated (RVD), chronically treated with atrasentan (RVD+a, 0.75 mg/kg/day, oral), RVD+PTRA (performed at 6 weeks), and RVD+PTRA+a (n=4 each). All pigs were observed for 4 additional weeks. At 10 weeks, in vivo MDCT studies were repeated to determine the impact of treatments. Additional normal pigs were used as controls.

Results: Renal stenosis and hypertension were similar in all RVD pigs before treatments. PTRA similarly resolved renal artery stenosis in RVD+PTRA and RVD+PTRA+a. Atrasentan and PTRA alone reduced blood pressure and improved RBF and GFR in RVD pigs (Figure). However, combination of PTRA+a resulted in a normalization of renal function and a significant decrease in blood pressure, suggesting augmented renoprotection from this combined approach (Figure).

Conclusions: These preliminary results suggest that a concomitant treatment with atrasentan may induce a synergistic beneficial effect on the outcomes of renal angioplasty in chronic experimental RVD. This study shows promising effects of atrasentan as a potential co-adjuvant intervention to improve the recovery of renal function and blood pressure control after PTRA.

TO004
PREDICTORS FOR THE BLOOD PRESSURE LOWERING EFFECT OF RENAL DENERVATION

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Introduction and Aims: Percutaneous renal denervation (pRDN) is a promising treatment for resistant hypertension. However there is a wide range in the BP-lowering effect and ~15% of the treated patients do not respond to pRDN. No predictors for the BP-lowering effect have been identified yet. The aim of this current study is to find predictors for the BP-lowering effect of pRDN. We hypothesize that parameters related to sympathetic activation could predict the BP-lowering effect.

Methods: 53 patients, from a prospective cohort of patients treated with pRDN, are included in this current analysis. Secondary causes of hypertension were excluded. Prior to pRDN, patients collected 24-h urine (creatinine and catecholamines), blood samples were taken (creatinine, plasma renin activity(PRA) and plasma aldosterone concentration(PAC) in supine- and standing-position), and 24-h ambulatory BP (ABPM) was taken. When considered safe, anti-hypertensive drugs were stopped before these tests, since most drugs interfere with the tests. For analysis of the predictive value of these laboratory parameters, only data of patients who stopped antihypertensive drugs are included.

Results: At moment of submission 6 months follow-up data are available of 52 patients (31 males). Mean age was 63 yrs (±12), mean BMI 28.8 (±5.6), mean eGFR 73 mL/min/1.73m², ABPM 165(±21)/98(±12)mmHg, office BP 202(±24)/109(±14)mmHg. Despite the use of on average 3.8 (±1.8) antihypertensive drugs(all at baseline). 30 patients did stop antihypertensive drugs prior to the tests. Univariate analysis shows a positive correlation between respectively office SBP(n=52), PAC (standing)(n=26), norepinephrine(24-h urine)(all at baseline), and a SBP-reduction 6 months after pRDN with regression coefficients of respectively β=0.622(p<0.01), β=0.065(p=0.077). Univariate analysis shows an inverse correlation between respectively eGFR(n=28), the percentage of dipping in the ABPM (1-nighttime SBP/mean daytime SBP)*100%(n=26)(both at baseline), and a SBP-reduction 6 months after pRDN with regression coefficients of respectively β=1.137(p<0.05) and β=0.630(p<0.01). Other parameters show no significant relation with the BP-lowering effect of pRDN.

Conclusions: We have identified possible easily available predictors for the BP-lowering effect of pRDN. More data are needed for a multivariate analysis.

TO004
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Eva E. Vink1, Willemien L. Verloop2, Rianne B.C. Bost1, Michiel Voskuil2, Wilko Spiering3, Evert-Jan Vonken4 and Peter J. Blankestijn1
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Conclusions: We have identified possible easily available predictors for the BP-lowering effect of pRDN. More data are needed for a multivariate analysis.
**RENAL REGENERATION**

**BENEFITS AND RISKS WHEN PUSHING REDifferentiation in the renal cell carcinoma. Wnt/β-catenin pathway in the differentiation process.**

**Introduction and Aims:** miRNA let-7e is considered a global regulator of the differentiation and loss of let-7e results in a reversion of embryogenesis and dedifferentiation in the renal cell carcinoma. Wnt/β-catenin signalling is essential during kidney development as well as in cell differentiation towards renal lineage. But Wnt is also believed to stimulate embryonic stem cell (ESC) proliferation and maintain pluripotency, and its improper regulation is associated with cyst formation in the kidney. Thus, Wnt/β-catenin activation should be tightly regulated. β-catenin production is dependent on Glycogen synthase kinase 3beta (GSK3β) phosphorylation. Serine phosphorylation of GSK3β during stem cell differentiation downregulates miRNA let-7e and the expression of the Wnt9b and Notch2 by RT-PCR. Western blot analysis of GSK3β results of the array. Total RNA was extracted and assayed for gene specific expression Northern Blot tested for the mature miRNA let-7e were analyzed to confirm specific phosphorylation, destabilizing Wnt/β-catenin and PKCβ activity, contributing to tightly regulate Wnt/β-catenin pathway in the differentiation process.

**Methods:** Embryoid bodies (EBs) were cultured with a combination of ATRA and activin A for 1 to 10 days. Silencing miRNA let-7e protocol was performed on differentiated EBs. Cells were collected on day 10 of differentiation and LNA-antiLet-7e was added on days 7 and 9 of differentiation. miRNAs microarray were performed and Northern Blot tested for the mature miRNA let-7e were analyzed to confirm specific results of the array. Total RNA was extracted and assayed for gene specific expression of Pax2, WT-1, Wnt9b and Notch2 by RT-PCR. Western blot analysis of GSK3β serum phosphorylation, β-catenin and PKCβ protein was also performed.

**Results:** miRNA let-7e expression levels were significantly upregulated in cells cultured with retinoic acid and activin A. The differentiation markers Pax2, WT-1, Wnt9b and Notch2 were upregulated and PKCβ protein, GSK3β serum phosphorylation and β-catenin were significantly decreased. miRNA let-7e silencing during stem cell differentiation downregulates miRNA let-7e and the expression of the differentiation markers and upregulates GSK3β phosphorylation, β-catenin production and PKCβ protein. Inhibition of PKCβ in let-7e silenced cells abolished let-7e-derived effects in differentiation markers, and reversed the increase in GSK3βP and β-catenin, thus indicating the direct relationship between PKCβ, GSK3βP and β-catenin.

**Conclusions:** miRNA let-7e is involved in renal differentiation via the modulation of GSK3β phosphorylation and β-catenin production. The inhibitory effect of miRNA let-7e on PKCβ reduces GSK3β phosphorylation and β-catenin production during the differentiation process in mouse embryonic stem cells (mESCs).

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**HUMAN LIVER STEM CELLS CONTRIBUTE TO RENAL REGENERATION AFTER ACUTE INJURY**

**Introduction and Aims:** We recently identified and characterized a mesenchymal stromal cell like population resident in the human liver. This human liver stem cell (HLS) population expresses specific mesenchymal stem cell markers (CD29, CD73, CD44, CD105 and CD146), specific hepatic cell markers (albumin, cytokeratin 8 and 18) and embryonic markers (Oct4, Nanog, Musashi). Moreover, HLSs are able to differentiate into osteocytes, condrocytes, hepatocytes and beta-like cells. When injected in an experimental model of fulminant liver failure, HLSs protect from death and improve liver function and morphology by a paracrine mechanism. The aim of this study was to test whether the action of this unique cell population is limited to the liver or has a broad regenerative potential as a tool for cell therapy of acute kidney injury (AKI). Studies in vivo experimental AKI was induced by intramuscular injection of glycerol in SCID mice and different concentration of HLSCs (75,000, 350,000 and 1x10⁶) or vehicle were intravenously injected at day 3 after injury. Mice were sacrificed 2 days after HLS injection (day 5 after injury). Renal morphology and function were evaluated by histology and by blood urea nitrogen (BUN) and creatinine plasma levels. Tubular cell proliferation was evaluated by 5-bromo-2′-deoxy-uridine (BrdU) incorporation and by staining with antibody against proliferating cell nuclear antigen (PCNA). Apoptosis was evaluated by Tunel. The engraftment capacity of CFSE-labelled HLSCs in the kidney and the possible mechanism of protection were investigated.

**Results:** The lesions observed in mice with AKI injected with vehicle alone at day 5 after glycerol injection, included tubular hyaline casts, vacuolization, and necrosis of proximal and distal tubular epithelium. In AKI mice injected with different doses of HLSCs the tubular lesions were less severe in comparison to those of mice treated with vehicle alone. The morphological recovery was associated with a significant reduction of plasma levels of creatinine and BUN. At 48 hours after HLS administration, we observed a significant increase in tubular cell proliferation. The best results were obtained with the injection of 350,000 HLSCs.

**Conclusions:** The regenerative potential of HLSCs, a mesenchymal stromal cell population resident in human liver, is not limited to liver injury but they are able to accelerate in vivo the recovery of glycerol-induced AKI in SCID mice.

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KIDNEY IN SEPSIS

THE PREDICTIVE VALUE OF URINARY TUBULAR PROTEINS COMPARED TO NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN FOR SEPTIC AND NON-SEPTIC ACUTE KIDNEY INJURY IN THE CRITICALLY ILL

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Introduction and Aims: Acute kidney injury (AKI) is common in critically ill patients and associated with poor outcome, particular when induced by sepsis. There is an ongoing search for biomarkers for early AKI detection and prediction to guide preventive and therapeutic measures to benefit patients. The aim of this study was to find alternative biomarkers than neutrophil gelatinase-associated lipocalin (NGAL) for predicting development of AKI, dependent on predominant etiology and site of renal injury.

Methods: We conducted a prospective observational study in a university hospital intensive care unit (ICU). Seven hundred adult patients were prospectively included for urine measurements at four time-points (T=0,4,8 and 24h) straight after entry. Samples were analyzed after study completion for biomarker expression. Patients were stratified according to the presence of sepsis at entry. We compared urinary NGAL with another up regulated low molecular weight protein, kidney injury molecule-1 (KIM-1), and with the constitutive cytoplasmatic enzymes α- and γ-glutathion-S-transferase (GST). Since, NGAL and α-GST reflect distal and KIM-1 and α-GST proximal tubular injury. Results: Of the 710 patients, 508 subjects were eligible for further analysis. Fifty-seven patients developed AKI (8 septic patients) in de first 48h versus 451 patients without AKI (19 septic patients). The development of AKI in septic patients was significantly higher than in non-septic patients (p<0.008). The rise in excretion of α- and γ-GST preceding AKI was earlier compared to NGAL and KIM-1. However, the predictive values (area under the receiver operating characteristic curve, AUC) for AKI of NGAL and α-GST were above 0.70 and comparable, in contrast to those for γ-GST (AUC=0.60) and KIM-1 (AUC=0.64), suggesting greater distal than proximal tubular injury. The performance difference was similar in predicting septic and non-septic AKI, despite higher biomarker concentrations in sepsis, even in non-AKI (figure 1). Nevertheless, γ-GST was the best predictor of septic AKI (AUC=0.91).

Conclusions: The urinary biomarker excretion preceding AKI differs between constitutive versus up regulated proteins. The data suggest that urinary α-GST is at least as good as NGAL. In predicting AKI and its severity, particular in sepsis, although enhanced release from distal tubusls in the latter increases optimal cutoff values. Differential expression of biomarkers may help to differentiate septic from non-septic AKI.

ASSOCIATION BETWEEN REGIONAL CITRATE ANTICOAGULATION AND ENHANCED PERMEABILITY HEMODIALYZERS LIMITS SEPSIS-ASSOCIATED ACUTE KIDNEY INJURY THROUGH THE INCREASED CLEARANCE OF INFLAMMATORY CYTOKINES (IL-6) AND MICROVESICLES

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Introduction and Aims: During extracorporeal blood purification for sepsis, regional citrate anticoagulation (RCA) inhibits inflammation and decreases mortality. Enhanced permeability (EP) hemodialyzers reduce plasma levels of inflammatory mediators including IL-6. Microvesicles (MVs) are small particles released from activated leukocytes and platelets involved in tissue injury. MVs can transfer proteins and genetic information to target cells. The aims of this study were: 1) to quantify IL-6 and to characterize MV from plasma of septic patients correlating their concentration with outcome; 2) to define a potential role of MVs in the mechanisms of sepsis-associated AKI; 3) to evaluate the synergic role of RCA and EP hemodialyzers in the limitation of sepsis-associated AKI.

Methods: Plasma samples were collected from 10 septic patients to analyze IL-6 (ELISA) and MVs (FACS, Nanosight and RNA profiling). RIFLE/SOFA scores were calculated. CVVH or CVVHD with heparin or citrate (CiCa Multifiltrate, Fresenius Medical Care) and with EP hemodialyzers (Emmi2, Fresenius Medical Care) were performed. In vitro, whole blood or separated leukocytes and platelets were activated by LPS and cytokines in presence or absence of citrate or heparin to evaluate MV release. The biological effects of septic plasma MVs were studied on cultured human kidney-derived endothelial and tubular epithelial cells.

Results: Plasma IL-6 and MV concentrations were higher in septic than non septic or healthy subjects and correlated with severity of illness and mortality. MVs from septic patients expressed HLA antigens Fas-L, CD40-L, integrins and carried mRNAs and microRNAs involved in inflammation and apoptosis. Plasma MVs induced functional alterations and apoptosis of kidney-derived endothelial and tubular epithelial cells. Association between RCA and EP hemodialyzers significantly decreased plasma IL-6 and MV levels. This effect was less marked using heparin as anticoagulant. Similar findings were observed in vitro during CVVH or CVVHD with LPS-activated blood. Citrate significantly reduced the release of MVs from leukocytes and platelets activated by LPS and their ability to induce apoptosis of cultured kidney cells.

Conclusions: During sepsis, MVs are released by activated leukocytes and platelets and their concentrations associated with severity of illness and mortality similarly to IL-6. MVs play a potential role in the pathogenetic mechanisms of AKI. Association between RCA and EP filters may inhibit sepsis-associated AKI through the removal of pro-apoptotic MVs and inflammatory mediators.
MANAGEMENT OF DIABETES IN ADVANCED CKD

TO025

THE NATURAL HISTORY OF PREDIABETES AND NEW ONSET DIABETES AFTER TRANSPLANTATION

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1Research Unit Hospital Universitario de Canarias La Laguna Spain, 2Nephrology Unit Fundació Puigvert Barcelona Spain, 3Nephrology Hospital de Cruces Bilbao Spain, 4Nephrology Hospital Vall d’Hebron Barcelona Spain, 5Nephrology Hospital Virgen de las Nieves Granada Spain

Introduction and Aims: The long-term evolution, beyond 12 months after transplantation, of prediabetes and new onset diabetes after transplantation (NODAT) is scarcely known. Moreover, in stable patients little evidence is available on the evolution from prediabetes to NODAT or the reversibility of both alterations to normal glucose metabolism or the incidence of prediabetes.

Methods: Eight Spanish centers contributed 50-100 non-diabetics scheduled for renal transplantation. Post-operatively, patients underwent oral glucose tolerance test (OGTT) at 3 months and annually during 5 years. Patients were categorized in each period as Normal, Prediabetic: impaired fasting glucose (IFG: glucose ≥ 100 <126 mg/dL), impaired glucose tolerance (IGT: 2 h glucose ≥140 <200 mg/dL) or NODAT (ADA criteria). Prevalence, incidence and changes between these three categories were analyzed. Immunosuppressive therapy was CNI+MMF+low dose steroids in 82.9%.

Results: We evaluated 656 patients at 3 months; 597 at 1yr, 427 at 2yr, 261 at 3yr, 121 at 4yr and 100 at 5yr. At each period 50% had NODAT or prediabetes. NODAT ranged from 14% (3-m) to 25.3% (5yr), and prediabetes from 37.4% (3-m) to 17.6% (5yr). The most frequent prediabetic alteration was IGT: 23.8% (3-m) to 13.6% (5yr). Prediabetes evolved into NODAT (16.3%) or normality (37.2%) and 46.5% remained prediabetic (3 year incidence). Most normal and NODAT patients remained stable during follow-up.

Conclusions: NODAT and prediabetes are highly frequent after renal transplantation. The prevalence of prediabetes seems higher than in the general population (6-8% in Spain). So, its consequences (cardiovascular disease, evolution to diabetes) deserve further study.

TO026

VILDAGLIPTIN IN NEW-ONSET DIABETES AFTER KIDNEY TRANSPLANTATION IS SAFE AND EFFICIENT - RESULTS FROM THE VIENNA VINDOAT TRIAL

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Introduction and Aims: New-onset diabetes after transplantation (NODAT) is a severe complication after kidney transplantation. Randomized studies that evaluate anti-diabetic drugs in these patients are sparse. In spite of the impaired kidney function, β-cell function were assessed by an OGTT one month after study drug discontinuation.

Methods: This randomized, placebo-controlled, double-blind, phase II trial was performed to assess the glycemic control in patients with newly diagnosed NODAT as defined by a 2-hour plasma glucose (2HPG) level ≥ 200 mg/dL. A total of 32 patients were randomized to receive vildagliptin or placebo for 3 months. Patients were counseled regarding life-style interventions. After three months oral glucose tolerance tests (OGTTs) were performed and Hba1c levels along with body mass index (BMI), metabolic and safety parameters were evaluated. Furthermore, possible long-lasting effects of vildagliptin on β-cell function were assessed by an OGTT one month after study drug discontinuation.

Results: There were no differences in baseline data with regard to fasting plasma glucose levels, Hba1c, 2HPG, time after transplantation, immunosuppression, and BMI. In the vildagliptin group 2HPG (vildagliptin: 182.7 mg/dL; placebo: 231.2 mg/dL; p ≤ 0.05) and Hba1c (vildagliptin: 6.1%; placebo: 6.5%; p ≤ 0.05) values were significantly reduced. Furthermore, Hba1c was still significantly reduced one month after study drug discontinuation. Adverse events were mild in nature and occurred at a similar rate in both groups. Life-style modification alone was not sufficient to improve glycemic control.

Conclusions: Vildagliptin was safe and effective in patients with newly diagnosed NODAT after renal transplantation in addition to life-style modification. Trial registration: ClinicalTrials.gov NCT00980356.
ACID-BASE / CELL PHYSIOLOGY

SP001 MDMA (ECSTASY) INCREASES AQUAPORIN 2 EXPRESSION AND REACTIVE OXYGEN SPECIES (ROS) IN NORMAL RATS

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Introduction and Aims: 3,4-Methylenedioxymethamphetamine (MDMA or Ecstasy-Ec) is an amphetamine derivative used popularly as a recreational drug of abuse due to its psychotropic properties. However, Ec also produces hyperthermia, strong seduress, intense thirst, an inappropriate antidiuretic hormone secretion and also a multisystemic toxicity with oxidative stress. The intense thirst induces high ingestion of free water, and together with the increased water absorption produced by vasopressin, an acute hypotension is developed, frequently causing death. As the hypotension is induced rapidly it was carried out experiments to investigate a possible effect of the Ec directly on the water transporter in the rat Inner Medullary Collecting Duct (IMCD), measuring the Aquaporin 2 (AQ2P) expression. At the same time, Oxidative Stress (OS) was studied since it was already reported that Ec can induce the appearance of ROS, which can cause renal tissue damage. OS will be determined by measuring the thiobarbituric acid reactive substances (TBARS) and Glutathione reduced form (GSH). To try to decrease the OS, the antioxidant inhibitor N-acetylcysteine (NAC) was used.

Methods: AQ2P Group - AQ2P expression - rats were maintained on lithium (Li) diet for 5 days to block the Vasopressin action before Ec addition. AQ2P expression was determined by Western Blot techniques in IMCD and measured by densitometric analysis.

Results: AQ2P Group - The densitometric Western Blot AQ2P expression bands analysis revealed that Ec was able to increase the water transporter expression decreased by Li therapy (absence of Vp action): control- 100.00±5.08, Li- 68.28±2.39, Li+Ec- 76.40 ± 0.80 % p<0.05 (n=11). Ec and Ec+NAC Groups - The table shows that Ec increased the TBARS, decrease the GSH evidencing ROS appearance that was protected by NAC.

Conclusions: These results showed that the AQ2P abundance was decreased in the presence of lithium but increased in presence of Li+Ec evidencing a proper effect of this drug to increase IMCD water absorption. The increase of water transporter AQ2P expression in the IMCD, demonstrated that there is another mechanism contributing to the rapid hypotension that occurs with Ec use. The increase of the TBARS and the decrease of GSH showed an Ec-mediated oxidative stress that was prevented by the previous use of NAC. These results showed that the two effects studied can contribute, at least in part, to a rapid malaise, which in turn can lead to a lethal outcome if not corrected correctly and as soon as possible. HCFMUSP, FMUSP, FFM, FAPESP, CNPq, ICPTUSP.

SP003 HYPERKALEMIA(HK) IN CHRONIC RENAL FAILURE PATIENTS (CRF) NOT IN DIALYSIS (ND) AND IN DIALYSIS (5D): NATIONAL OBSERVATIONAL COHORT

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Introduction and Aims: Hyperkalemia (HK) in CRF patients ND or 5D is a dreaded complication prevented by diet, drugs (resin K+ exchangers, loop diuretics, potassium concentration in dialysate) and treated by drugs (insulins, b2-mimetics…) or dialysis. A national observational cohort (Kamescope ®) was launched in January 2012 (n = 700 patients targeted, follow up = 1 year) to assess medical practices and outcomes in the management of HK in CRF ND and 5D.

Methods: Demographic, clinical, biological and therapeutic data of the first 535 patients included in this cohort are analyzed (Criteria of inclusion = Serum K+ > 5.5 mmol / l). This analysis individualized two sub-groups: CRF ND and CRF 5D patients.

Results: 535 patients included (CRF 5D = 428 / CRF ND = 97), mean age = 66.4 ± 17.2 years, mean eGFR (MDRD) in CRF ND patients = 25.6 ± 14 ml / min, mean BP in CRF ND patients (137.7 (s) / 74 (d) ± 14.1 / 9 mmHg), mean BP in CRF 5D patients = 145.6 (syst.) / 72.6 (diast.) ± 15.7 / 17 mmHg). Between “measured weight” and “dry weight” was 1.27 ± 0.6 kg in CRF ND and 2.42 ± 0.6 kg in CRF 5D patients. 32% of CRF 5D patients are treated by Haemodialatation. The average number of session is 3.02 ± 0.35 / week; each session lasts 4.09 ± 1.4 hours. Mean Blood flow of Arteriovenous fistula = 370.3 ± 340 ml / min. The breakdown of vascular access in CRF 5D patients is: arteriovenous fistula: 83% or graft = 5%, Central Catheter = 13%. 5% of CRF ND and 10% of CRF 5D patients had significant clinical event (hospitalization, infection, surgery) 2 months before the onset of HK. Baseline serum potassium level = 6.18 ± 0.2 mmol / l and 6.03 ± 0.4 mmol / l in CRF ND and 5D patients respectively. Concerning acidosis and nutritional status, SDCA= 32.7 ± 3.4 for CRF ND and 21.1 ± 4 mmol / l in CRF 5D; serum creatinine = 397.5 ± 328.2 for CRF ND and 867 ± 279 mmol / l for CRF 5D. Among the potential factors of HK, 13 % had a complication of vascular access and 9 % had been hospitalized in the previous 2 months.

Conclusions: Kamescope ® represents a cohort of 355 CRF ND and 5D patients included in January 2013. From this interim analysis we confirm as expected a higher prevalence of HK in dialysis. For CRF ND patients, HK concerns CRF stage 4-5. The ongoing follow up of this cohort will allow to (1) assess natural history of HK in CRF ND and 5D patients, (2) confirm factor involved in HK and (2) place of preventive and curative measure.

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**SP004**

**ALTERATION OF EXTRA- AND INTRA-CELLULAR CALCIUM CONCENTRATION INDUCED ENDOThelial-TO-MESEnchymal TRANSITION VIA AN INDUCTION OF OXIdATIVE STRESS**

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**Introduction and Aims:** Phenotype transition of endothelial cells (ECs), especially endothelial-to-mesenchymal transition (EndoMT) is suggested as one of the earliest phenomena of vascular complications in chronic kidney disease. EndoMT is a complex process in which ECs lose their specific markers such as vascular endothelial cadherin (VE-cadherin) with an acquisition of mesenchymal cell markers such as α-smooth muscle actin (α-SMA). Extracellular calcium plays a key role in maintaining endothelial cell integrity by an establishment of stable interaction of VE-cadherin between neighboring ECs. In addition, extra- and intra-cellular calcium also functions as the first messenger triggering intracellular signaling cascades in ECs. We investigated the role of extracellular Ca²⁺ depletion in endothelial dysfunction with an elucidation of potential mechanism linking an alteration of Ca²⁺ concentration and endothelial cell dysfunction.

**Methods:** EndoMT was evaluated by morphological changes and an enhanced migration of BAEC as well as a quantitative analysis of VE-cadherin and α-SMA protein by western blot and real-time PCR after exposure of BAECs to different concentration of Ca²⁺. Oxidative stress, the activation of MAPK, and the expression of Src kinase and Snail/slug were evaluated. Intracellular calcium concentration was assessed by Fluo3/AM fluorescence intensity.

**Results:** Ca²⁺ depletion in culture media induced EndoMT of BAEC in a time- and concentration-dependent manner, which was reversible with Ca²⁺ repletion from 6 to 24 hours. Ca²⁺ depletion resulted in reactive oxygen species (ROS) generation via activation of NADPH oxidase and mitochondrial oxidation. Exposure of BAEC to Ca²⁺ depleted media activated ERK1/2 MAPK phosphorylation at 15 minutes. Antioxidants such as NAC, DPI and MitoQ as well as an inhibitor of ERK1/2 MAPK (PD98059, 10 μM) partially inhibited endoMT. A decrease in VE-cadherin expression was associated with an increase in Snail/slug expression as well as an increased degradation of VE-cadherin and Src phosphorylation. Interestingly, Ca²⁺ depletion induced a transient increase in intracellular Ca²⁺ concentration via the release of calcium store from endoplasmic reticulum (ER). Xestospong C (10 μM), an inhibitor of calcium efflux from ER, blocked endoMT induced by Ca²⁺ depletion with an inhibition of ERK phosphorylation.

**Conclusions:** Ca²⁺ depletion induced endoMT by a transient increase in intracellular calcium concentration via Ca²⁺ release from ER, which was followed by ERK MAPK activation. Concomitant increase in ROS generation induced a decreased production of VE-cadherin and an increased degradation, which impaired endothelial cell integrity. This study suggests the key role of Ca²⁺ homeostasis in endothelial function.

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**SP005**

**INVESTIGATION OF THE ASSOCIATION BETWEEN BLOOD SODIUM AND CALCIUM IONS**

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**Introduction and Aims:** Total blood calcium consists of free or ionized calcium (IC) (50%), protein (40-45%) and anion-bound calcium (5-10%). The active part at the cellular level is the IC. When blood becomes alkalotic, hydrogen ions dissociate from albumin and decrease the freely ionized part of the total calcium. In acidemia, the opposite occurs. These have some clinical implications such as hypocalcemia and Chvostek’s sign in respiratory or metabolic alkalosis. We aimed to investigate the effects of blood pH (pH) on IC levels.

**Methods:** We recruited 21811 separate arterial blood gas analysis reports in the study, obtained in different time points and mainly from different patients. Reports were taken in a raw digital format from the blood gas analyzer devices. Results: 4941 (22.65%) reports were gathered from biochemistry laboratory, 4430 (20.3%) from the internal medicine intensive care unit (ICU), 4952 (22.7%) from the anaesthesia ICU, 2540 (11.6%) from chest diseases department and 4984 (22.68%) from cardiovascular surgery ICU. pH levels were between 4.60-7.599 (7.391±0.10), IC levels were between 0.25-2.181 (1.003±0.181) mmol/L, Na levels were between 136,6-148,5 (140,59±7.13) meq/L. Ca²⁺ ion levels were between 0.25-2.181 (1.003±0.181) mmol/L. There was a significant positive correlation between serum Ca²⁺ and Na ions (Spearman’s rho, r=0.241, p<0.001). At the linear regression analysis in the whole group, total Ca²⁺ ion levels fell 0.005 mmol/L in any 1 meq/L increase in Na ions (Figure).

**Conclusions:** Our results show that the levels of total Ca²⁺ and Na²⁺ ions have a significant correlation according to the blood gas analysis reports. The decreasing Na ions reflect increasing Ca²⁺ ions. These data may point to the function of the membrane Na/Ca²⁺ exchanger protein and the neuromuscular functions of these ions. Chart showing the linear, logarithmic and quadratic associations between blood levels of Na and Ca²⁺ ions on 21811 separate blood gas analysis reports.

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**SP006**

**ARTERIAL BLOOD pH SEEMS TO BE LESS IMPORTANT IN DETERMINING THE SERUM IONIZED CALCIUM LEVELS**

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**Introduction and Aims:** We recruited 21811 separate arterial blood gas analysis reports in the study, obtained in different time points and mainly from different patients. Reports were taken in a raw digital format from the blood gas analyzer devices. Results: 4941 (22.65%) reports were gathered from biochemistry laboratory, 4430 (20.3%) from the internal medicine intensive care unit (ICU), 4952 (22.7%) from the anaesthesia ICU, 2540 (11.6%) from chest diseases department and 4984 (22.68%) from cardiovascular surgery ICU. pH levels were between 4.60-7.599 (7.391±0.10), IC levels were between 0.25-2.181 (1.003±0.181) mmol/L, Na levels were between 136,6-148,5 (140,59±7.13), 7.493±0.032) and 9578 (43.9%) pointed to a normal pH (7.405±0.028). There was a significant, but very weak negative correlation with IC levels (Pearson r=0.019, p=0.009). IC levels were significantly different between pH groups; 0.997±0.18, 0.982±0.01, 1.023±0.08, 1.023±0.08 mmol/L in acidemic, alkalenic and normal pH reports, respectively (p<0.001). In acidemic group, pH had a very weak but significant positive correlation with IC levels (Pearson r=0.040, p=0.006). In alkalenic group, pH had a negative very...
weak negative correlation with IC levels (Pearson r = -0.073, p < 0.001). In the normal bpH group, bpH had a very weak negative correlation with IC levels (Pearson r = -0.061, p < 0.001). At the linear regression analysis in the whole group, total IC levels fell 0.0033 mmol/L in any 0.1 increase in bpH (Figure).

Conclusions: Our results show that bpH is not the only determinant of IC levels, beyond binding to serum albumin. There should be other points which change IC levels like renal/endocrine regulatory mechanisms. It is another important point of discussion that the correlation between bpH and IC changes from negative to positive directions with bpH changes. There should be a more dynamic condition than solely binding to serum albumin. We think that further studies should be designed to reveal these associations. Chart of the linear, logarithmic and quadratic associations between bpH and IC levels on 21811 blood gas analysis reports.

EFFECTS OF CITRATE ON PRESSURE-NATRIURESIS IN CRF RAT KIDNEYS

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Introduction and Aims: Correction of metabolic acidosis may ameliorate the progression of renal injury. Renal injury can increase salt-sensitivity of blood pressure. We evaluate whether alkali therapy may affect pressure-natriuresis relationship in chronic renal failure (CRF).

Methods: Sprague-Dawley rats were treated with standard diet (0.9% sodium), and consumed 3% sodium citrate (NaCitrate) or 3% sodium chloride (NaCl) with 20% casein diet after a 5/6 nephrectomy or sham operation, which were sacrificed at week 4.

Results: After 5/6 nephrectomy, the NaCitrate-treated group had higher levels of serum bicarbonate, and glomerular filtration (GFR), and less tubulointerstitial damage indices (TI) than those in the NaCl group (bicarbonate, 21.1 ± 1.0 vs. 28.1 ± 1.78 mmol/L; GFR, 0.19 ± 0.01 vs. 0.15 ± 0.01; TI, 1.55 ± 0.09 vs. 1.94 ± 0.11, respectively). In pressure-natriuresis relationship, NaCl-treated CRF rats were more salt-sensitive than NaCitrate-treated CRF rats. Expression of NHE3 and NKCC2 in the NaCitrate-treated CRF group was significantly decreased, whereas expression of H-ATPase and sodium/bicarbonate cotransporter was not different between the groups. Renal endothelin-1 levels were also decreased in the NaCitrate-treated CRF group, compared to the NaCl-treated CRF group (32.2 ± 3.88 vs. 45.7 ± 1.27 [pg/mL]/[mg/mL], respectively).

Conclusions: We found that citrate as alkali therapy may improve impaired pressure-natriuresis relationship in CRF, which can be mediated with decreased in expression of NHE3 and NKCC2 and renal endothelin-1 levels.
Renaissance Development and Cystic Diseases

SP008 CLINICAL FACTORS PREDICTING RENAL OUTCOME IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD): RESULTS OF THE GENKYST REGISTRY

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Introduction and Aims: Conflicting results have been published regarding clinical factors predicting renal outcome in ADPKD. The Genkyst cohort is a valuable resource for an accurate description of ADPKD, as it aims to include the totality of consenting patients followed in public and private nephrology centers of a unique geographic region, the western part of France.

Methods: All ADPKD consenting patients were included between late 2009 and December 2012, either in nephrology, dialysis, or post-transplantation consultations. Clinical data were collected and molecular analysis of PKD1 and PKD2 genes was conduced.

Results: 1017 patients (551 women and 466 men) from 755 pedigrees were included. Mean age at inclusion was 53.9 years [5.45-89.5, SD = 14.2]. Genkyst cohort is representative of ADPKD at each stage: 13.1% of the patients were at stage 1 of chronic kidney disease (CKD), 15.8% at stage 2, 19.4% at stage 3, 10.7% at stage 4 and 41% at stage 5. Median age at diagnosis was 35 years, and only 28% of the patients were diagnosed during a family survey, whereas 26.2% were diagnosed following radiologic examination for another disease, 23.8% following urological complications and 13% following the diagnostic of hypertension.

Patient at CKD stage 1 were often symptomatic: 48% had already presented urological complications (including flank pain, gross hematuria, cyst infection, kidney stones, or cyst hemorrhage) and 42% had high blood pressure. Median age at ESRD in the total cohort, obtained by Kaplan-Meier curve, was 65 years [0.95 CI: 62.7-67.2] without any influence of the gender (p = 0.243). Patients with PKD1 mutations (81.8% of the pedigrees) reached ESRD at the median age of 57.9 years [56.4-59.5], whereas patients with PKD2 mutations (18.2% of the pedigrees) reached ESRD at 79.7 years [76.9-82.6] (p<0.001). First episode of gross hematuria before 35 years was associated with an earlier onset of ESRD (median age 52.2 years [0.95 CI: 44.9-59.6] vs 66.4 years [63.2-69.5], p<0.001). Patients with early management of hypertension, before 35 years, were the ones diagnosed earlier for ADPKD (median age at diagnosis 27 years vs 38.6 years, p<0.001), and who had the best renal outcome (median age at ESRD 68.8 years [CI 0.95 = 66.7-71.5] vs 54 years [CI 0.95 = 51.6-56.9]). We did not demonstrate the influence of smoking status. In the 551 women, 1132 pregnancies and 1044 births were recorded, fertility rate was similar to general population (51-56.9). We did not demonstrate the influence of smoking status. In the 551 women, 1132 pregnancies and 1044 births were recorded, fertility rate was similar to general population (51-56.9). We did not demonstrate the influence of smoking status.

Conclusions: Thanks to one of the largest cohort of ADPKD patients with clinical and genetic data available, we were able to evaluate clinical factors of evolution to ESRD. Such studies are important in order to define which patients should benefit from the upcoming targeted therapies at an early stage of the disease.

SP009 THE ROLE OF RENAL FUNCTION IN PLASMACOPEPTIN LEVELS IN HEALTHY KIDNEY DONORS AND ADPKD PATIENTS

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1Nephrology UMC Groningen Groningen The Netherlands, 2Clinical Chemistry UMC Groningen Groningen The Netherlands

Introduction and Aims: Plasma copeptin has been shown to be a reliable, stable surrogate of plasma vasopressin. Plasma levels of copeptin are elevated in ADPKD patients and higher levels have been found to predict disease progression. It is presently unknown whether elevated copeptin levels are the result of decreased renal clearance or increase as compensation for an impaired urinary concentration. The aim of this study was to disentangle the role of these two processes using data of ADPKD patients and healthy kidney donors before and after donation in whom GFR decreases without a concomitant impairment in renal concentrating capacity.

Methods: Plasma copeptin levels were measured using a sandwich immunoassay, GFR as 125I-iothalamate clearance and renal concentrating capacity as urine to plasma ratio of urea (U/P urea). In ADPKD patients we measured total kidney volume (TKV) as measure of disease severity with magnetic resonance imaging. Associations were adjusted for age and gender.

Results: ADPKD patients (n=122, age 40±12 yr, male 56%) had significant higher copeptin levels (6.8 lQR (3.4-15.7) pmol/L) when compared to donors (n=134, age 52±10 yr, male 49%), pre- and post-donation (3.8 (2.8-6.3), p<0.001 and 4.4 (3.6-6.1) pmol/L, p<0.001). In donors, copeptin levels did not change significantly after donation (p = 0.17) despite a significant fall in GFR (from 105±17 to 66±10 ml/min, p<0.001). No significant association was found between GFR and plasma copeptin in donors pre- or post-donation (p=0.84 and p=0.41, left figure) whereas a significant association was found in ADPKD patients (St.β=0.50, p=0.001, right figure). When including only ADPKD patients with a GFR range similar as in donors (GFR=34-74 ml/min), this remained significant (St.β=0.28, p=0.008). In ADPKD patients U/P urea was significantly negative associated with copeptin (St.β=0.31, p=0.001), whereas in donors this association was not present pre-donation (p=0.40) and significant, but positive, post-donation (St.β=0.29, p=0.001).

Conclusions: Reduced renal clearance is not the main determinant of elevated plasma copeptin levels in ADPKD. We hypothesize that renal damage and an associated impaired urinary concentration are of greater importance.

SP009 EFFICACY AND SAFETY OF SIRILIMUS IN REDUCING CYST VOLUME IN PATIENTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

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Introduction and Aims: ADPKD is the most common hereditary renal disease, responsible for 8% to 10% of ESRD. Progression is due to the growth of cysts and disruption of the normal tissue. At present there is no definitive treatment for reducing cyst volume and prevent progression. Sirolimus exerts antiproliferative effect and inhibit cyst growth in ADPKD. Animal studies have proved this. AIMS To assess the efficacy and safety of 6 month treatment with sirolimus (along with conventional therapy) as compared to conventional therapy alone in patients with ADPKD.

Methods: Study type and design: Interventional Randomized open label, active control Duration - 6 months Randomized at 2:1 ratio to sirolimus or standard treatment alone.

Inclusion criteria: ADPKD type 1 - after genetic typing Age 18 - 60 years GFR>40ml/min/1.73m2 Urinary protein <0.5g/24hrs Informed consent Exclusion criteria: Urine protein 0.5g/24 hrs or abnormal urinalysis Diabetes mellitus Malignant Psychiatric disorders Hepatitis B,C, HIV Pregnancy and lactation Increased liver enzymes Dyslipidemia Granulocytopenia or thrombocytopenia Co-medication with strong inhibitor of CYP3A4 Hypersensitivity Conventional therapy limb: Patients on RAAS blockers, statins and calcitriol, with target BP<135/85 mmHg, sirolimus limb: sirolimus arm - 20 patients enrolled in sirolimus arm - 40 Patients enrolled in conventional treatment arm - 20 Dropped out due to sirolimus side effects - 5 Lost to follow up - 1 Completed treatment in sirolimus arm - 34 Completed treatment in conventional treatment arm - 20. There was statistically significant increase in proteinuria, total cholesterol and decrease in hemoglobin in sirolimus arm
**SP011 SUCCESSFUL PERCUTANEOUS SCLEROTHERAPY FOR SYMPTOMATIC RENAL CYSTS**

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**Introduction and Aims:** The most common benign masses of the kidney in an adult, renal cysts, are usually clinically silent and do not require specific therapy. Symptomatic renal cysts are associated with flank pain, hypertension (HT)/aggravation of previous HT, hematuria, infection, and obstruction of the collecting system. We have decided to continue the evaluation, started in 2009 in our Nephrology Department, of the safety and efficacy of percutaneous ultrasound guided sclerosing therapy with 96% ethanol of giant, uncomplicated renal cysts. Significant, persistent lumbar pain, associated reducing QoL, and repeated episodes of uncontrolled hypertension were the most frequent indications for the intervention.

**Methods:** Ultrasound guided renal cyst puncture was performed in 48 patients (50 cysts), followed by 96% ethanol intracystic instillation (except in 6 cases, 12.5%, with macroscopic aspect suggesting intracystic infection/hemorrhage), between March 2009 and December 2012. In 10 cases there were giant, highly symptomatic, pericystic cysts in patients diagnosed with Adult Polycystic Kidney Disease. All cysts presented the ultrasound criteria of simple renal cysts and a variable diameter between 6-12.5 cm. We used 96% ethanol for its capacity to safely sclerose the secreting epithelial layer of the renal cyst wall, without affecting the renal parenchyma. The technique consisted of ultrasound-guided puncture with an 18-G needle under local anesthesia with lidocaine 1%, partial aspiration of the content (over 75% of total volume), injection of 96% alcohol solution (up to 25% of the original cyst volume) into the cyst cavity under ultrasound guidance, with partial aspiration of the alcohol solution after 10 to 15 minutes.

**Results:** The median follow-up period after procedure was 22 months (range 3 to 42 months). Cystic lesions were significantly reduced in diameter after sclerotherapy in all 48 patients: the ratio between post and pre-procedural maximum cyst diameter was between 0.21 and 0.87. In two cases, ultrasound examination could not detect anymore the location of the previous cyst, 3 months after the sclerotherapy (100% rate of success), with persistent effect until now. The functional renal parameters (urea and creatinine, eGFR) where not influenced by our procedure, and no other serious local or systemic complication (i.e. infections, hemorrhages, etc) occurred. Local complications, like mild local pain related to ethanol instillation was reported in four cases. Caliceal deformation and/or pelvis compression improved in 2-3 days after instillation of ethanol and episodes of uncontrolled hypertension decreased/disappeared in symptomatic patients (25/48).

**Conclusions:** Ultrasound-guided ethanol sclerotherapy for symptomatic simple renal cysts is a simple, cost-effective, minimally invasive outpatient procedure. Therefore, we recommend it as a therapeutic option only in selected cases, in order to increase the quality of life for this patients.

**SP012 UMOD GENE POLYMORPHISMS AFFECT GFR DECAY IN ADPKD**

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**Introduction and Aims:** Autosomal dominant polycystic kidney disease (ADPKD) is the most common monogenetic nephropathy and an important cause of ESRD, accounting for about 5% of patients requiring dialysis. The number of cysts and their complications are variable among single patients as well as the renal outcome. Phenotypic variability is due to the genetic heterogeneity, with the more common PKD1. However, in ADPKD, eGFR decay (Δ) is related to other “gene modifier” involved in Na handling and hypertension. Uromodulin (Tamm-Horsfall glycoprotein) is the most common protein excreted in the urine of healthy individuals, yet its function remains unclear. Mutations in the UMOD gene result associated to CKD and hypertension. Aim of the study is to evaluate the influence of UMOD in renal outcome in APKD.

**Methods:** 108 pts with APKD regularly followed in outpatient clinic of Nephrology Division of our Hospital, DGF was evaluated at the follow up. Statistical analysis has been performed by GLM adjusted for sex, age, blood pressure, comorbid conditions, therapy and previous renal function.

**Results:** ADPKD patients carrying UMOD CC genotype present a significant (p=0.013) loss of renal function vs TT ones, after 18 months of average follow up. Recoding patients in two groups (UMOD CC+GC vs TT) data were further confirmed (AGFR: -25.5 ml/min (<0.004)).

**Conclusions:** Mutations in the UMOD gene result in a marked decrease in the synthesis of uromodulin, as well as the accumulation of abnormal uromodulin in tubular cells, leading to tubular cell death. This phenomena may play a key role in the worsening of renal failure in APKD.

**SP013 SIGNIFICANCE OF URINARY ANGIOTENSINOGEN AS A BIOMARKER FOR RENAL FUNCTION IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE**

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**Introduction and Aims:** Intrarenal renin-angiotensin-aldosterone system (RAAS) activation has been suggested to contribute to hypertension and renal failure in autosomal dominant polycystic kidney disease (ADPKD). This cross-sectional study evaluated urinary angiotensinogen (AGT) as a potential biomarker to assess renal function in ADPKD.

**Methods:** Urinary AGT was measured in 233 ADPKD patients aged between 18 and 60. Human ADPKD tissues were acquired from two patients with different renal function (case 1, rcr 0.98 mg/dl; case 2, rcr 5.4 mg/dl, predialysis). The glomerular filtration rate (eGFR) was estimated using IDMS-MDRD equation. The association between urinary AGT and both eGFR and total kidney volume (TKV) were evaluated and the localization of intrarenal RAAS components was identified using immunohistochemical study in human ADPKD tissues.

**Results:** The mean age at enrollment was 43.3 ± 9.7 years and 176 (75.5%) were hypertensive. Among them, 115 (65.3%) patients were taking either angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB). Mean serum creatinine (Cr) and eGFR at baseline were 1.1 ± 0.5 mg/dl and 72.5 ± 23.5 ml/min/1.73m2, respectively. The median values of baseline TKV and urinary AGT/Cr were 1126 ml (min. 194.6, max. 5900.9) and 13.7 µg/g (interquartile range, 7.5–35.1), respectively. Urinary AGT/Cr was negatively correlated with eGFR (r = 0.12, P<0.001) and positively correlated with TKV (r= 0.101, P<0.001). Urinary AGT/Cr was significantly elevated in hypertensive group (n= 176, 298 ± 11.2 g/l, P<0.001), but there was no difference between patients with and without the use of RAAS blockers. Immunohistochemical study revealed that AGT was highly expressed in both proximal and distal tubules of ADPKD kidneys. The degree of AGT expression was stronger in ADPKD tissue from early stage (case 1) than from later stage (case 2).

**Conclusions:** Urinary AGT/Cr can be a potential early biomarker to represent concurrent renal function and kidney volume in ADPKD. Strong AGT expression in both proximal and distal tubules around cysts suggests that intrarenal RAAS activation may be caused by cystic compression and ischemic injury in pericystic tubules.

**SP014 APELIN, COPEPTIN AND AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE: TWO OPPOSITE BIOMARKERS ASSOCIATED WITH KIDNEY FUNCTION DECLINE AND CYST GROWTH**

Antonio Lacquanti1, Michèle Buemi1, Rosaria Lupica1, Silvia Lucisano1 and Valeria Chirico1

1Inter Med University of Messina Messina Italy

**Introduction and Aims:** Vasopressin (AVP) plays a detrimental role in autosomal dominant polycystic kidney disease (ADPKD). Copeptin represents a measurable marker of vasopressin secretion and its increased plasma levels seem to be linked to increased cardiovascular events in patients with ADPKD. Apelin represents a vasoprotective hormone, which is known to reduce blood pressure and stimulates renal vasodilation. We therefore hypothesized that in ADPKD patients apelin levels would be increased while copeptin levels would be decreased, and we performed a cross-sectional study to investigate this hypothesis.

**Methods:** 52 ADPKD patients were enrolled and followed until the end of the observation period or the primary study endpoint was reached, defined by the combined outcome of decrease of GFR associated with a total renal volume (TRV) increase.
Abstracts

***SP014***

**Abstracts**

DECLINE IN APELIN CONCENTRATION IN ADPKD PATIENTS IS ASSOCIATED WITH DECLINE IN RENAL FUNCTION AND IMPAIRMENT OF AUDITORY PROPERTIES

**Introduction and Aims:** Growing body of evidence suggests that primary cilium plays a key role in normal physiologic function and defects in cilary function contribute to pathogenesis of autosomal dominant polycystic kidney disease (ADPKD). Outer hair cells of the cochlea convert the motion to electrical activity via their cilia. The aim of this study was to assess the outer hair cell function in ADPKD patients with distortion product otoacoustic emissions (DPOAE).

**Methods:** 34 volunteers (68 ears) followed by the nephrology clinic were enrolled in the study. Hyperlipidemia, diabetes mellitus, history of otologic operation, acoustic trauma, ototoxic drug and presbycusia in high frequencies as well as receiving renal replacement therapy were exclusion criteria. Group 1 ADPKD (n=26 ears), group 2 non-polycystic chronic kidney disease (CKD) patients (n=18 ears) and group 3 healthy control group (n=15 ears) of similar age. They were evaluated in terms renal functions and outer hair cell function. Serum sodium, potassium, urea nitrogen and creatinine levels were detected and blood pressure was evaluated.

**Results:** Apelin levels were significantly lower in ADPKD patients when compared with HS. ADPKD patients, who suffered from a severe CKD (stages IV-V), were characterized by the lowest levels of apelin and the highest copeptin values. Apelin was strictly correlated with osmolality and with markers of diseases severity. Using apelin as dependent variable in a multiple regression model, only the associations with serum sodium, TRV, mGFR and copeptin remained significant. The association between baseline apelin concentration and start of renal replacement therapy (RRT) was associated with a 5% increased risk of ADPKD progression. The decrease of apelin concentration over time demonstrated that the diagnosis of progression of ADPKD is possible by using apelin as marker. Kaplan-Meier curves were generated to assess renal survival in subjects with serum apelin values above and below the optimal ROC-derived cutoff levels. Subjects with apelin values below 68.5 pg/ml experienced a significantly faster evolution to end-stage renal failure. [Figure 2] To identify putative risk factors associated with incidence of ADPKD progression, we performed Cox regression analysis. The decrease of apelin was associated with a 5% increased risk of ADPKD progression. The association between baseline apelin concentration and start of renal replacement therapy (RRT) during follow-up was investigated. Apelin was associated with a hazard ratio for start of RRT of 0.88.

**Conclusions:** In ADPKD subjects, low apelin level is associated with kidney function decline during follow-up, suggesting that it may be a new marker to predict kidney outcome in ADPKD.

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***SP015***

**CILIARY DYSFUNCTIONAL EFFECT OF AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE ON HEARING**

**Berke Ozucu¹, Fumeyza Kazancioglu², Burak Öztürk³, Murat Alay⁴, Bayram Veyiseler⁵, Orhan Ozturan⁶ and Reha Erkoç⁷**

¹Department of Otolarygology Bezmialem Vakif University Istanbul Turkey, ²Department of Nephrology Bezmialem Vakif University Istanbul Turkey, ³Department of Audiology Bezmialem Vakif University Istanbul Turkey

**Introduction and Aims:** Growing body of evidence suggests that primary cilium plays a key role in normal physiologic function and defects in cilary function contribute to pathogenesis of autosomal dominant polycystic kidney disease (ADPKD). Outer hair cells of the cochlea convert the motion to electrical activity via their cilia. The aim of this study was to assess the outer hair cell function in ADPKD patients with distortion product otoacoustic emissions (DPOAE).

**Methods:** 34 volunteers (68 ears) followed by the nephrology clinic were enrolled in the study. Hyperlipidemia, diabetes mellitus, history of otologic operation, acoustic trauma, ototoxic drug and presbycusia in high frequencies as well as receiving renal replacement therapy were exclusion criteria. Group 1 ADPKD (n=26 ears), group 2 non-polycystic chronic kidney disease (CKD) patients (n=18 ears) and group 3 healthy control group (n=15 ears) of similar age. They were evaluated in terms renal functions and outer hair cell function. Serum sodium, potassium, urea nitrogen and creatinine levels were detected and blood pressure was determined. Each patient was evaluated by means of DPOAE and pure tone audiometry (PTA).

**Results:** Apelin levels were significantly lower in ADPKD patients when compared with HS. ADPKD patients, who suffered from a severe CKD (stages IV-V), were characterized by the lowest levels of apelin and the highest copeptin values. Apelin was strictly correlated with osmolality and with markers of diseases severity. Using apelin as dependent variable in a multiple regression model, only the associations with serum sodium, TRV, mGFR and copeptin remained significant. The association between baseline apelin concentration and start of renal replacement therapy (RRT) was associated with a 5% increased risk of ADPKD progression. The decrease of apelin concentration over time demonstrated that the diagnosis of progression of ADPKD is possible by using apelin as marker. Kaplan-Meier curves were generated to assess renal survival in subjects with serum apelin values above and below the optimal ROC-derived cutoff levels. Subjects with apelin values below 68.5 pg/ml experienced a significantly faster evolution to end-stage renal failure. [Figure 2] To identify putative risk factors associated with incidence of ADPKD progression, we performed Cox regression analysis. The decrease of apelin was associated with a 5% increased risk of ADPKD progression. The association between baseline apelin concentration and start of renal replacement therapy (RRT) during follow-up was investigated. Apelin was associated with a hazard ratio for start of RRT of 0.88.

**Conclusions:** In ADPKD subjects, low apelin level is associated with kidney function decline during follow-up, suggesting that it may be a new marker to predict kidney outcome in ADPKD.

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***SP016***

**MUTATIONS OF PKD1, PKD2 AND PKHD1 GENES IN FAMILIES WITH POLYCYSTIC KIDNEY DISEASE IN THE CZECH REPUBLIC**

**Lena Obeclova¹, Jitka Stekrova¹, Jana Reiterova², Veronika Elišáková³, Miroslav Mert³, Milada Kohoutova⁴ and Vladimír Tesar⁵**

¹Institute of Biology and Medical Genetics of 1st Faculty of Medicine, Charles University and General Teaching Hospital Prague Czech Republic, ²Department of Nephrology General Teaching Hospital of 1st Faculty of Medicine, Charles University Prague Czech Republic

**Introduction and Aims:** Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary renal disorder caused by mutations of PKD1 and PKD2 genes and affecting approximately 1 in 500–1,000 births. ADPKD is a systemic disorder causing decline in renal function which often results in renal failure in adulthood. The autosomal recessive form of polycystic kidney disease caused by mutations in the PKHD1 gene is less common than ADPKD but it usually presents in early childhood when up to 50% of affected neonates die of pulmonary hypoplasia. The aim of this work is the optimization of the molecular methods to provide reliable and fast presymptomatic, prenatal and preimplantation diagnostics of polycystic kidney disease.

**Methods:** Presymptomatic DNA analysis has been performed in our laboratory for over 20 years by the linkage analysis using highly polymorphic markers. Nowadays the analysis performed within research projects also includes detection methods as heteroduplex analysis, Multiplex Ligation-dependent Probe Amplification (MLPA) and high resolution melting analysis (HRM). Recently we have added the next generation sequencing as well as a new mutational detection method in the PKHD1 gene which is too complex for conventional detection methods. The mutational analysis of the whole PKD1 gene has been already performed in 66 suspected patients and the duplicated region of the PKD1 gene has been analyzed in 78 patients. The mutational detection in PKD2 has been carried out in approximately 300 patients. Patients for mutational detection were selected on the basis of linkage analysis.

**Results:** So far, probably causal mutations of the PKD1 gene have been detected in 57 families. Only described nonsense mutation p.R401X1 was detected in three nonrelated families and described missense mutation p.E377K1 was detected in two families; other mutations are unique for individual families. 42 mutations are unique for Czech population. The mutational analysis of the PKD2 gene has so far detected probably causal mutations in 38 families. The frameshifting mutation c.203_204insC was identified in 9 families and nonsense p.Q140X in 7 families. Fourteen mutations are unique for Czech population. More than 50% of mutations of the PKD2 gene were localized in the first exon.

**Conclusions:** Determination of localization and type of mutations within the PKD1 and PKD2 genes and their genotype-phenotype correlation improves DNA diagnostics together with the assessment of the clinical prognosis of patients. Supported by the grant project IGA MZCR NT 13090-4 and P2YSK- P25/LF1/2.

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**SP017**

<table>
<thead>
<tr>
<th>Sodium</th>
<th>Potassium</th>
<th>Calcium</th>
<th>Blood-urea-nitrogen</th>
<th>Creatinine</th>
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<td>Group 1</td>
<td>140.7</td>
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<td>Group 2</td>
<td>140.7</td>
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<tr>
<td>Group 3</td>
<td>140.5</td>
<td>4.6</td>
<td>9.6</td>
<td>22.7</td>
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</table>
INCREASED FGF23 AND DECREASED ARTERIAL COMPLIANCE IN EARLY AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

Bülent Gül, Selime Çekiç, Burak Asiltas, Selda Doğan, Nimet Aktaş, Aysegül Oruç, İbrahim Doğan, Alparslan Ersoy, Mustafa Güllülü, Mustafa Yurtkuran and Abdülmecit Yıldız

Nephrology Çekirge State Hospital Bursa Turkey, Nephrology Uludag University Bursa Turkey, Biochemistry Uludag University Bursa Turkey, Cardiology Uludag University Bursa Turkey, Nephrology Şevket Yılmaz Hospital Bursa Turkey

Introduction and Aims: Normotensive (NT) autosomal dominant polycystic kidney disease (ADPKD) patients with preserved kidney functions have left ventricular hypertrophy (LVH) and increased cardiovascular risk (CVR). Elevated levels of FGF23 have been linked to LVH and CVR. Recent studies report elevated levels of FGF23 in ADPKD. We investigated FGF23 levels in ADPKD patients and sought their association with arterial stiffness.

Methods: 54 ADPKD patients with preserved renal functions and 26 healthy subjects were included. Arterial elasticity was assessed by applanation tonometry and serum FGF23 level (Immutopics) was measured. Comparison of the groups was performed with Student t or Mann Whitney U test and correlation analysis was done with Pearson or Spearman test according to normality of the parameters tested.

Results: In the ADPKD group, 23 patients were hypertensive (HT) and using RAS blockers. The mean levels of FGF23 were higher in ADPKD patients compared to controls (Table 1). FGF23 levels were similar in NT-ADPKD and HT-ADPKD patients. Large and small vessel compliances (C1 and C2, respectively) were lower in the ADPKD patients compared to controls. NT-ADPKD patients (n=31) had lower C2 and tended to have lower C1 compared to controls (Table 1). HT-ADPKD patients tended to have lower C1 and C2 compared to controls. HT-ADPKD and NT-ADPKD patients had similar arterial function values. There was no correlation between arterial elasticity parameters and FGF23 levels.

Conclusions: FGF23 was found substantially elevated and arterial compliance was found significantly decreased in early ADPKD patients regardless of hypertension. However there was no significant correlation between FGF23 levels and arterial function parameters. Additional studies are required to determine possible mechanisms of these disturbances and cardiovascular effects of FGF23 in ADPKD patients.

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=26)</th>
<th>NT-ADPKD (n=31)</th>
<th>HT-ADPKD (n=23)</th>
</tr>
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<tr>
<td>Age (years)</td>
<td>35 (24-53)</td>
<td>28 (19-64)</td>
<td>44 (29-68)</td>
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<tr>
<td>eGFR (ml/min/1.73m²)</td>
<td>116.9±12.8</td>
<td>104.4±16.8</td>
<td>95.9±12</td>
</tr>
<tr>
<td>FGF23 (RU/ml)</td>
<td>39.8 (4-82.6)</td>
<td>423.4 (65.3-1770)</td>
<td>333 (60.4-927.7)</td>
</tr>
<tr>
<td>C1 (ml/mmHgx10)</td>
<td>14.8±5</td>
<td>12.1±4.3</td>
<td>12.8±4.3</td>
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<tr>
<td>C2 (ml/mmHgx100)</td>
<td>6.5 (2.8-15.7)</td>
<td>4.9 (1.6-10.2)</td>
<td>4.9 (1.8-11.8)</td>
</tr>
</tbody>
</table>

eGFR: estimated glomerular filtration rate. C1: large artery elasticity index, C2: small artery elasticity index. ADPKD: autosomal dominant polycystic kidney disease, NT: normotensive, HT: hypertensive, NS: not significant

*p* comparison between controls and NT-ADPKD, controls and HT-ADPKD, and NT-ADPKD and HT-ADPKD respectively
HYPERTENSION - HUMAN STUDIES

SP018 PATIENT-LEVEL FACTORS ASSOCIATED WITH CEREBROVASCULAR EVENTS IN MAINTENANCE HEMODIALYSIS

Albert Power1, Neill Duncan1, Charles Pusey1, Len Usyvay1, Cristina Marrilli1, Peter Kotanko2 and MONDO Consortium.

1 Imperial College London United Kingdom, 2 Renal Research Institute New York United States, 3 Fresenius Medical Care Bad Homburg Germany, 4 Fresenius Medical Care Latin America Buenos Aires Argentina, 5 MONDO Consortium New York United States

Introduction and Aims: Stroke remains a major cause of disability and mortality in hemodialysis (HD) patients with studies deriving predominantly from US & Japanese cohorts. By contrast the worldwide variability in stroke epidemiology is poorly characterized and associations between treatment parameters and stroke are not well explored.

Methods: The MONitoring Dialysis Outcomes [MONDO] consortium consists of HD databases from Renal Research Institute [RRI] clinics in the US, Fresenius Medical Care [FMC] clinics in Europe, Asia Pacific [AP], Latin America [LA], RII clinics in Germany, Imperial College in UK, Hadassah Medical Center in Israel, and University of Maastricht, Netherlands [Usyvay et al, Blood Purif 2013]. Databases from RRI, FMC Europe [17 countries] & FMC Latin America [FMC LA, 5 countries] identified all patients with in-center treatments [1/2000-12/2012] who survived ≥12 months on HD. Only those with ≥1 all-cause hospitalizations were included [assuring proper recording] and hospitalizations for stroke were studied. The mean of clinical & laboratory parameters were computed for the whole patient exposure time.

Results: We studied 27,252 patients [FMC Europe n=14,742; FMC LA n=6,690; RRI n=5,620]. Overall 2% of the cohort [n=575] experienced stroke events [Table 1; p-values shown if <0.1]. Older age, cerebrovascular comorbidity, higher mean pre-diastolic systolic blood pressure [SBP] and variability in SBP, and lower serum creatinine levels were associated with stroke across all databases. Diabetes was associated with stroke in Latin America & RRI but not in Europe. Lower EDWG was associated with stroke in Europe & Latin America but not in the US. Albumin and nPCR appeared to be lower in the patients with stroke events although not always significant.

Conclusions: Higher predialysis SBP variability is associated with stroke on HD populations suggesting a potential role for cerebral perfusion instability. We confirm known associations between age, diabetes, pre-existent cerebrovascular disease and hypertension. In contrast to studies in non-dialysis patients we do not find an association between EPO dose and stroke. Interventional trials of blood pressure management on stroke are recommended.

Table 1. Cochrane Systematic Review

<table>
<thead>
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<th>Parameter</th>
<th>MD</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office Systolic BP (mm Hg)</td>
<td>135.4±12.7</td>
<td>134.4±10.7</td>
<td>NS</td>
</tr>
<tr>
<td>Office Diastolic BP (mm Hg)</td>
<td>84.9±8.0</td>
<td>84.4±5.3</td>
<td>NS</td>
</tr>
<tr>
<td>Home Systolic BP (mm Hg)</td>
<td>127.9±11.6</td>
<td>122.5±8.6</td>
<td>NS</td>
</tr>
<tr>
<td>Home Diastolic BP (mm Hg)</td>
<td>80.4±6.6</td>
<td>75.0±6.9</td>
<td>0.002</td>
</tr>
<tr>
<td>Central BP (mm Hg)</td>
<td>132.5±15.7</td>
<td>132.7±14.1</td>
<td>NS</td>
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<tr>
<td>24-h Ambulatory Systolic BP (mm Hg)</td>
<td>129.2±14.3</td>
<td>123.3±8.8</td>
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<tr>
<td>Night-time Ambulatory Systolic BP (mm Hg)</td>
<td>125.8±16.2</td>
<td>117.4±11.5</td>
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</tr>
<tr>
<td>Day-time Ambulatory Systolic BP (mm Hg)</td>
<td>130.2±14.0</td>
<td>125.7±9.1</td>
<td>NS</td>
</tr>
<tr>
<td>24-h Ambulatory Diastolic BP (mm Hg)</td>
<td>80.6±8.5</td>
<td>79.3±5.9</td>
<td>NS</td>
</tr>
<tr>
<td>Night-time Ambulatory Diastolic BP (mm Hg)</td>
<td>77.0±10.0</td>
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<td>Day-time Ambulatory Diastolic BP (mm Hg)</td>
<td>81.6±8.5</td>
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<tr>
<td>24-h Systolic Blood Pressure Variability</td>
<td>8.8±2.3</td>
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<td>24-h Diastolic Blood Pressure Variability</td>
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<td>6.6±1.3</td>
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<tr>
<td>24-h Mean Arterial Blood Pressure Variability</td>
<td>7.3±1.9</td>
<td>6.3±1.2</td>
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SP019 URINARY PODOCYTE PREDICTS EARLY PHASE OF HYPERTENSION-INDUCED GLOMERULAR INJURY

Zong Li1,2, Xiaojiao Wang1, Xiaoli Yuan1, Juan Wang1 and Lining Wang1,2

1 Department of Nephrology, First Hospital of China Medical University Shenyang, China, 2 Institute of Nephrology, China Medical University Shenyang China

Introduction and Aims: Hypertension can induce chronic kidney disease with proteinuria and loss of renal function. Urinary podocyte excretion has been shown to associate with proteinuria and severity of active glomerular injury in several glomerular diseases. In the present study, we aimed to investigate whether podocyte was present in urine of hypertensive patients with negative proteinuria, and could be used in clinical as a predictor for early phase of glomerular injury induced by hypertension.

Methods: Urine samples clean-catch in the morning were obtained from 18 primary hypertension patients with negative proteinuria (9 male and 9 female) and 10 age-matched normotension subjects (5 male and 5 female) as control. To identify podocyte excretion in urine, urinary sediment was detected by immunocytochemistry staining using anti-Nephrin and anti-CD2-associated protein (CD2AP) antibodies. The concentration of urinary microalbumin (U-mALB), serum creatinine (Cr), serum uric acid (sUA), low-density lipoprotein cholesterol (LDL-C) and triglycerides (TG) were also measured.

Results: Urinary podocyte with either Nephrin or CD2AP positive expression was detected in 11 of total 18 hypertension patients (61.1%), while there was no Nephrin and CD2AP expression in normotension subjects. During the urinary podocyte positive subset, Nephrin was detected in 10 patients, CD2AP in 6 patients and both of them in 5 patients. The concentration of U-mALB was significantly higher in urinary podocyte positive subset compared with negative subset (P<0.005), and urinary podocyte was detected even in patients with U-mALB concentration lower than measurable range. There was no significant difference in age, blood pressure, sCr, sUA, LDL-C and TG between the two subsets of hypertension patients. According to Pearson correlation analysis of urinary podocyte with other clinical features, it showed a positive correlation between urinary podocyte and U-mALB (r=0.645, P=0.004).

Conclusions: Podocyte can be detected in urine of hypertension patients with negative proteinuria, suggesting that urinary podocyte excretion, as a sensitive marker, may be used in clinical for predicting early phase of hypertension-induced glomerular injury.
an increased risk of target organ damage independent of blood pressure. We aimed to evaluate the relation among endothelial functions determined by flow mediated vasodilatation (FMD) with blood pressure levels obtained by OBP, HBPM, CBP, ABPM and BPV in renal transplant recipients.

Methods: OBP, HBPM, CBP, ABPM were obtained from renal transplant recipients with a diagnosis of hypertension. BPV was calculated using the average real variability index. Patients were divided into two groups as patients with or without endothelial dysfunction according to FMD. Predictive value of different measurement techniques and BPV on endothelial functions were investigated.

Results: Seventy-three kidney transplant recipients were enrolled. 68.5% of the patients had endothelial dysfunction. Blood pressure values measured by different techniques in both groups are presented in Table. Patients with endothelial dysfunction had significantly higher ambulatory blood pressure values and higher BPV. There was no difference in other blood pressure values. There was a negative correlation between FMD with 24-h mean and systolic ARV (r=−0.262; p=0.02 and r=−0.376; p=0.001 respectively). Other blood pressure parameters were not correlated with FMD.

Conclusions: ABMP and BPV are the most closely related blood pressure parameters with endothelial functions in renal transplant recipients.

**SP021**

**THE EFFECT OF PERCUTANEOUS RENAL DENERVATION ON MUSCLE SYMPATHETIC NERVE ACTIVITY IN HYPERTENSIVE PATIENTS**

Eva E. Vink1, Laima Siddiq2, Willemlen L. Verloop3, Leonard J. van Scheven3, P. Liam Cey1 and Peter J. Blankestijn1

1Nephrology University Medical Center Utrecht Utrecht The Netherlands, 2Cardiology University Medical Center Utrecht The Netherlands, 3Medical Technology and Clinical Physics University Medical Center Utrecht Utrecht The Netherlands

Introduction and Aims: The rationale of percutaneous renal denervation (pRDN) is based on extensive studies suggesting that efferent and afferent renal nerves contribute to hypertension and that they comprise a sensible target treatment. Muscle Sympathetic Nerve Activity (MSNA) by microneurography is a reliable method to quantify sympathetic activity. An important limitation of the available studies investigating the effect of pRDN on MSNA is that patients used diverse antihypertensive drugs with various effects on MSNA during the recordings. The aim of this current study is to determine the effect of pRDN on MSNA in a standardized fashion: after cessation of antihypertensive treatment or under the exact same medication.

Methods: 13 patients with a systolic BP of ≥160 mmHg despite the use of ≥3 antihypertensive drugs or the inability to follow a stable drug regimen due to unacceptable side-effects, meeting inclusion- and exclusion criteria for treatment with pRDN were included in this study. Before pRDN and 6 months after pRDN MSNA was determined. Anti-hypertensive medication was stopped before MSNA. If cessation of medication was considered unsafe, a patient was instructed to use the exact same medication twice.

Results: 12 patients completed follow-up. In total 10 (6 female) sets of measurements were of good quality and were used for analysis. The mean age at study entry was 57 yrs (±10), mean BMI was 30.2 (±5.8), mean GFR was 85 (±18) mL/min/1.73 m². Mean 24-h ambulatory BP was 175 (±19)/100 (±7) mmHg despite the use of on average 4.3 (±1.5) different antihypertensive drugs. MSNA was determined twice during a medication free interval in 5 patients, 1 patient used the exact same medication and 4 patients used different drugs. No pRDN-related serious adverse events were observed. Resting BP was 206 (±23)/116 (±12) mmHg before and 186 (±20)/106 (±9) mmHg 6 months after pRDN (p=0.10). 7/10 patients showed clinically relevant reductions in BP (decrease of systolic BP ≥10 mmHg) 6 months after pRDN. Resting heart rate was 70 (±10) bpm before and 67 (±6) bpm after pRDN (p=0.75). Resting MSNA was 40 (±18) bursts/min and 44 (±12) bursts/min (p=0.344) after pRDN. Changes in BP did not correlate with changes in MSNA (p=0.336) or heart rate (p=0.521)(fig. 1). GFR did not change (p=1.0).

Conclusions: Treatment with pRDN did not result in a change in MSNA. Changes in BP did not correlate with changes in MSNA. More research on the effect of pRDN on MSNA has to be done.
resistant HTN-dedicated outpatient clinic, 135 patients were evaluated, of whom 23 (17%) were submitted to RDN with radiofrequency catheters (Symplify®; n=21; EnligHTN®; n=2).

**Results:** Mean age was 62.8 years, 61% were men, 62% were obese (mean body mass index 31.5±6.8 kg/m²), 78% had diabetes, 44% had vascular disease (any territory), 9% had sleep apnea syndrome and 95% had left ventricular hypertrophy (95% mean left ventricular mass index 170±57 g/m²). Most of the patients (83%) had normal renal function, had sleep apnea syndrome and 95% had left ventricular hypertrophy. Before RDN, the mean SBP was 172 ±24 mmHg and diastolic BP (DBP) 90±20 mmHg. In the 24th ambulatory BP monitoring the mean SBP was 150±22 mmHg and the DBP was 84±17 mmHg. Patients were taking on average 5.7±1.0 BP drugs. Regarding safety, there were no vascular access complications and no renal artery dissections; There was one case with significant renal artery stenosis after RDN (accessory artery with diameter <4 mm). Of the 13 patients with complete 6 months follow-up, 9 were responders (69% response rate). A significant office SBP reduction was documented - 169±25 to 140±18 mmHg, p=0.004 (Figure) and there was a trend for reduction in DBP (93±19 to 83±10 mmHg, p=0.052), and a significant reduction in albuminuria/creatinuria (mg/g) ratio was reported (678±216 to 322±96).

**Conclusions:** In this cohort of patients with resistant hypertension, renal sympathetic denervation was safe and effective, with a significant blood pressure reduction and proteinuria at six months follow-up.

<table>
<thead>
<tr>
<th>SP023</th>
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</thead>
<tbody>
<tr>
<td><strong>Mean age</strong></td>
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<td><strong>BMI</strong></td>
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<tr>
<td><strong>Diabetes</strong></td>
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<td><strong>Vascular disease</strong></td>
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<td><strong>Sleep apnea syndrome</strong></td>
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| **Introduction and Aims:** Peritubular capillary (PTC) loss has been proved to be associated with renal function in diabetic nephropathy patients, but has never been studied in malignant hypertension (MHT). This study is aimed to observe the PTC loss as well as clinico-pathological characteristics of essential MHT (EMHT) and IgA nephropathy associated MHT (IgAN-MHT).

**Methods:** 1.9% (34) IgAN-MHT patients were diagnosed in the 1765 cases of IgA nephropathy in the past 10 years in our hospital. 52 patients with EMHT confirmed by renal biopsy were enrolled as the EMHT group. The clinical records were reviewed and the lesions of 482 renal small arteries and 818 arterioles were re-evaluated. The peritubular capillary (PTC) was demonstrated by immunohistochemical staining of CD34 (a specific marker for vascular endothelium) and compared with 19 glomerular minimal lesion (GML) patients.

**Results:** Both the IgAN-MHT and EMHT patients were mainly young males (71% vs 92% male, p=0.0088) and have very high blood pressures. When compared with EMHT patients, the IgAN-MHT patients showed more severe urinary proteins and glomerular sclerosis lesions, but less severe scripture (Scl) erosion and tubulo-interstitial injuries. The lesions of renal small arteries and arterioles were also less severe among IgAN-MHT patients than the EMHT group. Among all the vascular lesions, only the arteriolar occlusion proportion in EMHT group correlated with renal function. The PTC proportion was decreased in both IgAN-MHT (2.98±0.51%, P=0.001) and EMHT (2.24±0.73%, P=0.001) patients compared with the GML control group (3.75±0.79%), and was lowest in the EMHT group. The PTC proportion correlated well with renal function in EMHT group and all MHT patients.

**Conclusions:** Our IgAN-MHT patients had a less prominent PTC loss than the EMHT patients. And the PTC proportion, instead of renal vascular lesions of small arteries and arterioles, correlated well with renal function impairment in malignant hypertension patients.

**SP025**

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<th>SSHTN</th>
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<th>C-NSD</th>
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<tr>
<td><strong>CD4</strong>&lt;sup&gt;+&lt;/sup&gt; cells/mm&lt;sup&gt;3&lt;/sup&gt;</td>
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<td>17.9±2.29&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>0.25±0.01</td>
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<td><strong>IL-2</strong>&lt;sup&gt;+&lt;/sup&gt;</td>
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<td><strong>IL-6</strong>&lt;sup&gt;+&lt;/sup&gt;</td>
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**Methods:** We studied male SD rats that received LNAME (70 mg/100 ml in the drinking water) for 3 weeks followed by 4 weeks of a high salt (4% NaCl) diet (SSHTN group, n=17) and rats treated similarly given in addition 20mg/kg/day of furosemide compared with the control group (C-NSD group, n=20). Pressure natriuresis was evaluated after 6 weeks in the test diets by standard methods using an aortic clamp to modify renal artery pressure (RAP) and standard methods using an aortic clamp to modify renal artery pressure (RAP) and obtained stable measurements at 90, 110, 130 and 150 mmHg of RAP. Angiotensin II (AII) levels were followed every 2 weeks, and was lowest in the EMHT group. The PTC proportion correlated well with renal function in EMHT group and all MHT patients.

**Conclusions:** Impairment in pressure natriuresis and hypertension correlate with the severity of renal inflammation in SSHTN.
Baseline patient characteristics and clinical data were collected. The pathological scores under went renal biopsy and ambulatory blood pressure monitoring. Patients were The study involved 341 adult IgAN patients in CKD1 -3 stage, all of whom had blood pressure rhythm variation in IgAN patients.

We aimed to determine renal pathological and clinical parameters associated with subsequent deterioration in renal function than dippers, which is independent of blood pressure level and other risk factors for renal impairment. However, it is still unclear upon the contributing factors for blood pressure rhythm variation in CKD patients. We aimed to determine renal pathological and clinical parameters associated with blood pressure rhythm variation in IgAN patients.

Methods: The study involved 341 adult IgAN patients in CKD1 -3 stage, all of whom underwent renal biopsy and ambulatory blood pressure monitoring. Patients were excluded if they were taking antihypertensive drugs, glucocorticoids for treatment. Baseline patient characteristics and clinical data were collected. The pathological scores were performed according to the IgAN Oxford score. Influencing factors of blood pressure rhythm abnormality were determined by Spearman correlation analysis and logistic regression analysis.

Results: The prevalence was 73.0% (249 cases) for IgAN patients with non-dipper blood pressure, 73.8% (93 cases) for IgAN patients with non-dipper blood pressure combined with hypertension and 72.4% (156 cases) for patients with normal blood pressure.Age, uric acid, Up/Cr, 24 h urinary sodium and urinary C3 excretion levels were significantly increased in patients with non-dippers blood pressure, compared with those with dippers blood pressure. Regardless of blood pressure level normal or not, the male non-dipper patients had significantly higher uric acid levels than those with non-dippers blood pressure, while the female patients showed difference only in the hypertension group. The prevalence of non-dippers blood pressure was gradually increased along with higher IgAN MEST score in IgAN patients. The prevalence of non-dippers blood pressure was positively related with age, serum creatinine, uric acid, Up/Cr, 24 h urinary sodium, tubular atrophy/interstitial fibrosis, arteriolar hyalinosis and arteriolar hyalinosis but negatively correlated with eGFR. Results of logistic regression analysis showed that no matter with or without hypertension, Up/Cr, 24 h urinary sodium, tubular atrophy/interstitial fibrosis, arteriolar hyalinosis were associated with abnormal blood pressure rhythm. For the patients combined with hypertension, eGFR, uric acid and interstitial inflammatory infiltration were correlated with abnormal blood pressure rhythm besides of the factors mentioned above.

Conclusions: Excretion of urine protein and sodium, tubulointerstitial injury including tubular atrophy/fibrosis and arteriolar hyalinosis are associated with abnormal regulation of blood pressure rhythm. eGFR, uric acid and interstitial inflammatory infiltration are related not only to hypertension but also to abnormal rhythm of blood pressure.

Introduction and Aims: Hypertension is a complex disease influenced by multiple factors. One of them is sympathetic nervous system hyperactivity which correlates with increased of vascular resistance and systemic blood pressure (BP). The hormone named renalse, secreted by the kidney to the blood, may degrade catecholamines and play a role in the regulation of sympathetic tone and BP. The aim of the study was to assess circulating level of renase in 96 hypertensive patients and the correlation of renase with eGFR (estimated glomerular filtration rate), heart rate (HR), BP control, a type of hypotensive therapy and the presence of diabetes and coronary artery disease.

Methods: The plasma concentration of renase was assessed in 96 (median age 56 yrs) hypertensive patients. The medical history, BP measurements twice a visit during three visits and 24 hour ambulatory blood pressure measurement (ABPM), HR, laboratory tests and the echocardiography were taken. The connection between renase and eGFR, HR, BP control, a type of hypotensive therapy and the presence of diabetes and coronary heart disease was analyzed.

Results: Mean BP was 132±17/76±10.4 mmHg and HR - 68,7±13,3 beats/min. The main used hypotensive drugs were diuretics - 67,7% and ACEI (angiotensin converting enzyme inhibitor) – 64,5%. Circulating renase level was significantly higher in patients with hypertension comparing to healthy individuals (Me 11,18 vs 3.86 ug/mL, p=0.001). It was higher in patients treated with ARB (angiotensin receptor blocker) than without (Me 13.14 vs 10.7 ug/mL p=0.046). Renase correlated with systolic blood pressure measured in 24 hour ABPM. There were no significant differences in renase level in patients with and without diabetes and with and without coronary artery diseases. No correlation between circulating renase and eGFR, heart rate or echocardiography parameters was found.

Conclusions: Renase still poses an interesting and intriguing protein. Its elevated circulating level in hypertensive patients may prove the role of renase in the pathogenesis of hypertension. It is probably related to the sympathetic nervous system hyperactivity found in this population, especially if the main used hypotensive drug was beta-blocker.

Introduction and Aims: Blood pressure circadian rhythm variation is rather common in patients with existing CKD. Non-dippers with renal disease are associated with a subsequent deterioration in renal function than dippers, which is independent of blood pressure level and other risk factors for renal impairment. However, it is still unclear upon the contributing factors for blood pressure rhythm variation in CKD patients. We aimed to determine renal pathological and clinical parameters associated with blood pressure rhythm variation in IgAN patients.

Methods: The study involved 341 adult IgAN patients in CKD1 -3 stage, all of whom underwent renal biopsy and ambulatory blood pressure monitoring. Patients were excluded if they were taking antihypertensive drugs, glucocorticoids for treatment. Baseline patient characteristics and clinical data were collected. The pathological scores were performed according to the IgAN Oxford score. Influencing factors of blood pressure rhythm abnormality were determined by Spearman correlation analysis and logistic regression analysis.

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Conclusions: Excretion of urine protein and sodium, tubulointerstitial injury including tubular atrophy/fibrosis and arteriolar hyalinosis are associated with abnormal regulation of blood pressure rhythm. eGFR, uric acid and interstitial inflammatory infiltration are related not only to hypertension but also to abnormal rhythm of blood pressure.
Methods: Fifty MO patients with normal renal function, with biopsy proven early stages of obesity-related glomerulopathy. Twenty-four hour ambulatory monitoring was recorded before bariatric surgery. Ambulatory arterial stiffness index (AASI) was defined as 1 minus the regression slope of diastolic on systolic blood pressure during 24h ambulatory monitoring. Renal lesions observed were: glomerulomegaly, mesangial lesions (mesangial matrix increase, podocite hypertrophy and mesangial cell proliferation) and vascular lesions (renal arteriosclerosis and renal arteriolesclerosis). Control group: 51 MO patients with normal renal function, with biopsy proven type 1 obesity. Ambulatory arterial stiffness index (AASI) was defined as 1 minus the regression slope of diastolic on systolic blood pressure during 24h ambulatory monitoring.

Results: MO patients: mean age 39.98 ± 9.75 years; mean BMI was 52.68 ± 8.9 Kg/m2, 60% were female, 58% had clinical hypertension; 60% were non dipper, 30% were dipper and 6% were diper; mean AASI was 0.405 ± 0.202 and 32% had arterial stiffness (defined by AASI ≥ 0.5). Compared with the control group, there were no difference between age and sex. Mean BMI was 26.88 ± 4.03 Kg/m2. There were 23% non dipper patients, 76.5% dipper and one no was diper. Mean AASI was 0.311 ± 0.158 and 9.8% had arterial stiffness. All differences between groups were statistically significant. Association between 24h-BPM and renal lesions: AASI was associated with glomerulomegaly (OR=4.08; IC 95% (1.204-16.14); p= 0.023) and diurnal Systolic blood pressure was associated with mesangial cell proliferation and CKD. Thus, there is a need for more efforts that implement public health programs targeting blood pressure during 24h ambulatory monitoring.

Conclusions: 1. MO patients had circadian pattern altered compared with control group. 2. Percentage of non dipper and riser pattern were higher in MO patients compared with the control group. 3. MO patients although they are young patients, had higher AASI than control group. 4. AASI could be a risk factor for glomerulomegaly. 5. Diurnal systolic BPM could be a risk factor for mesangial cell proliferation.
renal function (CKD-EPI and MDRD) with metabolism (cholesterol, triglycerides, glucose, uric acid), risk markers (von Willebrand factor-antigen: VWF, fibrinogen -F- and C- reactive protein -CRP-), albuminuria (albumin/creatinine urinary ratio or albuminuria microalbuminuria), arterial intima-media thickness (IMT) and F/ E A echocardiography index. Statistical analysis was performed with SPSS 15.0.

Results: We observed greater association between CKD-EPI and CVR scores (P <0.001 r = 0.281, FR p < 0.001 r = 0.432, SC p <0.001 r = 0.551, SC p <0.001 r = 0.460) than with MDRD (P r <0.001 p = 0.223, FR p < 0.001 r = -0.235, SC p <0.001 r = -0.322, SC p < 0.001 r = 0.261). The CKD-EPI was better associated with IM thickness (P <0.001 r = 0.359, E/ A ratio (p <0.001 r = 0.401) and uric acid (p <0.001, r = 0.357), than MDRD (P <0.001 r = 0.170, (P <0.001, r = 0.308) and (P <0.001, r = 0.249). The association of both formulas is similar with LAALCR, CKD-EPI (P <0.001, r = 0.352) and MDRD (P <0.001, r = 0.308). The VWF was associated with LAALCR (P = 0.008, r = 0.237). Also F was associated with CRP (P <0.001, r = 0.479). The CKD-EPI stratified better GFR with CVR, showing significant increase below 90 ml / min (p <0.001). This effect depends on the age, associated with GFR (P <0.001), showing a significant drop in people older than 50 years. Table 1. Table 1. CKD-EPI >100 100-90 89-80 79-70 <69 PR 0.64 1.7 5.23 6.61 8.12 FR 5.27 5.66 14.3 16.29 21.72 SC 19.3 23.7 31.2 36.2 39.1 SCE 0.46 0.59 1.41 1.76 3.18 AEG (mean)41 40 50 52 67.

Conclusions: In healthy population there are association between CVR and renal function. A GFR below 90 ml / min in people aged over 50 years is associated with significant increase in CVR. The formula CKD-EPI allows evaluate the relationship between renal function and cardiovascular risk, better than MDRD.

Introduction and Aims: Many trials documented that renal index (RI) is elevated in hypertensive patients with no renal impairment (normal GFR, no microalbuminuria) = group A; 33 offsprings of hypertensive patients with no renal impairment (normal GFR, no microalbuminuria) = group B. The subjects were divided in two groups: 32 offsprings of patients with hypertensive nephropathies in (hypertensive individuals) and 46 healthy subjects, descendants of patients with documented essential hypertension for more than 15 years, underwent renal Doppler ultrasonography. Inherited high RI values represent a predictor of the future high blood pressure values. In essential hypertensive patients, it is hard to predict nephropathy without genetic studies pointing the renal susceptibility genes. The aim of our study was to determine an easier modality to establish the presence of nephroangiосclerosis in both healthy descendants of hypertensive patients. We conducted a study to assess the importance of renal index (RI) in prediction of the renal susceptibility in the evolution of essential hypertension.

Methods: 65 healthy subjects, descendants of patients with documented essential hypertension for more than 15 years, underwent renal Doppler ultrasonography. The subjects were divided in two groups: 32 offsprings of patients with hypertensive nephropathies (various grades of chronic renal disease) = group A; 33 offsprings of hypertensive patients with no renal impairment (normal GFR, no microalbuminuria) = group B. The two groups were matched for age and sex. RI was measured in all offsprings and echocardiography was performed in all parents (hypertensive patients with or without renal impairment).

Results: Mean descendants groups age 28 +/- 2.8 years, mean systolic BP 116 +/-5 mmHg, mean diastolic BP 71 +/-4 mmHg. Mean RI (group A and group B) 0.68 +/-0.05. Mean RI was 0.79 +/-0.03 in group A, significantly higher (p < 0.001) than mean RI 0.62 +/- 0.02 in group B. Mean EF (ejection fraction) measured in hypertensive patients was 46.4 +/-5.2 %, with a value of 39.3+/-1.2 % in parents of group A (patients with renal impairment) and 46.4 +/-5.2 % in parents of group B patients (hypertensive patients with no renal involvement). High values of RI in the descendants strongly correlate with low EF in the hypertensive parents (p < 0.001 r = 0.65).

Conclusions: Our study supports the hypothesis that significant high levels of RI preexist in parents of hypertensive patients before the hypertension onset and that high RI values represent a predictor of the future high blood pressure values. In essential hypertensive patients, it is hard to predict nephropathy without genetic studies pointing the renal susceptibility genes. The aim of our study was to determine an easier modality to establish the presence of nephroangiосclerosis in both healthy descendants of hypertensive patients. We conducted a study to assess the importance of renal index (RI) in prediction of the renal susceptibility in the evolution of essential hypertension.

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Preeclampsia is a life-threatening disorder of pregnancy. To date the underlying pathogenic mechanisms of preeclampsia remain uncertain. Aim of this study is to investigate the relation between urinary angiotensinogen levels which is an indicator of local renin-angiotensin-system (RAS) activity in kidney and blood pressure and urinary protein excretion in preeclamptic pregnant.

Methods: Sixty women ages between 20-39 years old (20 women with normotensive pregnancy, 20 women with new diagnosed preeclampsia and 20 control subjects) were recruited in the study. Morning spot urine samples were collected to measure urinary angiotensinogen/creatinine ratio (UAGT/Ucre). UAGT/Ucre was logarithmically transformed (log (UAGT/Ucre)) to make normal distribution. Log (UAGT/Ucre) was compared in pregnant with and without preeclampsia and control subjects. Factors affecting log (UAGT/Ucre) in pregnant were also investigated.

Results: There were no differences in demographic characteristics between control subjects and pregnant with and without preeclampsia. In all pregnant with or without preeclampsia; log (UAGT/Ucre) levels were significantly higher than in controls. Although, log (UAGT/Ucre) levels in pregnant with preeclampsia were slightly less than in normal pregnant, this difference did not reach statistical significance. Log (UAGT/Ucre) levels were correlated positively with proteinuria [Figure 2] and albuminuria in pregnant with preeclampsia. However, log (UAGT/Ucre) levels were not correlated with blood pressure, age, height, body weight, gestational age, body mass index, and serum creatinine.

Conclusions: This study showed that elevated local RAS activity was correlated with renal injury presented by proteinuria in women with preeclampsia, despite the lack of association with blood pressure measurements.
and in 32nd gestation week, an analysis of the resistance index of the Doppler of umbilical artery. According to the outcomes, groups were divided into a group with and a group without preeclampsia. The integrated prognostic model was calculated by the method of determination of apriori and aposteriori risk. Statistical analyses were made by the use of the SPSS 17.0 software.

Results: The examined population, was divided after delivery into 2 groups: a group with preeclampsia (N=51), and a group without preeclampsia (N=68). The integrated prognostic model comprised three steps: first, determination of apriori risk, from the risk factors that were significant at the univariable analysis, by the use of multivariable logistic regression, the following were determined as predictors of preeclampsia - age above 35 years and use of dual antihypertensive therapy (p=0.09 and p=0.032 respectively). The logistic regression is the basis of determination of the apriori risk of preeclampsia, which equals 3.95%. The second step in the model was logistic regression of biochemical parameters and determination of the likelihood ratio for preeclampsia, that equal LR=1.8 for the first, LR=2 for the second and LR=2.2 for the third trimester. The third step was determination of the log MoM for the 24 hour blood pressure analysis and D-dimers, entered into logistic regression, and equaling LR=+1.3 for the first trimester, LR=+2.1 for the second trimester and LR=+2.3 for the third trimester. The aposteriori risk was obtained by multiplication of apriori risk by likelihood ratios. Thus, aposteriori risks for the first trimester were 9,2 for the second trimester 16,6 and for the third trimester 19,9. The aposteriori model was able to detect preeclampsia correctly by 90% in the second trimester. The integrated prognostic model offers possibilities for an apriori and aposteriori assessment of risk, thus correctly detecting 90% of patients with preeclampsia from the second trimester of pregnancy.

Conclusions: The integrated prognostic model was able to detect preeclampsia correctly by 90% in the second trimester.

Abstracts

SP040 TAKAYASU ARTERITIS COMPLICATING PREGNANCY
Karima Boubaker1, Adel Kheder1 and Hayet Kaaroud1
1Internal Medicine A Charles Nicole Hospital Tunis Tunisia, 2Charles Nicole Hospital Tunis Tunisia

Introduction and Aims: Takayasu’s Arteritis is a rare inflammatory disease of medium and large size arteries that affects women of reproductive age ; therefore, the management of pregnancies with this disease is of great importance in clinical obstetrics. However, only a limited number of such cases have been reported in the literature. Our aim in this study was to investigate the clinical features of pregnant women with Takayasu arteritis.

Methods: This retrospective study was carried out in the Department of Internal Medicine A from 1982 to 2011. Six patients with 19 pregnancies were included.

Results: The mean age of these patients at delivery was 34.7 years (27-44 years). One pregnancy resulted in spontaneous abortion, and one pregnancy was legally terminated because there are fetus malformations. The remaining 18 pregnancies resulted in live births. Significant maternal complications included pregnancy induced preeclampsia in 8 cases. None maternal mortality was present. Neonatal outcome showed 14 live births with increases incidence of intratineer growth restriction in 9 cases and neonates requiring NICU admissions in 1 case.

Conclusions: Although Takayasu arteritis is a potentially severe condition during pregnancy, successful pregnancy is possible if extreme caution is followed. Blood pressure should be strictly controlled and the delivery should be planned for favorable maternal and fetal outcomes.

SP041 ASSOCIATION OF DIETARY POTASSIUM INTAKE WITH SUBCLINICAL CORONARY ARTERY DISEASE IN KOREAN ADULTS
Seung Min Lee1, Hyo Eun Park1, Min Kyung Kim1, Nam Ju Heo1, Su-Yeon Choi1, Kwon Wook Joo1 and Jin Suk Han1
1Internal Medicine Seoul National University Hospital Seoul Republic of Korea

Introduction and Aims: Although several previous studies have evaluated the relationship between potassium intake and stroke or cardiovascular disease, but the results have been conflicting. The objective of this study was to investigate the relationship between dietary potassium intake and the prevalence of subclinical coronary artery disease in Korea.

Methods: We conducted a cross-sectional study of 1,495 subjects without history of cardiovascular disease or stroke, who underwent routine health checkups including computed tomography (CT) coronary angiography at the Healthcare System Gangnam Center of Seoul National University Hospital from 2007 through 2010.Dietary potassium intake was assessed by the Korean version of food frequency questionnaires. Significant coronary artery stenosis was defined as more than 50% of luminal stenosis of any major coronary artery on CT coronary angiography.

Results: Among 1,495 subjects, 68 (3.5%) had significant coronary artery stenosis. Individuals with lower potassium intake showed higher prevalence of significant coronary artery stenosis (p for trend 0.028). After adjustment for age, sex, body mass index, hypertension, diabetes mellitus, and dyslipidemia, the lowest quintile group of potassium intake was associated with higher risk of significant coronary artery stenosis (odds ratio [OR] 2.96; 95% confidence interval [CI] 1.12-7.79). In subgroup analysis, among individuals without diabetes, the lowest quintile group of potassium intake was still associated with higher risk of significant coronary artery stenosis (odds ratio [OR] 4.42; 95% confidence interval [CI] 1.21-16.19).

Conclusions: Our findings suggest that lower dietary potassium intake is significantly associated with higher prevalence of subclinical coronary artery disease. Among non-diabetic adults, the harmful effect of lower potassium intake on subclinical coronary artery disease may be even larger than that among general population.

SP042 WORLD KIDNEY DAY (WKD): FOUR YEAR ANALYSIS OF HEALTH EVENTS IN UK
Sohan Shah1 and Bhavna Pandya1,2
1University of Liverpool Liverpool United Kingdom, 2Nephrology Aintree Hospital Liverpool United Kingdom

Introduction and Aims: WKD is an annual kidney awareness event. For the past 4 years, health clinics have been held for the staff and shoppers in Liverpool. The aim was to determine their general health: blood pressure, blood glucose, urine abnormality, heart rate and cholesterol.

Methods: Individuals who attended annual WKD events from 2009-2012 came forward for blood pressure (electronic blood pressure monitor), capillary blood glucose monitoring (CBGM), urinalysis (automated urinalysis machine), heart rate (manual radial pulse) and cholesterol readings.

Results: A total of 871 patients were included in the analysis. The median age was 54 (range 12-102) with a M:F ratio of 1:3. The median systolic and diastolic blood pressure was 137 mmHg (range 83-217; SD 22) and 81 mmHg (range 40-128; SD 12) respectively. Defining hypertension as blood pressure >140/90, 361 (51%) patients were identified to be hypertensive. A systolic BP >180 was found in 37 patients. Median heart rate from 395 patients was 76 bpm (SD 13). Of the 585 patients who had a random blood glucose test, 5 patients were found to have glycosuria. Two of these had severe glycosuria (+++). Twelve patients showed mild positive (+) nitrate results suggesting infection. Random cholesterol was measured in 174 patients (median 5.00 mmol/L; range 3.00-7.76; SD 0.87). Twelve patients had high cholesterol >6.5.

Conclusions: The above analysis shows that hypertension, urine abnormalities and hypercholesterolaemia are prevalent throughout the community. Regular events like this help to discover undiagnosed patients and increase confidence in the community thus improving health check-up attendances. It also helps to identify and prevent severe consequences of undiagnosed and prevalent risk factors in the community.

SP043 BLOOD PRESSURE CONTROL AND RESISTANT HYPERTENSION IN DIABETES MELLITUS AND CKD ASSOCIATED DIABETES PATIENTS
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Introduction and Aims: Suboptimal blood pressure(BP)control is an important risk factor for death in cardiovascular disease and resistant hypertension (RHT) is one of the main causes of suboptimal BP control.Data about RHT and BP control in RHT (more than 3 hypertensor agents) are scarce.This study investigates RHT and BP control in diabetes(DM) and CKD associated DM patients.

Methods: 993 in hospital DM patients have been randomly assigned to this study (429 male,564 female,mean age 60.2 years).Standard evaluation for a diabetes management secondary care unit was performed for all patients. RHT was defined according to 2008 AHA criteria.Patients were considered to have RHT if at discharge (after actively targeting blood pressure control by adjusting hypertensive therapy)the target BP (<130/80 mmHg) was not reached using adjusted doses of 3 hypertensor agents (one being a diuretic).GFR was estimated by MDRD 4 formula.Data have been processed using SPSS16.

Results: Chronic hypertension was present in 812 (81.77%) of the hospital admitted DM patients and CKD in 659 (66.3%).From the CKD patients 4.09% were in stage 1, 2.05% in stage 2,34.1% in stage 3, 5.1% in stage 4 and 2.4% in stage 5 (pre-dialysis).The prevalence of chronic hypertension was significantly higher in the CKD DM patients compared to the non CKD DM patients (5.5% vs. 3.2% p=0.0004).In CKD DM patients RHT prevalence increased with the progression of the CKD (stage 1 - 42.1%, stage 2 - 38.7%, stage 3 - 56.8%, stage 4 - 57.5%, stage 5 – 73.3%) and the possibility of controlling BP by adjusting therapy (3> hypertensor agents)
decreased (prevalence of RHT IT stage 1 – 37.5%, stage 2 – 33.6%, stage 3 – 28.9%, stage 4 – 21.03%, stage 5 – 9%). From the CKD DM patients 80.8% (533) presented proteinuria/albuminuria and 90.4% (482) of them had HT also. The prevalence of RHT was significantly higher in the group with proteinuria as compared to the non-proteinuric one (53.1 vs. 42.1%, p=0.043).

Conclusions: The prevalence of RHT in DM patients is high, being more prevalent in CKD DM patients. II. CKD complicates DM: the prevalence of RHT increases with the CKD progression and the presence of proteinuria, thus the possibility of BP control (with more than 3 hypotensive agents) decreases accordingly.

SP044

RENAI FUNCTION IN PREHYPERTENSION

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Introduction and Aims: Our aim was to analyse kidney function in prehypertensives comparing to subjects with optimal blood pressure and patients with untreated stage 1 hypertension.

Methods: Out of 2489 subjects enrolled in Croatian rural study, 693 were eligible for further analysis. Exclusion criteria were antihypertensive treatment, hypertension stage 2, and isolated systolic hypertension, diabetes mellitus, pregnancy, chronic terminal diseases, dementia, immobility and missing data. Blood pressure (BP) was measured following the ESH guidelines. Antropometric measurements (height, weight) were determined. Fasting blood was analysed for serum creatinine. Urine was analysed for alpha1microglobulin, albumin, creatinine, sodium and potassium. Abbreviated MDRD formula was used to estimate glomerular filtration rate (eGFR). Albumin to creatinine ratio (ACR), alpha1microglobulin to creatinine ratio (alpha1ICR) and sodium to potassium ratio (S/P ratio) were determined. Renal ultrasound was performed assessing longitudinal and transversal diameters and parenchymal thickness. Subjects were divided in three groups: optimal BP (<130/80, N=316), prehypertensives (130/85-130/89, N=210), and untreated hypertensives stage 1 (140-159/90-99, N=167).

Results: Significant differences were found between the three groups in alpha1ICR and eGFR (p=0.001; p=0.012, respectively). Optimal BP group showed to have significantly lower alpha1CR values than prehypertensives and hypertensives (4.2 vs. 4.7 vs. 5.3, p<0.001), as well as serum creatinine (79 vs. 83 vs. 83, p=0.0001); while differed significantly only from hypertensives in eGFR (82.1 vs. 80.1 vs. 77.8, p=0.0022). No differences between prehypertensives and hypertensives were observed either in those parameters or kidney size determined by ultrasound, urine potassium and urine sodium, and ACR, although a trend of increment in ACR related to BP was observed (4.0 vs. 4.5 vs. 4.6).

Conclusions: No differences were found in markers of kidney function between prehypertensives and untreated hypertensives stage 1. As we have already reported higher values of alpha1microglobulin excretion observed in prehypertension might point on early proximal tubule damage present in high normal BP stage.

SP045

MOLECULAR EFFECTS OF RENIN-ANGIOTENSIN-SYSTEM BLOCKADE IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Blockade of the renin-angiotensin-system (RAS) is standard antihypertensive therapy for hemodialysis (HD) patients. However, the ideal mode of RAS interference is still unclear as large clinical trials have shown divergent outcomes. Hence, a quantitative analysis of the RAS is warranted to decipher relations between clinical outcomes and molecular effects of RAS blockade and to establish optimal antihypertensive regimens for HD patients.

Methods: We performed a single-center, cross-sectional study to quantify RAS peptides in HD patients. 52 patients were recruited: ACEi (n=8), ARB (n=11), dual RAS blockade (n=8), no RAS blockade (n=16) and anephric patients (n=9). RAS peptides were analyzed with a novel mass spectrometry-based assay. Angiotensin/renin ratios were calculated and compared.

Results: Patients without RAS blockade had similar RAS activity compared to healthy controls, while anephric patients completely lacked angiotensins (Ang). ACEi blocked ACE-mediated conversion to Ang 1-8 and Ang 1-5; this led to increased Ang 1-10/renin and Ang 1-7/renin ratios. Patients treated with ARB had high levels of Ang 1-8 and Ang 1-5, while Ang 1-7 was absent. Dual RAS blockade led to highly increased Ang 1-10/renin ratios and absence of all other peptides.

Conclusions: We demonstrate strongly divergent effects of several modes of RAS blockade on Ang levels in HD patients. We could show that i) anephric patients completely lack a systemic RAS, ii) a boosting of the alternative RAS represented by Ang 1-7/renin ratios occurs following ACE inhibition and iii) ARB therapy leads to high Ang 1-5/renin ratios. In conclusion, this differential expression of RAS patterns might be implicated with clinical outcomes and should be investigated in future clinical trials.

SP046

INFLUENCE OF “ENERGY DRINKS” ON THE BLOOD PRESSURE IN APPARENTLY HEALTHY YOUNG ADULTS

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Introduction and Aims: The growing interest in so called “energy drinks” (ED) is observed among young adults. These drinks contain among others caffeine, taurine and inositol. The aim of the study was to determine the influence of an ED on the pulse rate and blood pressure (BP) in apparently healthy young adults.

Methods: Study was performed using double blind method, with two concentrations of ED and placebo. Eighteen healthy volunteers aged 20-35 years were enrolled into the study. During the visits three solutions were administered: placebo and ED with 120 mg and 360 mg of caffeine. Measurements of BP and pulse rate were performed before (30, 15 and 1 minute) and after (2, 5, 10, 15, 30, 45, 60, 75, 90 minutes) ingestion of each of these solutions.

Results: Twelve volunteers completed entire study. Oral intake of ED containing 120 mg of caffeine didn’t influence significantly blood pressure and pulse rate. However oral intake of ED containing 360 mg of caffeine leads to significant increase of BP (systolic BP increase 9.0±12.9 mmHg, p=0.033; diastolic BP increase 9.4±5.1 mmHg, p=0.028) and a pulse rate (increase 5.2±2 beats/min, p=0.042). Three hours after ingestion of ED with 360 mg of caffeine all participants revealed cardiac arrhythmia with tachycardia, anxiety and insomnia.

Conclusions: 1. ED in larger amounts increase of blood pressure and pulse rate in apparently young healthy adults. 2. It seems very possible that ingestion of larger amount of ED may create a health status deterioration, particularly in patients with arterial hypertension or other cardiovascular diseases.
Introduction and Aims: Prehypertension is characterized with increased cardiovascular and renal risk. Our aim was to analyse parameters of renal function in prehypertensive men and women.

Methods: We enrolled 689 subjects (409 females and 280 males). Blood pressure (BP) and heart rate (HR) were measured following ESH guidelines. Fasting blood samples were drawn for glucose (FBG), insulin, creatinine and lipids. Urine samples (albumin, α1 microglobuline, sodium, α1 microglobuline/creatinine ratio (A1CR) and albumin/creatinine ratio (ACR) were calculated. Glomerular filtration (eGFR)-MDRD, HOMA index, and BMI were calculated. Renal ultrasound was performed. Subjects were divided in three groups according to the BP – group I - optimal BP (<120/80 mmHg), group II - prehypertension (130-138/80-85 mmHg), group III - hypertension (≥140/90 mmHg).

Results: There were 209 prehypertensive subjects (115 males and 94 females). We failed to find differences in age, FBG, HOMA index and HR between men and women (p=0.05). However, prehypertensive men had significantly higher values of total cholesterol, LDL, triglycerides. There were no differences in A1C and albuminuria between men and women (p=0.05). However, women had higher values of ACR and lower values of eGFR (p<0.05). Prehypertensive men excreted more sodium than women.

Conclusions: Observed differences in eGFR and ACR between men and women might point on earlier renal damage in women. However, in women ACR values could be influenced by lower values of urine creatinine, and probably eGFR based on MDRD equation underestimates true GFR. This should be taken into account not only in research but also in routine clinical work.

Introduction and Aims: Current knowledge indicates that hyperuricemia predicts the development of hypertension and is strongly linked to cardiovascular disease. Additionally, serum uric acid (SUA) is also higher in other high-risk groups (obesity, black race and CKD). Taking into account that some subjects have a relative defect in their ability to excrete sodium, which is called salt-sensitivity (SS), and that an increase in blood pressure response to sodium intake was observed in hypertensive and hyperuricemic subjects, the aim of this study was to evaluate SUA level in a cohort of normotensive subjects characterized on the basis of SS.

Methods: Seventy living kidney donors (both genders) without history of kidney disease, diabetes, cardiovascular events or hypertension, who participated in the donation screening protocol with subsequent donation, were included. They were placed on a low-salt period, laboratory test was performed (SUA and 24hs CrCl). Data were obtained if we use ambulatory blood pressure monitoring with a) clinician’s office obtained if we use ambulatory blood pressure monitoring with b) clinician’s office blood pressure.

Conclusions: Contrary to reported in hypertensive patients, the SUA level observed in normotensive subjects seems not follow the SS pattern. On the other hand, SUA correlated significantly with obesity in this cohort of subjects.
Introduction and Aims: Ambulatory blood pressure monitoring (ABPM) is thought to be more reliable than casual office blood pressure measurements. This method has frequently been used for the diagnosis and follow-up of hypertension in children with advanced chronic kidney disease (CKD). We aimed to evaluate BP status using ABPM in children with early stage of CKD.

Methods: This cross-sectional clinical study enrolled 28 children (15 boys, aged between 6-17.5 years) with CKD stage 2 (eGFR: 60-89 ml/min/1.73 m²) and 28 healthy children of comparable age and gender as controls. All of the subjects were evaluated by casual and ABPM measurements. For the casual measurements, indexed systolic (s) and diastolic (d) BP were calculated by dividing the observed BP by gender- and height-specific 95th percentile value and casual HT was defined as indexed sBP-and/or dBP>1. For the ABPM, the height-specific SD scores were calculated for each patient. Ambulatory hypertension was defined as 24-hr mean arterial BP (MAP) greater than 2 SD scores. Furthermore, all patients using antihypertensive medications were considered to be hypertensive regardless of being hypertensive or normotensive by causal or ABPM measurements.

Results: The mean SD scores of 24-hr MAP was significantly higher in the patients than the controls (0.65±1.44 vs. 0.01±0.76, p=0.010). Patients also had higher 24-hr MAP compared to the controls (0.43±1.68 vs. -0.33±0.82, p=0.002); however, there was no difference in 24-hr sBP-SD scores between the two groups. Both sBP- and dBP-SD scores in the patients were significantly higher than the controls during daytime (p=0.035 and p=0.004, respectively); however, neither sBP-, nor dBP-SD scores differed between the patients and controls during nighttime. Overall, 13 patients were considered as hypertensive. Of these, four were classified as hypertensive by ABPM measurements; three of these particular patients found to be hypertensive by causal measurements as well. Nine patients were considered as hypertensive because of using antihypertensive medications.

Conclusions: Our results suggest that hypertension is prevalent among children with early stages of CKD. Diastolic high blood pressure seems to be more prominent in this patient group. ABPM is not a "must" for diagnosis of hypertension in these children since most of hypertensive patients can be detected by casual BP measurements as well.
AKI - EXPERIMENTAL MODELS

SP053 Cysteine-rich protein 61 mediates kidney fibrosis after ischemia reperfusion injury

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Introduction and Aims: Clinical studies have demonstrated the risk of chronic kidney disease after the occurrence of an acute kidney injury (AKI). Experimental works indicate that AKI result in incomplete repair, persistent tubulointerstitial inflammation and fibrosis. Cysteine-rich protein 61 (Cyr61), a secreted matrix-associated protein, has been found to be up-regulated in the kidney ischemia reperfusion injury (IRI) animal model. The present study aimed to investigate the role of Cyr61 in the kidney after IRI.

Methods: Using mouse unilateral IRI model, we analyzed gene and protein expression of Cyr61. We further investigated the effect of blockade of Cyr61 in unilateral IRI mice by treating polyclonal anti-Cyr61 antibody or non-specific IgG. In addition, we used proximal tubular epithelial (NRK-52E) cells for cell culture studies.

Results: After IRI, kidney Cyr61 expression increased significantly in both mRNA and protein level. Immunofluorescence staining indicated Cyr61 was predominantly expressed in renal proximal tubular epithelial cells. This was supported by in vitro studies showing hypoxia condition stimulate Cyr61 expression in NRK-52E cells. Daily treatment with anti-Cyr61 antibody produced a decrease in the renal type 1 collagen, PAI-1, MCP-1, and IL-1 gene expression, as well as a-SMA protein production at day 14 after IRI. The degree of collagen fibril accumulation, evaluated by picrosirius red staining, and macrophage infiltration were both attenuated by the Cyr61 blockade on day 7 and 14. Concurrently, renal VEGF-A gene expression was enhanced and vessel density was more preserved at day 14 in the treatment group.

Conclusions: Renal Cyr61 expression by tubular epithelial cells is enhanced after IRI. Our findings suggest that Cyr61 contributes to the renal inflammation, vascular rarefaction, and fibrosis after ischemic AKI.

SP054 Pretreatment with rituximab prevents subsequent ischemia-reperfusion injury in mice kidney

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Introduction and Aims: There is growing evidence of the roles of B-cell after Ischemia-reperfusion (IRI) renal injury, and IRI is unavoidable event in renal transplantation. We investigated whether rituximab is renoprotective in a mouse model of IRI and whether potential mechanism is related with modulation of renal inflammatory infiltration.

Methods: Rituximab (10 mg/kg) was administered to male C57BL/6 mice 7 days before IRI, and mice were killed at 72 hours after IRI. Pretreatment with rituximab decreased blood urea nitrogen and serum creatinine at 1 and 3 days postischemia.

Results: Tubular necrosis scores were lower in mice kidney with rituximab treatment than in those of mice kidney with IRI only. Rituximab did not reduce the serum immunoglobulin (Ig) G and IgM levels. The infiltration of CD19-positive B-cells and CD40-positive antigen-presenting cells were decreased in the rituximab-treated kidneys, which was accompanied with decreased production of interleukin (IL)-12. Rituximab inhibited the infiltration of T-cells and macrophages and its immunomodulatory effects also affected the decreased production of Th1 cytokines IL-12, interferon-g and tumor necrosis factor-a. Of the Th2 cytokines, IL-4 expression was decreased in rituximab-treated kidneys, but rituximab had little effect on IL-10 expression in the mice kidneys with IRI.

Conclusions: Rituximab has a protective effect on renal IRI and that this effect is associated with reduced antigen presentation and decreased activation of inflammatory cytokine associated with Th1-pathway.

SP055 The study on the protective effect and mechanism of neutrophil gelatinase-associated lipocalin (NGAL) to the rats ischemia/reperfusion renal injury

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Introduction and Aims: To investigate the protective effect and mechanism of NGAL on rats ischemia/reperfusion renal injury.

Methods: Renal I/R models of rats were established, rats were randomly divided into 3 groups, including the shame operation, IRI model group and NGAL group; the pathological changes of kidney tissue were investigated by hemotoxylin-eosin staining; renal tubular epithelial cell apoptosis was detected by TUNEL method; After 24 hours of reperfusion, blood samples were harvested from inferior vena cava. The Scr and Bun were measured on automatic biochemistry analyzer. The expressions of Bax, and CC3 were detected by immunohistochemistry expression of Fas, Bcl-2 were measured by Western Blot.

Results: Compared with IRI group, NGAL group showed the values of Scr and Bun (63.400±11.908 versus 121.857±17.151)umol/L, (14.840±2.868 versus 14.568±1.956)umol/L respectively; NGAL group showed a decreased number of renal tubular epithelial cell apoptosis(7.800±1.924 versus 15.400±3.049), down-regulated Fas mRNA (2.34±0.51 versus 6.84±3.24), Bax protein(7.44±1.956) versus 5.30±1.48); the results had statistical significance(P<0.05).

Conclusions: NGAL can protect renal tubular epithelial cells in renal I/R, may be related to decrease cell apoptosis and adjust protein expression by apoptosis-regulating cytokines,thus protect renal from I/R injury.
**SP056**

**THE ROLE OF CYSTEINYL LEUKOTRIENE-1 (CysLT1) IN RENAL ISCHEMIA-REPERFUSION INJURY**

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**Introduction and Aims:** The pathogenesis of ischemia-reperfusion (I/R) injury is known to involve cytokines and particularly surface adhesion molecules, the expression of which initiates the attachment of inflammatory cells. Renal I/R injury is also clinically important problem and invariable consequence of renal transplantation. The problem begins at the onset of acute tubular necrosis, when the transplantation takes a long ischemic interval by using the cardiac arrest donor's kidney. The cysteinyl leukotriene-1 (CysLT1) is a potent lipid mediator in allergic disease, acting through the receptor (CysLT1R). We researched the expressions CysLT1R in rat renal I/R injury as well as the degree of acute tubular necrosis.

**Methods:** Male Lewis rats (270-320g) were used in this study. Under laparotomy using pentobarbital sodium anesthesia, the right kidney was harvested and then the left renal artery and vein were clamped with a hemostasis clip for 90 minutes. The clip was subsequently removed to permit reperfusion. The abdomen was closed during I/R. The left kidneys were reperfused, the rats were sacrificed at 0, 3, 5, 12 and 24 hours after reperfusion. The kidneys were harvested for HE staining and immunohistochemistry. Samples of ischemic and nonischemic kidney tissue were fixed in 10% buffered formalin for 24 hours immunohistochemical staining.

**Results:** CysLT1R expression was observed only in endothelial cells of normal kidney. From 0 to 3 hours after reperfusion, CysLT1R expression gradually became stronger on endothelial cells. CysLT1R expression was most intense on endothelial cells at 3 hours after reperfusion. 5 hour after reperfusion, internal spaces of the tubular epithelial cells were inflated, and the destruction of the tubular epithelial cells appeared. CysLT1R expression, necrosis extended throughout the ischemic kidney and nearly all of the tubular epithelial cells were destroyed, from 3 to 12 hours after reperfusion, CysLT1R expression became weaker on endothelial cells. 24 hour after reperfusion, CysLT1R expression was almost normal level of normal kidney. Naturally, renal I/R injury gradually progressed at time flow after reperfusion. Several hours after the maximum of CysLT1R expression, the maximum of renal I/R injury was observed.

**Conclusions:** These results suggest CysLT1R play very important roles on renal I/R injury in rat, and CysLT1R plays very important roles on renal I/R injury in rat.


**SP058**

**MALE GENDER IS MORE PRONE TO RENAL ISCHEMIA-REPERFUSION INJURY BY ENHANCED INFLAMMATORY RESPONSES**

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**Introduction and Aims:** Inflammation is known to key mediator of renal ischemia-reperfusion injury. Gender disparity has been reported in acute or chronic kidney disease. In particularly, male gender is known as more susceptible to renal ischemic injury compared to female in animal study. The purpose of this study is to investigate the effect of gender differences on the renal inflammatory responses after acute ischemia-reperfusion injury in mice.

**Methods:** Experiments were performed in male and female C57BL/6. Two weeks before study, castration or ovariotomy was performed. The males, testosterone propionate (100 ug/kg) and 17b-estradiol (100 ug/kg) were injected. Acute kidney injury was induced by bilateral clamping of renal pedicle for 23 min. Histologic examination, Western blot analyses and qRT-PCR were performed.

**Results:** 23 min ischemia-reperfusion injury, male mice were signficantly increased serum BUN and creatinine level. However, castration of male mice is more resistance to renal I/R injury. Replacement of testosterone to the castration male mice reversed this protective effect. In female mice, 23 min IR injury did not significantly change the renal function. However, estrogen depletion by bilateral ovariectomy increased serum BUN and creatinine level after 23 min IR injury. Estrogen replacement attenuated IR-induced renal dysfunction. The tubular injury and tubular inflammation were increased in male AKI group. However, castration of male group mice decreased IR-induced tubular injury and inflammation.

**Conclusions:** Supplementation of testosterone reversed this protective effect in male AKI model. In case of female mice, 23 min IR injury induced mild tubular injury compared to male mice. Depletion of estrogen by bilateral ovariectomy increased IR-induced tubular injury and inflammation. However, supplementation of estrogen in ovariotomized female mice attenuated the IR-induced tubular injury and decreased macrophage infiltration. The expressions of inflammatory cytokines such as TNF-α, MCP-1, IFN-γ, and CCL17 were increased at 2 d in male AKI group. However, castration of male group mice decreased IR-induced cytokine expression. Supplementation of testosterone increased IR-induced cytokine expression. In case of female mice, estrogen depletion by bilateral ovariectomy significantly increased renal TNF-α, MCP-1, IFN-γ and CCL17 expression.

**Conclusions:** Supplementation of estrogen attenuated these IR-induced inflammatory cytokine expressions in ovariotomized female mice. These results suggested that male gender is more susceptible to the ischemia-reperfusion renal injury by enhanced inflammatory response. Further studies are needed to address the underlying mechanism of gender differences in the AKI.


**SP057**

**COUPLED PLASMA FILTRATION AND ADSORPTION IN THE CORRECTION OF THE SYNDROME OF ISCHEMIA / REPERFUSION INJURY**

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**Introduction and Aims:** Cytokines play an important role in the development of ischemia / reperfusion injury. We used modern method of treatment for the correction of this syndrome.

**Methods:** We applied coupled plasma filtration and adsorption (CPFA) of cytokines to correct ischemia / reperfusion in renal transplant recipients. The study included 17 kidney transplant recipients. We investigated the concentrations of cytokines (TNF, IL-1β, IL-6, IL-10, IL-12) in the blood before surgery, after reperfusion, and 12 and 24 hours after the procedure. To study the concentration of cytokines used sets of reagents for ELISA. CPFA was performed on the unit Lynda (Bellco) c plasma filter and sorbent «Mediasorb-Selecta». Each patient had one treatment duration of 6-8 hours. The criterion for inclusion of patients in the study were marginal donors as source of organs and the duration of conservation for more than 18 hours. Also we have formed a comparison group, numbering 20 people.

**Results:** We found that the syndrome of ischemia / reperfusion injury is accompanied by a massive release of cytokines into the circulation, which peaks at 4-6 hours after reperfusion, with a gradual decrease of the concentration of cytokines to 12-24 hours in some patients. There was a moderate correlation between the severity of increasing the concentration of cytokines and duration of cold and warm ischemia. Typically, patients with a marked increase in the concentrations of cytokines immediately after start of blood flow or in 4-6 hours, we observed no initial graft function. Sorption of cytokines decreased the cytokine concentration immediately after the procedure. Increase the return kotsentratsiya cytokines typically observed within the first 24-36 hours after surgery in some patients. In the main group, we noted an increase in diuresis and glomerular filtration rate, improve of microcirculation of the graft (lower resistivity index). Delayed graft function was observed in 14 patients of the study group and in 10 patients of the comparison group. Because of the small number of sampling differences did not reach the level of statistical significance. The median of duration of anuria was significantly lower in the treatment group. However, we believe that the selective removal of cytokines in the early postoperative period after kidney transplantation is an effective and necessary procedure.

**Conclusions:** These results are needed to address the underlying mechanism of gender differences in the AKI.


**SP059**

**LACK OF EXTRACELLULAR (ec) SUPEROXID-DISMUTASE SOD IS DETERMINANT IN ISCHEMIC ACUTE KIDNEY INJURY – AN ecSOD-DEFICIENT MOUSE-MODEL**

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**Introduction and Aims:** Generation of reactive oxygen species is an important pathomechanism in iAKI. Here, superoxide radicals (O2·-) are responsible for e.g. inactivation of nitric oxide (NO) and generation of further oxygen derived radicals with detrimental effects on cellular or protein levels. The enzyme superoxide dismuate (SOD) initiates the first step of O2·- radical detoxification. Here, we analyzed the influence of the extracellular SOD (ecSOD) in iAKI with regard to renal function, inflammation and tubular epithelial transport in an ecSOD deficient mouse model.

**Methods:** WKY mice were subjected to 23-min IR injury the clearance of inulin (CIN, resp. GFR) and para-aminohippuric acid (CPAH, resp. OAT3). In parallel, markers of inflammation which include COX1/COX2, HO1/HO2, MCP1, IL6b and HO1 were unchanged at baseline. In iAKI, ecSOD -/- caused a more pronounced functional deterioration of CIN, CPAH and NSPAH with additional down regulation of tubular epithelial transporter capacities and respective transporter expressions (OAT1/ HSP70, MCP1, IL6b, Cx3Cl1/Cx3Cr1 and NO-synthases (iNOS/eNOS) were unchanged. In iAKI, expression of MCP1, IL6b, Cx3Cl1/Cx3Cr1 and NO-synthases (iNOS/eNOS) were unchanged. In iAKI, expression of HO1/HO2, MCP1, IL6b and Cx3Cl1/Cx3Cr1 was significantly increased.

**Conclusions:** Supplementation of ecSOD reversed this protective effect in male AKI model. In case of female mice, 23-min IR injury induced mild tubular injury compared to male mice. Depletion of estrogen by bilateral ovariectomy increased IR-induced tubular injury and inflammation. However, supplementation of estrogen in ovariotomized female mice attenuated the IR-induced tubular injury and decreased macrophage infiltration. The expressions of inflammatory cytokines such as TNF-α, MCP-1, IFN-γ, and CCL17 were increased at 2 d in male AKI group. However, castration of male group mice decreased IR-induced cytokine expression. Supplementation of testosterone increased IR-induced cytokine expression. In case of female mice, estrogen depletion by bilateral ovariectomy significantly increased renal TNF-α, MCP-1, IFN-γ and CCL17 expression.

**Conclusions:** Supplementation of estrogen attenuated these IR-induced inflammatory cytokine expressions in ovariotomized female mice. These results suggested that male gender is more susceptible to the ischemia-reperfusion renal injury by enhanced inflammatory response. Further studies are needed to address the underlying mechanism of gender differences in the AKI.
regulation of OAT1 and OAT3. Following I/R injury, eSSD deficient mice exhibit a differential regulated inflammatory pattern (COX1/COX2, HO1/2, HSP70, MCP1, IL6b, Cx3Cl1/Cx3Cl1), whereas inOS induction was abrogated.

Conclusions: These results emphasize the detrimental pathophysiological impact of the extracellular O2 radical in iAKI with regard to renal function in an eSSD deficient mouse model. Tubular epithelial transport might be additionally regulated by primary or secondary O2-dependent mechanisms in iAKI.

**SP060** PRETREATMENT WITH PARICALCITOL ATTENUATES INFLAMMATION IN ISCHEMIA-REPERFUSION INJURY VIA UPREGULATION OF CYCLOOXYGENASE-2 AND PROSTAGLANDIN E2

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**Introduction and Aims:** The effect of paricalcitol on renal ischemia-reperfusion injury (IRI) has not been investigated. We examined whether paricalcitol is effective in preventing inflammation in a mouse model of IRI, and evaluated the cyclooxygenase-2 (COX-2) and prostaglandin E2 (PGE2) pathway as a protective mechanism of paricalcitol.

**Methods:** Paricalcitol (0.3 mg/Kg) was administered to male C57BL/6 mice 24 hrs before I/R. Bilateral kidneys were subjected to 23 min of ischemia, and mice were killed 72 hrs after I/R. The effects of paricalcitol on renal IRI were evaluated in terms of renal function, tubular necrosis, apoptotic cell death, inflammatory cell infiltration and inflammatory cytokines. The effects of paricalcitol on COX-2, PGE2, and its receptors were investigated.

**Results:** Paricalcitol pretreatment improved renal function (decreased blood urea nitrogen and serum creatinine levels), tubular necrosis and apoptotic cell death in IRI mice kidneys. The infiltration of inflammatory cells (T cells and macrophages), and production of proinflammatory cytokine (RANTES, tumor necrosis factor-a, interleukin-1b and interferon-g) were reduced in paricalcitol-treated mice with IRI. Paricalcitol upregulated COX-2 expression, PGE2 synthesis and mRNA expression of receptor subtype EP4 in postischemic renal tissue. The coteatment of selective COX-2 inhibitor with paricalcitol restored functional injury and tubular necrosis in paricalcitol-treated mice with IRI.

**Conclusions:** Our study demonstrates that paricalcitol pretreatment prevents renal IRI via inhibition of renal inflammation, and upregulation of COX-2 and PGE2 is one of the protective mechanisms of paricalcitol in renal IRI.

**SP061** PHOSPHODIESTERASE-5 INHIBITION ATTENUATES EARLY RENAL ISCHEMIA-REPERFUSION-INDUCED ACUTE KIDNEY INJURY: ASSESSMENT BY QUANTITATIVE MEASUREMENT OF URINARY NGAL AND KM-1

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**Introduction and Aims:** Acute kidney injury (AKI) is a common clinical problem that still lacks effective treatment. PDE5 inhibitors possess anti-apoptotic and anti-oxidant properties, making it a promising therapy for ischemia-reperfusion (I/R) injury of various organs. The present study evaluated the early nephroprotective effects of Tadalafil, a PDE5 inhibitor, in experimental model of renal I/R.

**Methods:** Sprague-Dawley rats were divided into 2 groups: vehicle-treated I/R (n=10), and Tadalafil (10 mg/kg, PO)-treated I/R group (n=11). After removal of the right kidney and collection of 2 baseline urine samples, the left renal artery was clamped for 45 min followed by reperfusion for 60, 120, 180, and 240 min. Functional and histological parameters of the kidneys from the various groups were determined.

**Results:** In the vehicle-treated I/R group, glomerular filtration rate (GFR) was significantly reduced compared to that in normal kidneys. In addition, the ischemic kidney showed marked cast formation, necrosis and congestion, a consistent pattern of acute tubular necrosis. Furthermore, urinary excretion of NGAL and KM-1, two novel biomarkers increased following I/R insult. In contrast, Tadalafil treatment resulted in a significant improvement in kidney function and amelioration of the adverse histological alterations of the ischemic kidney. Noteworthy, the urinary excretion of NGAL and KM-1 markedly decreased in the Tadalafil treated I/R group.

**Conclusions:** These findings demonstrate that Tadalafil possesses early nephroprotective effects in rats kidney subjected to I/R insult. This approach may suggest a prophylactic therapy for patients with ischemic AKI.

**SP062** C/EPP HOMOLOGOUS PROTEIN (CHOP) DEFICIENCY ATTENUATES ISCHEMIA-REPERFUSION-INDUCED ACUTE KIDNEY INJURY: ROLES OF REACTIVE OXYGEN SPECIES

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**Introduction and Aims:** Renal ischemia-reperfusion (IR) is a major cause of acute kidney injury (AKI). The mechanism of IR injury includes inflammation, hypoxia, oxidative stress and endoplasmic reticulum (ER) stress. C/EPP Homologous Protein (CHOP) mediates a part of ER stress-dependent apoptosis, and is a downstream molecule of activating transcription factor (ATF)-6 and ATF-4. The study aim is to clarify the role of CHOP in IR-induced AKI.

**Methods:** This study applied the wild type and CHOP knockout mice in the IR model.

**Results:** CHOP deficiency retarded renal injury after IR-induced AKI. Both renal proximal tubule damage and collagen deposition were attenuated in CHOP deficiency mice. Furthermore, CHOP deficiency could decrease IR-induced caspase-3 cleavage and activity. Lipid peroxidation was enhanced after 24 hrs of IR, but it was reversed by CHOP deficiency mice. In addition to in vivo study, we evaluated the effects of reactive oxygen species in the CHOP knockdown renal tubule cells. CHOP silenced tubule cells were treated by H2O2, and shown more resistant to apoptosis. In spite of lesser cleavage of CHOP, in CHOP silenced tubule cells, treated with H2O2, did not influence by H2O2 and CHOP siRNA treatment. Finally, CHOP deficiency blocked NfEB activation and COX-2 expression, which suggested CHOP-related signals contributed to the oxidative stress-mediated inflammation responses.

**Conclusions:** To the best of our knowledge, this is the first report demonstrated that CHOP-related signals contribute to the IR-related AKI.

**SP063** PANCREATIC INJURY INDUCED BY RENAL ISCHEMIA-REPERFUSION (I/R) INJURY POSSIBLE ROLE OF OXIDATIVE STRESS

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**Introduction and Aims:** Recent studies demonstrated remote effects of renal ischemia/reperfusion (I/R) injury in some organs such as brain, liver, and lungs. We investigated the effects of renal I/R injury on pancreas.

**Methods:** Twenty –four male adult Sprague-Dawley rats were divided equally into 2 groups; sham group rats underwent all surgical procedures except renal ischemia. Acute kidney injury groups rats underwent bilateral renal ischemia for 45 min. Renal functions (serum creatinine and BUN), pancreatic functions (serum amylase, lipase and insulin) and fasting blood glucose were measured at 2 hrs, 1 day, 3 days and 7 days after ischemia. Also, pancreatic histology and malondialdehyde (MDA), catalase and reduced glutathione (GSH) were examined at 2 hrs and 7 days after ischemia.

**Results:** The ischemic rats showed significant increase in renal functions with significant increase in serum amyrase and lipase in control group at 2 hrs, 1 day, 3 days and 7 days after ischemia. Also, pancreatic histology and malondialdehyde (MDA), catalase and reduced glutathione (GSH) were examined at 2 hrs and 7 days after ischemia.

**Conclusions:** The ischemic rats showed significant increase in renal functions with significant increase in serum amyrase and lipase in control group at 2 hrs, 1 day, 3 days and 7 days after ischemia. Blood glucose and fasting insulin showed no significant change a part from significant increase in insulin in sham group at 1 day after ischemia. Pancreas isolated from control rats showed significant increase in histopathological damage score and significant increase in MDA and catalase enzyme and decrease GSH.

**Conclusions:** Bilateral renal ischemia for 45 min caused significant change in pancreatic functions and histology and increased oxidants with deficiency of antioxidants in pancreas.

**SP064** IMPACT OF COMBINATION OF ISCHEMIC PRECONDITIONING AND SULPHORAPHANE ON IN RENAL ISCHEMIA/REPERFUSION INJURY: ROLE OF NUCLEAR FACTOR-2 (NF-2) GENE AND ITSDEPENDENT GENES, INFLAMMATORY CYTOKINES, AND APOPTOSIS

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**Introduction and Aims:** Recently, it was demonstrated that nuclear factor -2 erythroid related factor 2 (Nrf2) gene and its dependent genes, are important endogenous
Adaptive mechanisms that protect organs against ischemic injury. The aim of this study was to investigate impact of combined effect of ischemic preconditioning (Ipre) and sulphoraphane on the expression of nuclear factor-2 erythroid related factor 2 (Nrf2) gene and its dependent genes; heme oxygenase-1 (HO-1) and NADPH:quinone oxidoreductase1 (NQO-1) and inflammatory cytokines TNF-α, IL-1β, and intercellular adhesion molecule-1 (ICAM1) and caspase-3 in renal ischemia/reperfusion (I/R) injury.

Methods: Ninety male Sprague Dawley rats were classified into 5 groups (each consists of 18 rats): sham, control, Ipre, sulphoraphane, and Ipre + sulphoraphane. Each group was subdivided into 3 subgroups each containing 6 rats according to time of kidney harvesting and taking blood samples; 2, 24, and 48 hrs subgroups. Renal functions including serum creatinine, BUN were measured at basal conditions and by the end of experiment. Expression of Nrf2, HO-1, NQO-1, TNF-α, IL-1β, and ICAM-1 was measured by real time PCR in kidney tissues by the end of experiment. Also, immunohistochemical localization of Nrf2 and caspase-3 was measured in kidney tissues.

Results: Both Ipre and sulphoraphane alone caused significant improvement in renal functions (p < 0.01), while combined caused more significant improvement of renal functions than each agent alone (p < 0.001). Also, the expression of nrf2, HO-1 and NQO-1 was increased in combined group compared to Ipre and sulphoraphane groups (p < 0.05). Also, all studied groups showed significant improvement of inflammatory (TNF-α, IL-1β) and ICAM-1 and apoptotic (caspase-3) markers (p<0.001). However, expression of inflammatory and apoptotic markers in control group did not show any significant difference with Ipre and sulphoraphane groups.

Conclusions: combination of Ipre and sulphoraphane caused more significant attenuation of renal injury in I/R than Ipre and sulphoraphane alone. This effect might be due to enhancement in expression and activation of Nrf2 gene and its dependent antioxidant genes; HO-1 and NOQ1.

Introduction and Aims: HIF-1 plays a critical role in tubular cells of both acute and chronic hypoxic kidney. Its protective role against tubular injury has been suggested and HIF activation is a potential therapeutic option in kidney diseases. We aimed to identify a novel gene involved in regulation of HIF-1 in kidney, a final common pathway to end stage kidney disease.

Methods: Microarray analysis of the renal cortex of rat renal artery stenosis (RAS) model (day 3 and day7) was used as in vivo screening for potential HIF-1 regulating genes. Hela cells transfected with shRNA plasmids against continuously regulated genes in RAS kidney were evaluated for potency of HIF-1 regulation, by HIF-1α protein expression, HIF-1 target gene expressions, and HRE reporter activity. Acute and chronic rat hypoxic mouse models were analysed for this gene’s expression to localize and identify its role in kidney. To confirm its relation to hypoxia in cultured human renal tubular cells, RNAi treated HK-2 cells under hypoxic condition were examined for HIF-1 regulation. Its regulating mechanism was investigated by RT-PCR, HIF-1 promoter assay, transcription or protein degradation inhibition experiments. To investigate if this novel HIF-1 regulating pathway gets activated under normoxia, inflammation was focused. Inflammatory stimuli were examined for this gene and HIF-1α induction. Finally, the mechanism by which this gene is induced by hypoxia or inflammatory stimuli was investigated.

Results: 150 genes were extracted from microarray analysis. shRNA library experiment revealed CEBPD to be the most promising HIF-1 regulator. CEBPD was up-regulated in RAS, 5/6 nephrectomy, ischemia reperfusion injury, and cisplatin nephrotoxicity. Its expression was prominent in the nuclei of tubular cells of S3 segment, the most hypoxic portion in ischemic renal injury. In HK-2, hypoxic treatment augmented CEBPD expression via HIF-1 independent pathway, which regulated HIF-1 protein expression and its target genes, VEGF and GLUT-1. CEBPD regulated HIF-1 by stabilizing its RNA. All of the above hypoxic models showed macrophage infiltration accompanied by up-regulation of its producing cytokines, which demonstrated that hypoxia and inflammation co-existed in kidney. As CEBPD is an inflammatory response gene, we hypothesized these two conditions are cross-linked by CEBPD/HIF-1 pathway. In vitro, correspondingly, interleukin-1β induced HIF-1 expression in CEBPD dependent manner. Furthermore, NF-κB pathway was proved to regulate CEBPD expression under hypoxia or IL-1β.

Conclusions: These results demonstrate that CEBPD is a novel HIF-1 regulator in kidney. We further identified that CEBPD was up-regulated via NF-κB pathway and regulated HIF-1 expression and its transcriptional activity in tubular cells. CEBPD is likely to contribute to protection of tubular cells from its injury through HIF-1, especially under co-existing condition of hypoxia and inflammation.
groups showed no effect on parameters of renal function and histology. KRG significantly decreased ROS production at day 10 (GSH 1.5±0.1 vs. 5.0±0.5 μM/g kidney wt, p<0.05; 8-OHdG in urine 3.0±0.1 vs. 2.0±0.5 ng/mg creatinine, p<0.05) and apoptosis. In in-vitro study GM induced ROS production with an increase in NOX activity and mitochondrial oxidation in NRK cells, which were ameliorated with KRG. GM-induced apoptosis was associated with an increased expression of Bax, cytochrome C, caspase 3 and -9, which was blocked by KRG as well as anti-oxidants, N-acetyl cysteine, DPI and MitoQ.

Conclusions: Our results suggest that KRG may protect the kidney from Gentamicin-induced AKI, possibly via the mechanism of modulation of oxidative stress. Further studies will be necessary to verify therapeutic potential of KRG with an investigation of renoprotective mechanisms in various spectrum of renal disease.

SP068 MITOCHONDRIA-TARGETED APPROACHES TO PREVENT GENTAMYCIN TOXICITY

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Introduction and Aims: The toxic effects of aminoglycoside antibiotics are realized via stimulating intercellular reactive oxygen species (ROS) overproduction. Oxidative damage of mitochondria results in the opening of mitochondrial permeability transition pore (MPTP). The signaling prevents opening of MPTP are known as preconditioning (PC) phenomenon. PC signaling pathways are converged on glycogen synthase kinase 3 (GSK3β) and results in its inhibition by phosphorylation. The aim of the study was to investigate whether mitochondria-targeted antioxidant SkQR1 and δ-opioid receptor agonist (dalargin) and GSK3β inhibitor (LiCl) are able to prevent gentamycin toxicity.

Methods: Male outbred rats were treated with gentamycin (i.p. 160 mg/kg) for 6 days. On 7th day the blood samples were obtained and concentration of creatinine and blood urea nitrogen (BUN) was measured. Western blotting of whole kidney homogenates and immunohistochemistry of kidney tissue were used to study the involvement of GSK3β. For in vitro studies primary cultures of renal tubular epithelium were incubated with gentamycin (from 0.6 to 10 mg/ml) for 24 h. Cells viability was assessed using the standard MTT test.

Results: In vitro gentamycin caused kidney cells death during 24 h. Preincubation with 50 nM SkQR1 for 24 h significantly increased the survival of the cells. In vivo gentamycin application resulted in pronounced nephrotoxicity (3.6-fold increase of blood urea nitrogen (BUN) and 3.9-fold increase of creatinine). The administration of SkQR1 and lithium significantly ameliorated the increase of BUN and creatinine levels. Western blotting of whole kidney homogenates and immunohistochemistry of kidney tissue showed a decrease in pro-apoptotic markers Bax and caspase-9 and an increase in anti-apoptotic marker BCL-2. The expression of GSK3 β was decreased by gentamycin and increased by lithium. SkQR1 administration resulted in a decreased expression of GSK3 β.

Conclusions: We conclude that mitochondria-targeted antioxidant SkQR1 effectively prevented nephrotoxicity of gentamycin. Partially this protective effect could be referred to induction of PC signaling. Moreover, different compounds that inhibits GSK3β thus protecting mitochondria, such as LiCl and dalargin, may serve as promising agents for preventing negative consequences of aminoglycoside therapy.

SP069 SOLUBLE HEMOJUVELIN, AN EARLY BIOMARKER PROMOTES IRON DEPOSITION DURING ACUTE KIDNEY INJURY

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Introduction and Aims: Free iron plays an important role in the pathogenesis of acute kidney injury (AKI) via the formation of hydroxyl radicals. Systemic iron homeostasis is controlled by the hemojuvelin (hemojuvelin)-ferroportin-hepcidin axis in the liver, but less is known about this process in AKI.

Methods: By proteomics, we have identified a 42 kDa soluble hemojuvelin (sHJV), a proteolytic form of the 50 kDa processed by furin protease from membrane-bound hemojuvelin (mHJV), was detected in the urine during AKI after cardiac surgery. Furthermore, the biopsies of the study was to investigate whether hemojuvelin-ferroportin-hepcidin axis in the liver, but less is known about this process in AKI. We conclude that sHJV relates to increase total kidney iron, secrete hepcidin, internalize ferroportin, whereas sHJV do the opposite and that the generation of sHJV is inhibited by furin in vitro.

Conclusions: Our findings link endogenous HIV inractically with kidney iron homoeostasis, add new significance to early predict AKI, and identify novel therapeutic targets to reduce the severity of AKI by furin inbitor.
SP074  
CHRONIC RENAL DAMAGE IS EXACERBATED IN THE CONTRALATERAL KIDNEY OF DB/DB MICE SUBJECTED TO 2K1C HYPERTENSION  

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Introduction and Aims: Hypertension is a major risk factor for progression of renal disease in patients with diabetes. However, few studies have addressed potential contributions of chronic inflammation on diabetic renal disease on renal injury and death. Furthermore, no previous study has addressed potential differential effects of renovascular hypertension on the renostatic versus contralateral kidney in diabetic mice. We therefore sought to test the hypothesis that renovascular hypertension promotes endothelial chronic renal disease in db/db mice, a model of type II diabetes.

Methods: Renovascular hypertension was established in db/db and wild-type control mice through placement of a cuff on the right renal artery.  

Results: At 17 weeks following surgery, mean systolic blood pressure was elevated to a similar extent in db/db and wild-type mice subjected to RAS. Although peak angiotensin 1 production was higher in db/db RAS mice (50 ng/ml/hr) than WT RAS mice at 4 weeks following surgery (9 ng/ml/hr, p<0.05), levels returned to baseline levels in all groups at 17 weeks after surgery. As expected, cuffed kidneys of db/db mice developed progressive interstitial fibrosis, tubular atrophy, and interstitial inflammation. Glomeruli from cuffed kidneys of db/db mice showed mesangial matrix expansion than age-matched sham db/db mice. In accordance with our previous observations, the contralateral kidneys of wild-type mice subjected to RAS showed minimal histopathologic abnormalities. Remarkably, the contralateral kidneys of db/db mice developed severe and progressive glomerular sclerosis, interstitial fibrosis, tubular atrophy, and interstitial inflammation. At 17 weeks following surgery, glomeruli from db/db RAS mice showed greater mesangial matrix expansion than wild-type RAS mice or db/db shams (PAS score 3.1 vs. 0.9 vs. 0.3, respectively on a 4 point scale; p<0.01). The mean glomerular basement membrane thickness of db/db mice subjected to RAS was 23% greater than that of age-matched sham db/db mice, as assessed by morphometric analysis of electron microscopic images, despite similar blood glucose levels in the db/db RAS and db/db sham mice. Gliomerul of db/db RAS, but not sham mice showed extensive effacement of glomerular visceral epithelial cell foot processes. db/db RAS mice showed greater interstitial fibrosis than age-matched db/db sham mice (7.9 vs 2.1%, p<0.05, as assessed by quantitative assessment of trichrome-stained slides), a process associated with increased fibrinogen and collagen III deposition. Urine albumin excretion in db/db RAS mice was 6-fold higher in db/db RAS mice than age-matched db/db sham mice. Finally, mean blood urea nitrogen levels were significantly elevated in db/db RAS, but not wild-type RAS or db/db sham mice at 17 weeks after surgery.

Conclusions: Renovascular hypertension superimposed on diabetes exacerbates the development of bilateral chronic renal disease in db/db mice.

SP075  
PATHOPHYSIOLOGICAL IMPLICATION OF A HIGH G1-TO-G0-PHASE CELL RATIO IN THE DEVELOPMENT OF PROLIFERATION OF PROXIMAL TUBULE CELLS  
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Introduction and Aims: Proximal tubule (PT) cells have high proliferative potential and are frequently observed to rapidly undergo cell cycle especially after acute kidney injury. However, little is known about the relationship between G1-to-G0-phase cell ratio and G1-S progression in PT cells. The purpose of this study is to evaluate kinetics of G0-G1-phase resting cells in PT in the initiation of undergoing cell cycle in response to proliferative and toxic stimuli.

Methods: We isolated PT cells and distal tubule (DT) cells [from normal male SD rats, rats 30 hours after injection of lead acetate (proliferative stimulus)] or rats 24 hours after injection of nephrotoxic dose of uranyl acetate (which can induce PT damage in association with proliferative activity of PT cells as early as day2)] by using Percoll density-gradient centrifugation, and analyzed the cell cycle by Flow cytometry. The separation of G0 and G1 was done by using combination of Hoechst33342 and Pyronin Y. Immunocytochemistry for cdt1 (a marker of G1-phase) was also applied.

Results: The proportion of G0-G1-, S- and G2-M-phase cells in normal PT was 98.3, 0.4 and 1.3%, respectively. G0 of G1-G0 phase progression in PT cells. The purpose of this study is to evaluate kinetics of G0-G1-phase resting cells in PT in the initiation of undergoing cell cycle in response to proliferative and toxic stimuli.

Methods: We isolated PT cells and distal tubule (DT) cells [from normal male SD rats, rats 30 hours after injection of lead acetate (proliferative stimulus)] or rats 24 hours after injection of nephrotoxic dose of uranyl acetate (which can induce PT damage in association with proliferative activity of PT cells as early as day2)] by using Percoll density-gradient centrifugation, and analyzed the cell cycle by Flow cytometry. The separation of G0 and G1 was done by using combination of Hoechst33342 and Pyronin Y. Immunocytochemistry for cdt1 (a marker of G1-phase) was also applied.

Results: The proportion of G0-G1-, S- and G2-M-phase cells in normal PT was 98.3, 0.4 and 1.3%, respectively. G0 of G1-G0 phase progression in PT cells. The purpose of this study is to evaluate kinetics of G0-G1-phase resting cells in PT in the initiation of undergoing cell cycle in response to proliferative and toxic stimuli.
approximately 2.3, indicating that the ratio of G1 to G0 in PT treated with unryl acetate increased when compared to that in normal PT. These suggest that stimuli inducing acute kidney injury can increase G0-G1 transition before G1-S progression.

Conclusions: A high G1-G0 ratio in normal PT and increase in G0-G1 transition in the development of PT cell proliferation may contribute to rapid and robust G1-S progression.

**Disclosure:**

**SP074**  
L-LYSINE AMELIORATES VASCULAR CALCIFICATION IN ADENINE-INDUCED UREMIC RATS  
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Introduction and Aims: Vascular calcification (VC) is common in patients with chronic kidney disease (CKD) and is associated with increased cardiovascular morbidity and mortality. In 2006, Price et al. reported that low protein diet exacerbates VC in adenine-induced uremic rats [Kidney Int. 2006;70(9):1577-83]. The results of this report prompted us to hypothesize that supplementation of certain amino acid would ameliorate VC. Because L-lysine is the first-limiting amino acid in the most of cereal grains, we examined whether L-lysine supplementation ameliorates VC.

Methods: Male Sprague-Dawley rats at age 12 weeks were divided randomly into four groups: no protein (LP) diet, LP diet + 0.75% adenine (group Ade), LP diet + 0.75% adenine + 2.5% L-lysine HCl (group Lys). We performed in vitro analysis using these amino acids. We further analyzed plasma levels of amino acids. We confirmed that plasma levels of L-lysine-metabolites, such as homoarginine, were elevated in group Lys, but the levels of alpha-aminoadipic acid and homoarginine, were not different among the LP, Ade, and Lys groups. Intragrually, serum calcium level in group Lys was slightly higher than that in groups Ade and Lys. We analyzed plasma levels of amino acids. We confirmed that plasma levels of L-lysine and its metabolic products were higher than those the basal level. Consequently, we hypothesized that plasma levels of L-lysine metabolites, such as homoarginine, were significantly higher than those in groups Ade and Lys. Hence, we performed in vivo analyses using these amino acids. In a solution of supersaturated calcium/phosphate, arginine significantly increased calcium phosphate precipitation, while L-lysine significantly decreased calcium phosphate precipitation. We analyzed the mechanism of this phenomenon and the results showed that plasma levels of L-lysine-metabolites, such as homoarginine, were significantly lower than those in group LP.

Results: At age 18 weeks, rats in group LP had no VC, whereas those in groups Ade and Lys had comparable levels of VC. L-lysine supplementation almost completely ameliorated VC. Because VC often coexists with bone loss, we also examined the bone morphology and found that L-lysine protected the femora from osteoporotic changes. Body weight, food intake, water intake, serum levels of creatinine, urea nitrogen, and phosphate were not different among groups Ade, Gly, and Lys. Intriguingly, serum calcium level in group Lys was slightly higher than that in groups Ade and Gly. We further analyzed plasma levels of amino acids. We confirmed that plasma levels of L-lysine metabolites, such as homoarginine, were significantly higher than those in groups Ade and Gly, and we performed in vitro analysis using these amino acids. In a solution of supersaturated calcium/phosphate, arginine and homoarginine attenuated spontaneous precipitation of minerals, thus suggesting that the elevation of plasma arginine and homoarginine explains the mechanism, at least in part, how VC was attenuated in group Lys.

Conclusions: L-lysine ameliorated vascular calcification in adenine-induced uremic rats. Our findings provide a novel approach for the treatment of VC in CKD.

**Disclosure:**

**SP075**  
CARDIAC MORPHOLOGY AND FUNCTION IN RATS WITH ADENINE-INDUCED CHRONIC RENAL FAILURE  
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Introduction and Aims: Cardiac disease is the major cause of death in patients with chronic kidney disease. An increased left atrial size is a sensitive marker of left ventricular (LV) dysfunction and clearly related to poor prognosis. Rats with adenine-induced chronic renal failure (ACRF) develop severe renal insufficiency and metabolic abnormalities that closely resemble those in patients with uremia. The aim of the present study was to characterize cardiac morphology and function in rats with ACRF. We hypothesized that this model may be valuable in the investigation of pathological mechanisms underlying uremic cardiomyopathy.

Methods: Male Sprague-Dawley rats (n=10 per group) received either chow containing adenine or were pair-fed an identical diet without adenine (controls, C). After 10 weeks animals were randomized to either remain on the same diet (normal 0.6% NaCl) or to be switched to high 4% NaCl (HNa) chow. Because four groups were investigated (n=8-10 per group): C-NNa; C-HNa, ACRF-NNa; ACRF-HNa. Two weeks after randomization renal clearance experiments were performed under isoflurane anesthesia and dynamic RBFA was assessed by transfer function analysis. Kidney and heart histology were analyzed. Data are means±SD.

Results: Rats with ACRF developed marked reductions in GFR (≤15% of control values) and RBF (<50% of control values) whereas mean arterial pressure was elevated by approximately 15 mmHg and accompanied by LV hypertrophy. High NaCl diet significantly increased transfer function gain values in the frequency range of the myogenic response (0.06-0.09 Hz) in ACRF animals (0.3±0.4 vs. 4.4±3.8 dB, P<0.05) but not in controls. Rats with ACRF animals showed severe tubulointerstitial injury but abnormalities were not significantly aggravated by high NaCl intake. High NaCl diet had no significant effects on LV morphology in controls but produced a marked increase in the size fraction of LV fibrosis (10.6±4.5 vs. 3.4±1.4 % in ACRF-HNa and ACRF-NNa, respectively, P<0.01).

Conclusions: A two week period of high NaCl diet in ACRF rats significantly impaired dynamic RBFA in the frequency range of the myogenic response. Hence, a high salt intake in chronic kidney disease may increase the vulnerability of glomeruli to hyperfiltration by facilitating pressure transmission to glomerular capillaries. In addition, high NaCl diet markedly aggravated LV fibrosis in this model of renal failure.
Methods: Mice were divided into three groups: 1) control diet (0.9 % phosphate), 2) adenine rich diet (0.9 % phosphate), 3) high phosphate diet (1.65 % phosphate in diet and 1mM in drinking water). Extracted kidney-RNA was hybridized to Affymetrix Mouse Genome 430 2.0 arrays. Raw data was pre-processed using Robust Multi-array Average, and e Klopp was applied to resulting data. Genes were considered differentially expressed when adjusted p-value was < 0.05 and fold change was >1.5 or <0.5 compared to controls. Data was analyzed with the Database for Annotation, Visualization and Integrated Discovery (DAVID) to identify overrepresented gene ontology groups. 

Results: Removal of duplicate genes and probes lacking annotation resulted in 2178 uniquely regulated genes in the adenine group, 427 in the high phosphate diet group and 199 commonly regulated genes. DAVID analysis revealed that biological processes such as extracellular matrix organization, regulation of cytokine production, response to wounding, inflammatory response and collagen fiber organization were enriched in both groups. In contrast, a majority of the uniquely and differentially expressed transcripts in the high phosphate group reflected diverse biological processes including oxidation-reduction, isoprenoid metabolic process, regulation of TGF-beta receptor signaling pathway, steroid metabolic process and lipid biosynthesis. These biological processes include genes identified as cardiovascular risk factors as well as genes involved in cardiovascular pathology.

Conclusions: Dietary phosphate loading evoked a transcriptional pattern distinct from adenine-induced uremia with differentially regulated genes involved in inflammation, lipid metabolism, hypertension and vascular calcification. Our data provides functional support for the observed relation between hyperphosphatemia and adverse cardiovascular outcomes in CKD.

Introduction and Aims: Liprotein glomerulopathy (LPG) is a unique disease characterized by intraglomerular lipoprotein thrombi. Previous reports have suggested that apolipoprotein E (apoE) variants play an important role in the development of LPG. In our recent study, we have shown that human FcγR IIIa−/−KO mice showed greater lipoprotein deposition in and lesser macrophage infiltration into the mesangial area than human apoE3-injected apoE−/−KO mice, although both groups showed similar dyslipidemia. These results suggest that FcγR deficiency also plays a principal role in the development of LPG in concert with apoE variants, and it may be linked to macrophage function. However, the mechanism by which FcγR deficiency causes LPG remains unclear. In this study, we attempted to clarify the mechanism of FcγR deficiency in the development of LPG.

Methods: We generated FcγR−/−apoE−/−KO mice by crossing apoE−/−KO mice with FcγR−/−KO mice, and subsequently introduced human recombinant apoE3 into FcγR−/−apoE−/−KO mice. At 21 days after infection, the mice were killed, and the kidneys and peritoneal macrophages were collected. To evaluate macrophage function, the harvested peritoneal macrophages were cultured with oxidized low-density lipoprotein (LDL) stained with Oil Red O, and observed under a light microscope. Cytokines in the supernatants were also examined by ELISA. In addition, mRNA transcription of the LDL receptor (LDLR), i.e., Ldr, and major scavenger receptors (SRs), i.e., Scara3, G3d6, Lox1, Scarf2, and Cxcl16, in the kidney were quantified using real-time polymerase chain reaction (PCR).

Results: Oxidized LDL uptake by macrophages was significantly lower in FcγR−/−apoE−/−KO mice than in apoE−/−KO mice (28.9 ± 12.8% vs. 79.3 ± 3.6%). The expression levels of MCP-1 and RANTES were decreased in the supernatants of samples in which peritoneal macrophages were incubated with oxidized LDL. Furthermore, real-time PCR examination of kidney samples showed no significant differences in the levels of SR mRNA transcripts, whereas the level of Ldr RNA transcripts was significantly lower in the FcγR−/−apoE−/−KO mice than in the apoE−/−KO mice. These results suggest that impairment of macrophage function is one of the causes of LPG. Moreover, the level of Ldr mRNA transcripts was reduced in the FcγR−/−apoE−/−KO mice. LDLR has been reported to be involved in the formation of foam cells through Fcγ receptor. Therefore, it is suggested that FcγR deficiency impairs the organic reaction responsible for the elimination of abnormal lipids and results in the deposition of these irremovable lipids as lipoprotein thrombi.

Conclusions: In this study, macrophage reactions for modified lipids, such as modified LDL, uptake and cytolysis, were elicited to a lesser extent in FcγR−/−apoE−/−KO mice than in apoE−/−KO mice. These results suggest that impairment of macrophage function is one of the causes of LPG. Moreover, the level of Ldr mRNA transcripts was reduced in the FcγR−/−apoE−/−KO mice. LDLR has been reported to be involved in the formation of foam cells through Fcγ receptor. Therefore, it is suggested that FcγR deficiency impairs the organic reaction responsible for the elimination of abnormal lipids and results in the deposition of these irremovable lipids as lipoprotein thrombi.

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Conclusions: Dietary phosphate loading evoked a transcriptional pattern distinct from adenine-induced uremia with differentially regulated genes involved in inflammation, lipid metabolism, hypertension and vascular calcification. Our data provides functional support for the observed relation between hyperphosphatemia and adverse cardiovascular outcomes in CKD.

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Methods: We generated FcγR−/−apoE−/−KO mice by crossing apoE−/−KO mice with FcγR−/−KO mice, and subsequently introduced human recombinant apoE3 into FcγR−/−apoE−/−KO mice. At 21 days after infection, the mice were killed, and the kidneys and peritoneal macrophages were collected. To evaluate macrophage function, the harvested peritoneal macrophages were cultured with oxidized low-density lipoprotein (LDL) stained with Oil Red O, and observed under a light microscope. Cytokines in the supernatants were also examined by ELISA. In addition, mRNA transcription of the LDL receptor (LDLR), i.e., Ldr, and major scavenger receptors (SRs), i.e., Scara3, G3d6, Lox1, Scarf2, and Cxcl16, in the kidney were quantified using real-time polymerase chain reaction (PCR).

Results: Oxidized LDL uptake by macrophages was significantly lower in FcγR−/−apoE−/−KO mice than in apoE−/−KO mice (28.9 ± 12.8% vs. 79.3 ± 3.6%). The expression levels of MCP-1 and RANTES were decreased in the supernatants of samples in which peritoneal macrophages were incubated with oxidized LDL. Furthermore, real-time PCR examination of kidney samples showed no significant differences in the levels of SR mRNA transcripts, whereas the level of Ldr RNA transcripts was significantly lower in the FcγR−/−apoE−/−KO mice than in the apoE−/−KO mice. These results suggest that impairment of macrophage function is one of the causes of LPG. Moreover, the level of Ldr mRNA transcripts was reduced in the FcγR−/−apoE−/−KO mice. LDLR has been reported to be involved in the formation of foam cells through Fcγ receptor. Therefore, it is suggested that FcγR deficiency impairs the organic reaction responsible for the elimination of abnormal lipids and results in the deposition of these irremovable lipids as lipoprotein thrombi.

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biochemical parameters, blood pressure (BP) and myocardium morphology in 5/6 nephrectomized (NE) Wistar rats.

**Methods:** Animals were divided into 3 groups: 1 – sham-operated (control, C); 2 – NE rats receiving standard diet; 3 – NE rats receiving LPD and Ketosteril. Haemo parameters, blood pressure (BP) and myocardium morphology in 5/6 nephrectomized (NE) Wistar rats.

**Results:** NE rats on the standard diet were associated with significant rise in BP (mean ±SE, 178±0.9 in group 2, vs 158±0.9 mmHg in group 3, p<0.001). LPD with Ketosteril prevented a significant increase in BP in rats after NE (p<0.001). PI level increased in rats after NE, receiving standard diet: 2.6±0.01 mmol/l in group 2 vs C – 2.05±0.05 mmol/l (p<0.01). Serum PI level in group 3 didn’t increase significantly (2.20±0.08 mmol/l). Total Ca level in group 2 was lower, than in group 3 (2.07±0.05 and 2.34±0.08 mmol/l respectively; p<0.01), whereas in C – 2.35±0.15 mmol/l (p=NS vs group 3). LPD didn’t influence on the TFP and Al levels. LPD with Ketosteril decreased proteinuria in rats after NE (in group 2 – 9.8±2.2 g/l in group 3 – 1.5±0.9 g/l; p<0.01). BP in group 2 was significantly higher, than in C (165±5 vs 125±10 mmHg, p<0.001). LPD with Ketosteril prevented increase in BP (130±5 mmHg) compared with NE rats on standard diet (p<0.001). LVH in group 3 was less than in other groups (1.96±0.15 mg/g vs 2.72±0.31 mg/g; p<0.01) in group 2, and vs 2.35±0.09 mg/g in C rats). After NE in groups 2 and 3 morphological findings showed disintegration of myocardium cells and signs of apoptosis, fragmentation of myocardium fibers, severe cellular cloudy degeneration, perivascular sclerosis. Hypertrophy of myocardium cells was not revealed. But increasing in conjunctive tissue area was significantly more in NE rats on standard diet (3636 ±8.41μm² vs 2750.5±6.57 μm²; p<0.01) and vs groups on LPD and Ketosteril (2837.6 ±6.2 μm², p<0.01). Vascular walls didn’t thicken in rats on LPD and Ketosteril.

**Conclusions:** Long term LPD with Ketosteril delayed myocardial fibrosis and showed anti hypertensive effects in 5/6 NE Wistar rats.

**SP081**  
PIRFENIDONE INHIBITS MACROPHAGE INFILTRATION IN 5/6 NEPHRECTOMIZED RATS

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**Introduction and Aims:** Tubulointerstitial macrophage infiltration is a hallmark of chronic kidney disease (CKD) involved in the progression of renal fibrosis. Pirfenidone is a newly identified anti-fibrotic drug, the potential mechanism of which remains unclear. The aim of this study was to investigate the effects of pirfenidone on M1/M2 macrophage infiltration in nephrectomized rats.

**Methods:** Nephrectomized rats were treated with pirfenidone by gavage for 12 weeks. We measured the MCP-1 concentration in HK-2 cells, which were treated with various concentration of Ang III, AT1 receptor antagonist and Ang III (10^{-9}M) for various time points. To explore the MAPK pathway, the phosphorylation states of p38, JNK and ERK were recorded.

**Results:** Pirfenidone significantly improved the elevated proteinuria and NAG activity with various concentration of Ang III, AT1 receptor antagonist and Ang III (10^{-9}M) for various time points. To explore the MAPK pathway, the phosphorylation states of p38, JNK and ERK were recorded.

**Conclusions:** Pirfenidone inhibits M1 and M2 macrophage infiltration in 5/6 nephrectomized rats, which suggests its efficacy in the early and late periods of renal fibrosis.

**SP082**  
ANGIOTENSIN III INCREASES MONOCYTE CHEMOTACTANT PROTEIN-1 EXPRESSION IN CULTURED HUMAN PROXIMAL TUBULAR EPITHELIAL CELLS

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**Introduction and Aims:** In cultured human proximal tubular epithelial cells (HK-2 cells), we investigated whether Ang III is involved in monocyte recruitment through the regulation of the chemokine, MCP-1.

**Methods:** We measured the MCP-1 concentration in HK-2 cells, which were treated with various concentration of Ang III, AT1 receptor antagonist and Ang III (10^{-9}M) for various time points. To explore the MAPK pathway, the phosphorylation states of p38, JNK and ERK were recorded.

**Results:** MCP-1 was increased in nephrectomized rats at mRNA and protein levels. Pirfenidone treatment significantly inhibited their expression. The TNF-α, IL-6 and iNOS expressed by M1 macrophages were increased in nephrectomized rats, and pirfenidone significantly attenuated their expression. Pirfenidone treatment also significantly decreased arginine-1, d-arginine, CD206 and CD86 expressed by M2 macrophages.

**Conclusions:** Pirfenidone inhibits M1 and M2 macrophage infiltration in 5/6 nephrectomized rats, which suggests its efficacy in the early and late periods of renal fibrosis.
**Introduction and Aims:** In sepsis, the local expression of TNF-α is very high, which causes systemic inflammatory response and multiorgan failure. Studies indicate that the possible mechanism of action of BMSCs may be due to paracrine modulation releasing biological factors such as microvesicles (MVs) type EXOs. The aim of this study is to evaluate the EXOs effect on the AKI induced by LPS in rats.

**Method:** The BMSCs were incubated with DMEM without SBF during 12 hours. Then, the conditioned medium (CM) were collected and EXOs were obtained from CM by ultracentrifugation technique and characterized by transmission electron microscopy (TEM). Groups include (n=10): LPS (10mg/Kg/BW) (LPS group); PBS (CTL) in 1 or 3 doses (1, 3 or 10mg/ml) injection, 1 or 3 doses either via the tail vein, 72 hr after first dose, the animals were sacrificed and samples of blood and urine 24 hours were collected for creatinine (Cr) and urea (U) evaluations. The kidneys were perfused and removed for HE, KI67 and caspase 3 analysis.

**Results:** EXOs were able to substantially reduce the impact of LPS on renal function, as seen by creatinine and urea. In LPS-group the kidneys showed a small marked Ki67 and intensive caspase 3 expression but it was highly marked for Ki67 and lower expression for caspase 3 in LPS+EXOs groups and no histological ATN lesions were observed. These effects were maximized when the doses of EXOs were given 3 times evaluated by Ki67 and caspase 3.

**Conclusions:** These results strongly suggest that EXOs derived from BMSC can minimize AKI in this sepsis model. This therapeutics EXOs effects have a significant impact on renal function and holds substantial promise for its use especially by avoiding to give cells with potential adverse effects.

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**SP084**

**CALCIUM-OXALATE CRYSTALS ACTIVATE RENAL CELLS TO SECRETE TNF WHICH DRIVES RENAL INFLAMMATION AND ACUTE KIDNEY INJURY**

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**Introduction and Aims:** Calcium oxalate (CaOx) crystal nephropathy results in renal failure. The involvement of inflammation and further tissue damage in CaOx nephropathy is speculative but not clear till the date. The aim of the study was to investigate whether CaOx crystals have the potential to activate the inflammatory signaling e.g. TNF signaling pathway during CaOx nephropathy in mice.

**Methods:** C57BL/6 male mice were procured from Jackson Laboratories (Bar Harbour, MA). TNFR1/-, TNFR2/- mice were generously provided by Volkert Vielhauer, Munich, Germany. All experimental procedures were approved by the local animal care authorities. Immunostaining and Paraffin Acid Schiff were used for analysing kidney pathology. Bone marrow-derived dendritic cells were generated by established protocols. Fluorescence Activated Cell Sorter, ELISA, and Immunoblot were used for further data analysis.

**Results:** Renal expression of TNF-α and its receptors viz. TNF receptor 1 (TNFR1) and TNF receptor 2 (TNFR2) increased during acute CaOx nephropathy. The increased levels of TNF-α, both systemic and local, were associated with increased plasma creatinine and BUN levels, increased infiltrating neutrophils, increased renal mRNA expression of Kim-1, CCLX-2, IL-6 and increased tubular damage. We further show that renal dendritic cells are the main source of TNF-α in the kidney during CaOx nephropathy by flow cytometry. These effects were abrogated in mice deficient in TNFR1 and TNFR2 despite a similar extent of CaOx crystal deposition in the kidneys. In addition, TNF-α antagonism with etanercept, a soluble decoy receptor for TNF-α, reduced plasma creatinine and BUN levels, reduced infiltrating neutrophils, reduced renal mRNA expression of Kim-1, CCLX-2, IL-6 and also reduced tubular damage.

**Conclusions:** We conclude that CaOx crystals induce renal inflammation via inducing the local expression of TNF-α and its receptors TNFR1 and TNFR2 in the kidney during CaOx nephropathy. TNF-α-dependent inflammation largely accounts for tubular necrosis and renal dysfunction of murine CaOx nephropathy. Therapeutic TNF-α blockade might be protective also in human CaOx nephropathy and potentially other crystal nephropathies, such as kidney stone disease, cast nephropathy, and rhabdomyolysis.

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**SP085**

**MITOCHONDRIA AS A TARGET TO TREAT KIDNEY PATHOLOGIES AND PREVENT ORGANISM DEATH**

Dmitry B. Zorov1,4, Egor Y. Potnikov1,4, Denis N. Slachev1,4, Stanislavov S. Janjukauskas2,4, Irina B. Pevzner2,4, Ljubava D. Zorova3,4, Sava D. Zorov2,4 and Maria A. Morsianova1,4

1Belozersky Institute, Moscow State University, Moscow, Russian Federation, 119992; 2Faculty of Bioengineering and Bioinformatics, Moscow State University, Moscow, Russian Federation, 119992; 3International Laser Center, Moscow State University, Moscow, Russian Federation, 119992 and 4Institute of Mitotechnology, Moscow State University, Moscow, Russian Federation, 119992

**Introduction and Aims:** Mitochondria carry various intracellular functions including production of pro- and anti-survival signals and are crucial to determine the incidence and progression of different pathologies where ROS play high role. ROS are a pathogenic factor in numerous renal pathologies. The down-regulation of the ROS levels in the tissue is a strategy for rescuing oxidative stress-mediated renal damage. Use of mitochondria-targeted drugs SkQ1 and SkQ0,1, antioxidants which minimize AKI in this sepsis model. This therapeutics EXOs effects have a significant impact on renal function and holds substantial promise for its use especially by avoiding to give cells with potential adverse effects.

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**SP082**

**THE PROTECT EFFECT OF EXOSSOMES (EXOss) DERIVED FROM BONE MARROW MESENCHYMAL STEM CELLS (BMSCs) IN RATS TREATED WITH LISPOLYSACCHARIDE (LPS)**

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**Abstracts**

JNK and ERK in Ang III (10-7M)-treated cells were measured. MCP-1 concentrations in the conditioned media of HK-2 cells were measured after pre-treatment with the transcriptional factor inhibitors, curcumin or PDTC.

**Results:** In HK-2 cells, Ang III increased MCP-1 protein production in a dose- and time-dependent manner and the increased MCP-1 level was inhibited by AT1 receptor blocker. p38 MAPK activities were significantly increased in HK-2 cells exposed to Ang III after 30 minutes and was sustained at higher levels after 60 minutes (p<0.05).

Pretreatment with p38 inhibitor, JNK inhibitor and curcumin significantly inhibited Ang III-induced MCP-1 production.

**Conclusions:** In HK-2 cells, Ang III increased MCP-1 synthesis via stimulation of the p38 and JNK MAPK activity and subsequent AP-1 activity. Our study provides a new insight into the RAS including Ang III.
ototoxicity. It gives an evidence that normalization of the ROS level normalizes organ functioning. The damaged area and the functional activity of ischemic brain were dependent on the kidney functioning with normalization by the measures quenching oxidative stress. Preconditioning of the kidney essentially diminished the brain damage and improved functional tests. Apparently, the cross talk between kidney and the brain is realized through a release of protective signaling molecules from the kidney which rescued neuronal structures from a damage caused by oxidative stress. Erythropoietin produced by the kidney may be one of these protectants. Under critical conditions, yielding a kidney failure and organism death mitochondrial antioxidants rescue the organism from a death.

Conclusions: ROS homeostasis in mitochondria and cells is a critical factor to be considered in the strategy to protect from a number of renal pathologies mediated by oxidative stress. The kidney plays important role in protective mechanisms and affords protection of other organs and organism itself. The analysis suggests that mitochondrially-derived patterns can hypertrope immune system and this overstimulation may be responsible for the multiple organ failure and the organism death.

Methods: Experimental animal groups: Sham: control without infusion of macrophages; 1/R: 45 min of bilateral ischemia followed by 24 h of reperfusion; 1/R + MACS; 1/R group with injection of untreated bone marrow derived macrophages (BMDMs); 1/R + b-gal: 1/R group injected with b-gal transduced BMDM; Lcn-2: I/R group with injection of untreated bone marrow derived macrophages (BMDMs); Lcn-2 + MACS: I/R group with injection of Lcn-2 BMDM, Lcn-2 + b-gal: I/R group injecting BMDM overexpressing Lcn-2.

Results: Renal function markers, regeneration tissue profile, inflammatory versus anti-inflammatory profile, gene array and histopathology was performed. Animals transferred with macrophage-derived Lcn-2 exhibited a special proliferation and repair ratio of tubular epithelial cells. Immunostaining for the regeneration markers Ki-67 and PCNA showed markedly positive expression in the kidney sections with Lcn-2-BMDM treatment. Real-Time RT-PCR of the proliferation marker BUN and creatinine were decreased upon adoptive transfer of these macrophages and the expression of pro-inflammatory mediators was attenuated. Animals transferred with macrophage-derived Lcn-2 exhibited a special proliferation and repair ratio of tubular epithelial cells. Immunostaining for the regeneration markers Ki-67 and PCNA showed markedly positive expression in the kidney sections with Lcn-2-BMDM treatment. Real-Time RT-PCR of the proliferation markers Ki-67 and PCNA further confirmed these effects. The recovered renal tissue treated with Lcn-2-BMDM modulates a different genetic expression compared to the damaged tissue or the one treated only with BMDM and provides a significant resistance to ischemic damage.

Conclusions: BMDM overexpressing Lcn-2 are capable of modulating injury and inflammation outcome in ischemic kidneys, promoting kidney repair and tissue regeneration in experimental renal ischemia/reperfusion injury. Our results indicate a possible target for further therapeutic use in disease, since Lcn-2-2 not only modulates the macrophage phenotype, but also its pro-repair properties. The provided results of this study have recently been patented and are expected to be soon translated into clinical approaches.

Methods: Renal ischemia reperfusion injury (IR) was induced in C57Bl/6 mice by transient bilateral clamping of pedicles for 35 min. Twice daily ip treatment with EA-230 at different doses (20, 30, 40, 50 mg/kg) was established 24 h after induction of the injury and continued for 4 days. Survival and renal function were monitored and histology (infiltrating cells, Ki-67, caspas-3) was analysed and renal blood flow was measured.

Results: Treatment with EA-230 improved survival in a dose-dependent manner. Doses of 30, 40 and 50 mg/kg EA-230 were most effective in reducing mortality due to IR-injury. Treatment with 50 mg/kg EA-230 gave 62.5% long-term survival (4 weeks) vs. 12.5% in saline-treated control mice. EA-230 improved renal blood flow (RBF) significantly. In spite of this, no differences in the amount of infiltrating cells or cleaved caspase-3 expression were detected. However, a significant increase in Ki-67 positive tubular epithelial cells two days after the IR injury in EA-230 treated animals was detected. This finding suggests that EA-230 improves regeneration of renal tissue after IR injury.

Conclusions: EA-230 is a novel and promising therapeutic agent for treating AKI. Its beneficial effect is associated to an increase in tubular epithelial cell proliferation.

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Conclusions: EA-230 is a novel and promising therapeutic agent for treating AKI. Its beneficial effect is associated to an increase in tubular epithelial cell proliferation.
Methods: 30 Sprague-Dawley rats were divided randomly into three groups: sham operation (SHAM) group, 5/6 subtotal nephrectomy (SNx) group, and 5/6 subtotal nephrectomy + Cordyceps sinensis (CS) group. Body weights were assessed and 24-h urine was collected before surgery. Rats were sacrificed 12 weeks after surgery, blood samples were taken for biochemical studies, and kidney tissues were used for HE and Masson's stains to assess histological changes. Immunohistochemical staining was used to detect the expression of TGF-β1, TGF-βR1, TGF-βRII and E-cadherin, FSP1 and α-SMA. The relative protein level of TGF-β1, TGF-βR1, TGF-βRII, p-Smad2/3, α-cadherin, α-SMA, FSP1 were examined by western blot.

Results: (1) CS treatment significantly reduced proteinuria, BUN and Scr level in SNx rats compared to the control group (p<0.05). (2) The glomerular and tubulointerstitial injury score were significantly reduced in CS group compared to SNx group (p<0.05). (3) The expression of TGF-β1, TGF-βRII, p-Smad2/3, were significantly attenuated, while Smad 7 markedly upregulated by CS treatment (p<0.05). (4) CS treatment upregulated the expression of E-cadherin and reduced the expression of α-SMA and FSP1 compared with SNx group (p<0.05).

Conclusions: Cordyceps sinensis has exerted an anti fibrosis fibrosis role in 5/6 subtotal nephrectomy rat through the suppression of TGF-β1 signal pathway.

**Abstracts**

**SP004**

**ERYTHROPOIETIN DELIVERED FOR PROTECTION FROM ACUTE KIDNEY INJURY MAY HAVE SECONDARY BENEFITS IN PREVENTING HEART FAILURE**

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Introduction and Aims: Acute kidney injury (AKI) is a common complication in hospitalized patients, especially those in the intensive care units. AKI and renal failure can lead to heart complications and concurrent worsening of structure and function in both organs. Erythropoietin (rEPO) is protective of AKI-induced functional and structural outcomes in both experimental animals and humans, but it is not known if treatment of the AKI with rEPO also protects the heart from injury. The aim of this study was to use isoproterenol (ISO) on cardiac cells in vitro as a model to mimic heart failure, to test whether rEPO modulates the outcome.

Methods: H9c2 cardiomyoblasts, seeded in 96-well plates, or on glass coverslips in combination group, rhEPO was added 60 seconds after the ISO treatment. Untreated or a combination of both. The compounds were dissolved in culture medium. In the in vitro study, the cardiomyocytes were exposed to ISO for 6 hours and were then exposed to different concentrations of rEPO and placebo (for rhEPO) groups served as controls. Forty-eight hours after treatment, repair of injured HKC.

Results: (1) CS treatment significantly reduced proteinuria, BUN and Scr level in SNx rats compared to the control group (p<0.05). (2) The glomerulosclerosis index and interstitial fibrosis deposition at the interstitial level (51.54±8.28, vs T0 p=0.04) and diffuse glomerular inflammation was monitored by plasma (7) IL-6 and (8) p40 (IL-12, IL-23) protein (if obtainable) is the most sensitive biomarker of ischemic injury of tubular epithelial cells. As plasma NGAL protein level could be influenced by other, simultaneous inflammatory foci, it should be used only in the absence of available urine samples.

Conclusions: NGAL is upregulated after IR injury and accumulates in vesicles at the apical cytoplasmic compartment of renal tubular epithelial cells. Thus, urine NGAL protein (if obtainable) is the most sensitive biomarker of ischemic injury of tubular epithelial cells. As plasma NGAL protein level could be influenced by other, simultaneous inflammatory foci, it should be used only in the absence of available urine samples.

Astragaloside-IV attenuates glycated albumin-induced epithelial-mesenchymal transition (EMT) via inhibiting oxidative stress in proximal tubular cells

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Introduction and Aims: Epithelial to mesenchymal transition (EMT) is a pathological process in chronic kidney disease, which leads epithelial cells to lose their polarization and specialized functional structures, and to acquire mesenchymal cells’ features. In tumors, it has been proved there is a deep relationship between oxidative stress and EMT. Astragaloside IV (A-IV), the major component isolated from Astragalus membranaceus, shows a wide range of biological activities. This study aims to assess whether A-IV could attenuate glycated albumin (GA), an AGEs precursor, induced EMT in NRK-52E cell line via oxidative stress.

Methods: GA and A-IV induced cytotoxicity was assayed by CCK-8, respectively. The intercellular reactive oxygen species (ROS) level was detected by H2DCFDA. Moreover, we investigated the activity of the oxidant enzyme, NADPH oxidase and antioxidant enzyme, superoxide dismutase (SOD) by using spectrophotometer in NRK-52E cell line cultured with GA. The morphology of NRK-52E cell line was examined by microscope. Cell mobility was determined by wound healing assay. The mRNA and protein expression of α-SMA and E-cadherin are determined by real-time PCR, Western blotting and immunocytochemistry in HUVEC exposed to Gb3. eNOS

Results: A-IV significantly attenuated GA-induced amplification of ROS (0.71-fold compared with GA group, P<0.05), reduced the level of NADPH oxidase activity (0.43-fold compared with GA group, P<0.01) and elevated the decreased level of SOD expression (1.33-fold compared with GA group, P<0.05). GA-induced NRK-52E cell line showed increased expression of α-SMA and decreased expression of E-cadherin in mRNA (2.14-fold, 0.18-fold respectively, P<0.01) and protein level (1.79-fold, 0.36-fold respectively, P<0.01), while A-IV could alleviate the expression of α-SMA to a 1.09-fold and increased the expression of E-cadherin to 1.07-fold.

Conclusions: Our data demonstrated that oxidative stress, tubular apoptosis and renal fibrosis in sepsis-induced AKI. CPA treatment might be pivotal to counteract the detrimental effects of LPs on renal tissue.

 Globotriaosylceramide (Gb3)-induced endothelial-to-mesenchymal transition (endo-MT) as a novel mechanism of renal damage in fabry disease

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Introduction and Aims: The lysosomal storage disorder Fabry disease is characterized by excessive Gb3 accumulation in major organs including kidney. Defective lysosomal alpha-galactosidase A (GAL) is responsible for Gb3 accumulation, and vascular endothelial dysfunction is one of the most vulnerable targets of the effect of Gb3. Endothelial dysfunction associated with microvascular disease is known as a key mechanism of progression of renal disease. However, it is not known whether Gb3 per se induced endothelial dysfunction. Recently, the phenotype transition of endothelial cells such as endothelial-to-mesenchymal transition (endo-MT) is emerged as one of the most promising phenomena of endothelial damage. We investigated whether Gb3 per se induced endo-MT in cultured endothelial cells with an evaluation of the evidence of endo-MT in the kidney of Fabry mouse.

Methods: Endo-MT was evaluated by the changes in cell morphology and a comparison of the expression of the endothelial markers, VE-cadherin or CD31 and the mesenchymal marker, alpha smooth muscle actin (α-SMA) by real time PCR, Western blotting and immunocytochemistry in HUVEC exposed to Gb3. eNOS phosphorylation and NO production were also assessed. Gb3-induced activation of Erk and p38 MAPK as well as production of reactive oxygen species (ROS) was evaluated as a mechanism of Gb3-induced endo-MT. In vitro evidence of endo-MT in the kidney was investigated in Fabry mouse using double immunofluorescence staining of CD31 and α-SMA.

Results: Stimulation of HUVEC with Gb3 (0.1-20 μM) down-regulated the expressions of CD31 and VE-cadherin with an up-regulation of α-SMA from 5 μM. Gb3 also induced an alteration of cell morphology from vonWillebrand cell to elongated fibroblastoid cell with a loss of cell contact. Gb3 decreased NO production with Ser-eNOS de-phosphorylation and Thr-eNOS phosphorylation in HUVEC. Gb3 also activated Erk and p38 MAPK from 15 minutes with an induction of ROS from 30 minutes of stimulation. In Fabry mouse, Gb3 accumulation was observed in glomerular podocyte, tubular cell and peri-tubular capillaries (PTC) with vascular generation in renal tubules. Immunostaining with CD31 and α-SMA revealed capillary rarefaction both in glomerular and PTC with de-novo expression of α-SMA in PTC, suggesting endo-MT in the kidney of Fabry mouse.

Conclusions: Gb3 per se induced a phenotypic transition of endothelial cells via a differential phosphorylation of eNOS, an activation of MAPK and an induction of oxidative stress, which could be one of the mechanisms of endothelial dysfunction and nephropathy in Fabry disease.

Cholicline ameliorates renal apoptosis in unilateral obstructive uropathy

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Introduction and Aims: In the kidney with unilateral ureteral obstruction (UUO), alteration of cytoskeleton can induce apoptosis. Cholicline, which inhibits microtubule polymerization, may reduce tissue injury. However, the effect of cholcine on renal apoptosis in UUO has not been explored.

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Methods: UUO was induced in C57BL/6 mice and colchicine (80 μg/kg, intraperitoneally, everyday) or vehicle was administered for 7 days. Results: UUO mice showed increased alpha-tubulin and renal apoptosis. Colchicine inhibited the expression of alpha-tubulin and decreased renal apoptosis 7 days after UUO. In colchicines treated UUO mice, the expression of phosphorylation glycogen synthase kinase-3β and phospho-p38 mitogen-activated protein kinase was decreased, while the expression of Akt and B-cell lymphoma-extra large was increased. Caspase 9 expression was also decreased. Intercalated fibrosis scores on Masson’s trichrome stain were not different between vehicle and colchicines treated UUO mice. Expression of alpha-smooth muscle actin, vimentin, collagen type 4 and fibronectin was not different between the two groups.

Conclusions: These data suggest that colchicine may have anti-apoptotic effect but lack of anti-fibrotic effect on obstructive kidney models.

SP087 ACTIVATION OF RENAL PI3K/Akt/mTOR SIGNALING PATHWAY IN OBSTRUCTIVE UROPATHY IN RATS

Seong Kwon Ma1, Soo Yeon Joo1, Chang Seong Kim1, Joon Seok Choi1, Eun Hui Baek1, Jong-Jin Lee2 and Soo Wan Kim1
1Internal Medicine, Chonnam National University Medical School, Gwangju, Republic of Korea, 2Physiology, Chonnam National University Medical School, Gwangju, Republic of Korea

Introduction and Aims: The present study was aimed to investigate the role of the mammalian target of rapamycin (mTOR) signaling pathway in the pathogenesis of tubulointerstitial fibrosis and apoptosis in the obstructed kidney of rats with unilateral ureteral obstruction.

Methods: Male Sprague-Dawley rats were unilaterally obstructed by the ligation of left proximal ureters for 7 days. Control rats were treated in the same way, except that no ligation was made. The expression levels of phosphorylated phosphatidylinositol 3-kinase (PI3K), Akt and mTOR were determined in the kidney by semiquantitative immunoblotting. The protein expression levels of transforming growth factor (TGF)-β1, Bax and Bcl-2 were also determined in the kidney.

Results: The phosphorylation of PI3K, Akt and mTOR was determined in the kidney of ureteral obstruction compared with the control. In the obstructed kidney, the protein expression of TGF-β1 and Bax was also increased, whereas Bcl-2 expression was decreased.

Conclusions: In conclusion, the upregulation of PI3K/Akt/mTOR signaling pathway may play an important role in the pathogenesis of tubulointerstitial fibrosis and apoptosis.

SP088 UROTENSIN AND RELAXIN: OPPOSITE ACTIONS AND POTENTIAL THERAPEUTIC APPLICATIONS IN RENAL FIBROSIS

Valeria Cernaro1, Maria Antonietta Medici2, Valentina Donato1, Domenico Trimboli1, Domenico Santoro1, Gaetano Montalto1 and Michele Bueni1
1Chair of Nephrology, Department of Internal Medicine, University of Messina, Messina, Italy, 2Department of Life Sciences “Marcello Malpighi”, University of Messina, Messina, Italy

Introduction and Aims: Tubulointerstitial fibrosis is the final common pathway of diseases that evolve towards chronic kidney disease (CKD). A key regulator of tissue fibrosis is TGF-β1 (transforming growth factor β1), whose expression is induced by numerous profibrotic stimuli. Our aim has been to evaluate the role of urotensin II (UII), urate (Ura) and relaxin (RLX) in an in vitro model of renal fibrosis.

Methods: We used an experimental model of renal tubular epithelial cells belonging to the cell line LLC-PK1, derived from the kidney of healthy male pig. We evaluated the effects on the fibrotic process of the addition of UII, Ura (powerful antagonist of UII's receptor) and RLX, by using antibodies against fibronectin, a marker of fibrosis, in western blot analysis.

Results: After addition of UII, the most potent vasoconstrictor present in mammals, we observed the formation of fibrotic tissue; this was documented by the increased expression of fibronectin, which was greater using a concentration of UII equal to 10^-6 M. The profibrotic action of UII at this concentration is even higher than that of TGF-β1. We have also observed, for the first time, that Ura is able to reduce fibronectin expression in the context of renal fibrosis; these data confirm the antifibrotic action that Ura seems to exert in myocardial fibrosis, where it abolishes the UII-induced TGF-β1 formation. Finally, we studied the effect of the addition of RLX, pleiotropic hormone able to interfere with the synthesis of collagen and other extracellular matrix components; we noted that this factor mimics the antifibrotic action of Ura in our model of UII-induced fibrosis.

Conclusions: Our data demonstrate that molecules such as Ura or RLX are able to reverse the tubulo-interstitial fibrosis induced by UII. These results are particularly important because UII and RLX are endogenous substances whose dysregulation (e.g., high UII, low RLX) has been linked to numerous pathophysiological states including atherosclerosis, heart failure, hypertension, renal impairment. Moreover, no data exist on the interactions between RLX and UII in the molecular pathways of renal fibrosis. Hence, it is possible to imagine a future pharmacological use of Ura and RLX in the treatment of pathological conditions, such as CKD, which are currently considered incurable precisely because secondary to the replacement of normal parenchyma with fibrotic and then not working tissue.

SP100 EFFECT OF VITAMIN D3 OVERDOSE AND CALCIUM SUPPLEMENTATION IN EXPERIMENTAL RAT NEPHROLITHIASIS MODEL

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1Federal University of Sao Paulo Sao, Paulo, Brazil

Introduction and Aims: Recent studies suggested that administration of calcium with vitamin D increases the risk of kidney stones development. To evaluate the effect of
overdose of vitamin D3 (Vit D) with calcium supplementation in an experimental model of foreign body lithiasis in rats.

Methods: Experimental model using pellets of calcium oxalate (P) surgically inserted into the bladder of rats. It was administered high doses of Vit D (200 IU), orally for 30 days with or without calcium supplementation (Ca) in a dose of 20mg/kg daily, by gavage. We evaluated 36 adult Wistar rats in 6 groups (n=6 for each): Group 1: Sham, without manipulation or drugs. Group 2: control P (CP); Group 3: control Vit D (CV); Group 4: P + Vit D (PV); Group 5: P + Calcium (PCa) and Group 6: P + Vit D + Ca (PVCa).

Results: Evaluated by ANOVA included: increase in the dosage of serum VitD (40.36 ng/ml ± 10.03) comparing with the control group (9.10 ng/ml ± 3.41, p < 0.0062) in the P + Vit D rats. However it was observed a 50% and 17% decreases bladder formation in the pellet groups (only calcium) and 6 (Vit D + Ca), p < 0.005 comparing with the P group. There was no detected hypercalciuria or hypercalcuria despite an overdose of Vit D and or Ca but for group 6 (PVCa) it was observed a significant decrease in calcium (p < 0.01). No significant differences in urine pH and density, creatinine, sodium and potassium in blood and urine at the beginning and at end of the experiments for all groups. The creatinine clearances showed no significant differences between groups.

Conclusions: Surprisingly, the administration of the Vit D associated with calcium supplementation significantly decreased the formation of stones and attended with a significant reduction in urinary calculus, suggesting a protection in the lithogenic pathophysiology. The effect in reducing calculus or the interference with other factors could be responsible for this mechanism and therefore, maybe, the supplementation of Vit D and calcium could be beneficial in the presence of osteopenia or osteoporosis despite the presence of urinary stones, a difficult medical decision.

Introduction and Aims: The considered pathophysiologic mechanisms of contrast induced nephropathy (CIN) are medullary hypoxia due to decreased renal blood flow secondary to renal artery vasoconstriction, tubular obstruction and direct tubular toxicity. Also, decreased production of nitric oxide (NO) and increased oxidative stress play important roles in the pathogenesis of CIN. Sildenafil, a type-5 phosphodiesterase (PDE-5) inhibitor which increases cGMP levels in response to NO, augments the relaxation of vascular smooth muscle. Moreover, sildenafil has been shown to reduce oxidative stress via inhibition of superoxide formation in vitro and to decrease the inflammatory response via improving oxygenation in vivo. We hypothesized that sildenafil may prevent CIN due to its renal vasodilatation and antioxidant effects.

Methods: Twenty-eight female Wistar albino rats were divided into 4 groups (n=7 each); control group, sildenafil group, CIN group, CIN+sildenafil group. Sildenafil (2.5 mg/kg) was given by gastric gavage one hour before the induction of CIN. CIN was induced at 48th hour by iv injection of indomethacin (10 mg/kg), L-NAME (10 mg/kg) and amiodarone (6 mg/kg). Renal function parameters and kidney histopathologic findings were determined.

Results: Mean serum creatinine level was found lower in CIN+Sildenafil group than in CIN group, but the difference was not significant (p=0.096). Mean creatinine clearance in CIN+Sildenafil group was significantly higher than in CIN group (p=0.04) and in control group (p=0.018). The mean scores of tubular necrosis, proteinaceous cast and medullary congestion in CIN group were significantly different from in CIN+Sildenafil group and in control group (p<0.05).

Conclusions: The present experimental study demonstrates that sildenafil prophylaxis is able to prevent deterioration of contrast induced renal functions and histopathological changes. Further studies are needed to determine the protective role of sildenafil against CIN.

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<th>SP0102</th>
<th>PROTECTIVE EFFECT OF SILDENAFIL ON EXPERIMENTAL CONTRAST-INDUCED NEPHROPATHY MODEL</th>
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<td>Atilla Uzman1, Rifki Ercsy1, Fujiya Cakalaqagocq2, Moral Karaman3, Etsun Kotelan3, Osman Sahin1, Osman Yilmaz2 and Mustafa Cirit1</td>
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<td>1Nephrology, Katip Celebi University Ataturk Training and Research Hospital Izmir, Turkey, 2Pathology, Katip Celebi University Ataturk Training and Research Hospital Izmir, Turkey, 3Laboratory Animals Doku Eylul University Medical School, Izmir, Turkey</td>
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Introduction and Aims: The considered pathophysiologic mechanisms of contrast induced nephropathy (CIN) are medullary hypoxia due to decreased renal blood flow secondary to renal artery vasoconstriction, tubular obstruction and direct tubular toxicity. Also, decreased production of nitric oxide (NO) and increased oxidative stress play important roles in the pathogenesis of CIN. Sildenafil, a type-5 phosphodiesterase (PDE-5) inhibitor which increases cGMP levels in response to NO, augments the relaxation of vascular smooth muscle. Moreover, sildenafil has been shown to reduce oxidative stress via inhibition of superoxide formation in vitro and to decrease the inflammatory response via improving oxygenation in vivo. We hypothesized that sildenafil may prevent CIN due to its renal vasodilatation and antioxidant effects.

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<th>SP0103</th>
<th>PROTECTIVE EFFECT OF ADRENOMEDULLIN ON CONTRAST INDUCED NEPHROPATHY IN RATS</th>
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<tr>
<td>Saith Inal1, Eypıc Kocy2, Gülyü U. Ökyay3, Özge Paçagı4, İpek Gönü5, Esen Oyar6, Hatice Paçagı5 and Galıp Gızı1</td>
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<td>1Nephrology Gazi University School of Medicine Ankara Turke, 2Nephrology Kırklareli University School of Medicine Kırklareli Turkey, 3Biochemistry Gazi University School of Medicine Ankara Turkey, 4Pathology Gazi University School of Medicine Ankara Turkey, 5Physiology Gazi University School of Medicine Ankara Turkey</td>
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Introduction and Aims: There is a considerable interest in strategies to prevent contrast-induced nephropathy (CIN) because of the increasing prevalence of renal insufficiency in our aging population and the increasing use of imaging studies using radiocontrast media. Some of the important mechanisms of CIN are renal vasconstriction and medullary hypoxia. It was shown that adrenomedullin, which has antioxident, vasodilatory and immunomodulatory effects, attenuated the renal ischemia-reperfusion injury. We aimed to investigate whether adrenomedullin might have a preventive role against the development of CIN.

Methods: Twenty-eight female Wistar albino rats (n=24) were allocated randomly into four equal groups of 6 each; Control (C), Adrenomedullin (A), contrast media (CM), and adrenomedullin plus contrast media (ACM). CIN was induced by intravenous administration of
Introduction and Aims: Although hypoxia attenuates renal injury induced by ischemia-reperfusion (IR), precise molecular pathways have not been elucidated. In our previous study, we showed that HIF phosphorylation may play an important role in hypoxic protection in renal IR injury. Hypoxia-inducible factor-1 (HIF-1) has been known as one of the potent protective proteins in IR injury. We evaluated whether HIF-1 phosphorylation plays an important role in hypoxic protection of renal IR injury.

Methods: 12-week-old male Sprague-Dawley rats were randomized to 4 groups: sham operated (CON); IR; IR + 50μg of tempol, a NO donor (IR + tempol); IR + PD098059, an ERK inhibitor (IR + PD). After the reperfusion phase, renal HIF-1α and HIF-1β expressions were evaluated by western blot and immunohistochemical stain, BUN and serum creatinine were measured 24 hr after IR injury. TUNEL staining and light microscopic examination of kidneys was performed to evaluate the magnitude of renal injury.

Results: Serum creatinine (s-Cr), tissue injury score, and 8-OHdG and TUNEL positive cells were significantly lower than those of sham operated rats (all, p<0.01). Tissue injury score and 8-OHdG and TUNEL positive cells in kidneys of PD098059 treated rats were significantly higher than those of sham treated rats (all, p<0.05). Renal HIF-1α, 1β and 8-Hydroxy-2-deoxyguanosine (8-OHdG) were evaluated by western blot and immunohistochemical stain. BUN and serum creatinine were measured 24 hr after IR injury. TUNEL staining and light microscopic examination of kidneys was performed to evaluate the magnitude of renal injury.

Conclusions: Our data indicate that rMnSOD is able to greatly reduce renal oxidative stress, and its associated reduction of GFR following CM administration. These preliminary data suggest that the use of rMnSOD may open new perspectives in the treatment of CIN, as well as in many pathological conditions associated with increased oxidative stress.

EFFECT OF A RECOMBINANT MANGANESE SUPEROXIDE DISMUTASE ON PREVENTION OF CONTRAST-INDUCED ACUTE KIDNEY INJURY

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Introduction and Aims: Contrast media-induced nephropathy (CIN) is an acute deterioration of renal function following administration of contrast media (CM), due to combined hypoxic and toxic renal parenchymal injury, mediated, to large extent, by an increased production of reactive oxygen species (ROS) within the kidney. The different isoforms of superoxide dismutase (SOD) have recently attracted researchers’ attention for a possible protective role in CIN. We have recently isolated a novel isoform of a recombinant Manganese Superoxide Dismutase (rMnSOD), derived from a human established liposarcoma cell line (LSA) which shares the same ability of physiological SODs in transforming free radicals into hydrogen peroxide, but shows peculiar structural and functional properties. The rMnSOD, in fact, is linked to an isoform of a recombinant Manganese Superoxide Dismutase (rMnSOD) derived from a human established liposarcoma cell line (LSA) which shares the same ability of physiological SODs in transforming free radicals into hydrogen peroxide, but shows peculiar structural and functional properties. The rMnSOD, in fact, is linked to an isoform of a recombinant Manganese Superoxide Dismutase (rMnSOD), derived from a human established liposarcoma cell line (LSA) which shares the same ability of physiological SODs in transforming free radicals into hydrogen peroxide, but shows peculiar structural and functional properties.

Methods: C57/B6 mice were divided into four groups: sham operated, cold IR mice (30°C), warmIR mice (37°C) and PD98059 (MAP kinase inhibitor) treated cold IR mice (IR injury; perfusion 27 minutes after clamping of both renal artery and vein). Kidneys were harvested at 10 minutes and 27 minutes after both renal artery ischemia and 24 hours after IR injury. Renal HIF-1α, Pexosome proliferator-activated receptor gamma coactivator 1-alpha (PGC 1-alpha), AMP-activated protein kinase (AMPK), and 8-hydroxydeoxyguanosine (8-OHdG) were evaluated by western blot and immunohistochemical stain, BUN and serum creatinine (s-Cr) were measured 24 hr after IR injury. TUNEL staining and light microscopic examination of kidneys was performed to evaluate the magnitude of renal injury.

Results: Serum creatinine (s-Cr), tissue injury score, and 8-OHdG and TUNEL positive cells were significantly lower than those of sham treated rats (all, p<0.01). Tissue injury score and 8-OHdG and TUNEL positive cells in kidneys of PD98059 treated rats were significantly higher than those of sham treated rats (all, p<0.05). Renal HIF-1α, 1β and AMPK expression were significantly increased in the kidneys of cold ischemic mice at 10 minutes and 27 minutes after both renal artery ischemia and 24 hours after IR injury. TUNEL staining and light microscopic examination of kidneys was performed to evaluate the magnitude of renal injury.

Conclusions: In conclusion, HIF-1 preservation induced by ERK phosphorylation may be involved in hypoxic protection of renal ischemia-reperfusion injury.

EFFECTS OF MENSECHYMAL STEM CELLS (MSCs) OR THEIR CONDITIONED MEDIUM (CM) IN UNILATERAL URETERAL OBSTRUCTION (UUO) IN RATS

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1Medicine/Nephrology Federal University of São Paulo - Unifesp São Paulo Brazil

Introduction and Aims: A substantial knowledge has been accumulated in relation to therapeutic potential of MSCs and its conditioned medium. It is known their ability to repair tissue and reduce local inflammation. A renal tubule interstitial inflammation is one of the principal causes that induce chronic damage, resulting in fibrosis. A model well established for fibrosis is UUO. In this study we evaluated the effects of MSCs or CM administrations.

Methods: MSCs extracted from rat’s bone marrow were cultivated in vitro and characterized by flow cytometry and cellular differentiation. Four groups of female rats were employed in vivo (n=7): SHAM, UUO, MSCs (UUO + MSCs) and CM (UUO + CM). The MSCs or their CM were administered via carotid artery after total left ureter ligation. After 7 days, the rats were sacrificed and serum and UUO kidney were collected. The fibrosis was assessed by depositions of collagen type I and III displayed on staining Picro Sirus Red.

Results: We observed a significant improvement in reduction of fibrosis progression in animals treated with MSCs or CM (UUO 1.2±0.2; MSC 0.3±0.1; CM 0.4 ±0.1, staining area %, p<0.05). The expression of molecules related to the progression of fibrosis, inflammation and Epithelial-Mesenchymal Transition were evaluated by real time PCR. It was observed reduction of molecules expression such as COL-1(UUO 4.5±0.5; MSC 2.3±0.3; CM 1±0.2, arbitrary units), α-SMA (UUO 5.2±0.5; MSC 3 ±0.5; CM 2±0.3, arbitrary units) and TNF-α (UUO 7.7±1.3; MSC 2±0.3; CM 1.7 ±0.1, arbitrary units) in animals treated with MSCs or CM, p<0.05. In immunohistochemical assays were observed reductions of 15% in staining area of capase-3 and α-SMA (UUO 7.2±1.1; MSC 1±0.2; CM 0.7±1.0, staining area %, p<0.05) in treated animals. We also observed a reduction in cell proliferation in the animals receiving MSCs or CM (UUO 3.1±0.7; MSC 0.4±0.1; CM 0.6±0.3, staining area %, p<0.05).

Conclusions: Results suggested that the IV administration of MSCs or its CM minimize the fibrosis progression and change factors involved in apoptosis.
Inflammation, cell proliferation and epithelial-mesenchymal transition in Wistar rats, subjected to unilateral ureteral obstruction.

**SP107 ONTOGENY OF THE CIRCADIAN MOLECULAR CLOCKWORK IN THE RAT KIDNEY**

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1Division of Pediatric Nephrology, Center for Pediatrics and Adolescent Medicine University of Heidelberg Heidelberg Germany, 2Department of Pathology University of Heidelberg Heidelberg Germany

**Introduction and Aims:** Most physiologic processes exhibit day/night rhythms driven by the circadian clockwork. The central circadian clock is located in the suprachiasmatic nucleus (SCN) and synchronizes peripheral clock systems operative in various tissues. They govern the adjustment of organ functions to daytime at the cellular level. In the kidneys, circadian oscillation of essential renal functions such as the maintenance of water and electrolyte homeostasis has been demonstrated. Recent studies have revealed the circadian expression of numerous genes critical for kidney functions (e.g. 

**Methods:** Pregnant SD rats were housed with free access to food and water at constant temperature under 12:12-hour light-dark cycles. Offspring (7 per group) were sacrificed at 4 hour intervals on embryonic day 20 (E20) and postnatal days 7, 30, or 84 (P7, P30, P84). The circadian expression patterns in the kidneys were probed by real-time RT-PCR for the canonical clock genes, Clock, Bmal1, Rev-Erb, Per1, Per2, Cry1, Cry2 and the kidney specific clock-controlled genes Scnn1a, Sf1a3, Scl1a2, Avpr2, and Sgk1.

**Results:** The core clock genes Clock (p<0.01), Rev-Erbα (p<0.01) and Per1 (p<0.01) showed significant circadian expression as early as E20. During early postnatal life, rhythmic expression increased in amplitude and showed a significant phase shift. Whereas the expression of Cry1, Cry2 and Per2 showed no variation at E20, circadian rhythmicity had developed by P7 for Cry1 (p<0.01) and by P30 for Per2 (p<0.05). All genes displayed distinct circadian rhythms at P84 (p<0.01). Among the clock-controlled genes, expression of Scnn1a (p<0.01), Sf1a3 (p<0.05) and Avpr2 (p<0.05) was observed at E20. The phase of the rhythms shifted along the observation time points. Scl1a2 showed rhythmic expression only at P84 (p<0.01), and Sf1a3 only transiently at E20 (p<0.01).

**Conclusions:** Our findings demonstrate a complex time course of development of the intrarenal molecular clockwork during pre- and early postnatal life in rats. Environmental factors affecting the maturation of kidney function are driven by this critical period of development which might impact on the organism's postnatal health and survival. The understanding of the molecular mechanisms involved in these processes is important for the development of novel therapies for renal diseases.

**SP108 PROTEINKINASE C alpha DELETION ATTENUATES RENAL ISCHEMIA REPERFUSION INJURY BY TGF-beta INHIBITION**

Daniel Walaicides1, Niele Rüskamp2, Song Rong1, Katja Hueper2, Hermann Haller1, Mario Schiffer1 and Faikah Gueler1

1Division of Pediatric Nephrology, Center for Pediatrics and Adolescent Medicine University of Heidelberg Heidelberg Germany, 2Department of Pathology University of Heidelberg Heidelberg Germany

**Introduction and Aims:** Renal ischemia reperfusion injury (IRI) leads to delayed graft function (DGF) after kidney transplantation and is a strong risk factor for progressive renal damage. Furthermore, renal IRI leads to acute kidney injury (AKI) after major cardiac surgery and contributes to increased post-operative mortality. In this study we analysed the role of PKC-α in a hypoxia induced impaired renal blood flow (RBF) and edema formation in PKC-α deficient mice compared to control mice.

**Methods:** Renal ischemia reperfusion injury (IRI) was induced in wildtype or PKC-α knock out mice by transient unilateral clamping of the right renal pedicle for 35 min. Functional contrast free magnetic resonance imaging (MRI) was performed at d1 and d7 to measure renal blood flow (RBF), edema formation and cell infiltration. Histologically, renal morphology and inflammatory cell infiltration (F4/80 and Gr-1 positive cells) were investigated by qPCR PAF1 and CTGF expression which are downstream targets of TGF-β were evaluated.

**Results:** PKC-α knock out mice had significantly better survival and less s-creatinine elevation than WT mice. By MRI techniques IRI induced renal perfusion impairment was markedly reduced in PKC-α knock out mice compared to WT mice at d1. Acute tubular necrosis (ATN) and inflammatory cell infiltration was significantly reduced in the PKC-α knock out mice. qPCR showed reduced up-regulation of PAF1 in PKC-α deficient mice pointing towards impaired TGF-β signaling in this model.

**Conclusions:** Our study proves that PKC-α deficiency attenuated hypoxia induced renal IRI by blocking TGF-β up-regulation. This results in improved renal tissue perfusion and less inflammation. Thus PKC-α inhibition might be a promising therapeutic option to reduce hypoxia induced IRI in solid organ transplantation.

**SP109 GOLD NANOPARTICLE SENSORS FOR DETECTING CHRONIC KIDNEY DISEASE AND DISEASE PROGRESSION**

Ophir Marom1, Hossam Haick2 and Farid Nahoul2

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**Introduction and Aims:** Chronic kidney disease (CKD) progresses less impact of kidney function over a period of many years. Recent professional guidelines classify the severity of CKD in five stages according to the reduction in glomerular filtration rate (GFR), with stage-1 being a mild illness and stage-5 being a severe illness. Uremic toxins, which are normally excreted by the kidney, are retained as GFR diminishes. Over 5000 potential toxins have been identified. Retained urea and Creatinine serve as markers of kidney failure. Moreover, up to 60% of the kidney function may be lost before serum Creatinine begins to rise. These limitations, and the asymmetric onset of the disease, contribute currently to delayed diagnosis and therapy of CKD. A novel approach that offers many advantages of the conventional diagnostic techniques relies on the detection of volatile organic compounds (VOCs). Some of the VOCs among the plasma CKD biomarkers, or their metabolic products, are transmitted to the alveolar exhaled breath through via the lung, even at the very onset of the disease, causing in later stages the fishy smell characterizing the breath of these patients. Rapid progress has been made in recent years in the field of nanotechnology and towards the standardization of breath sampling. This could lead to the development of efficient and cost-effective methods for diagnostic breath testing. To study the feasibility of a novel nanomedical method that is based on breath testing for identifying Chronic Kidney Disease (CKD) and disease progression.

**Methods:** Exhaled breath samples were collected from 62 volunteers. The breath samples were analyzed using sensors based on organically functionalized gold nanoparticles (GNPs), combined with support vector machine (SVM) analysis, to detect statistically significant differences between the sub-populations of the disease. Sensitivity and specificity with reference to CKD patient classification according to estimated GFR amplitude and rate (ΔGFR) were determined using cross-validation. The chemical composition of the breath samples was studied using gas chromatography linked with mass spectrometry (GC-MS).

**Results:** A combination of 2-3 GNP sensors provided good distinction between early stage-1 CKD and healthy (control) subjects.ΔGFR was p<0.01 and AVPR2 (p<0.05) was observed at E20. The phase of the rhythms shifted along the observation time points. Sc1a2 showed rhythmic expression only at P84 (p<0.01), and Sf1a3 only transiently at E20 (p<0.01).

**Conclusions:** 1. Breath testing using GNPs sensors holds future potential as a cost-effective, fast and reliable diagnostic test for early detection of CKD and monitoring of disease progression. 2. Combinations of GNP sensors and separate sensors can distinguish between: Early-stage CKD and healthy stages Stage 4 and 5 CKD states Early-stage (stages 2 and 3) and late-stage (stages 4 and 5) CKD.

**SP110 INHIBITION OF MITOCHONDRIAL DYSFUNCTION IS THE MECHANISM OF PIFREDINONE ANTI-TUBULOINTERSTITIAL FIBROSIS-AN IN VIVO AND IN VITRO STUDY**

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**Introduction and Aims:** Dysfunctional mitochondria participate in the progression of chronic kidney disease (CKD). Pifredinone is a newly identified anti-fibrotic drug, but its mechanism remains unclear. Mitochondrial dysfunction is an early event that occurs prior to the onset of renal fibrosis. In this study, we investigated the protective effect of pifredinone on mitochondria and its relevance to apoptosis and oxidative stress in renal proximal tubular cells in an in vivo and in vitro study.

**Methods:** A CKD rat model of 5/6 nephrectomy was established, and human renal proximal tubular epithelial cells (HK2) using mitochondrial respiratory chain inhibitors were further investigated in vitro to examine the protective effect of pifredinone on mitochondria.

**Results:** Pifredinone protected mitochondrial structures and functions by stabilizing the mitochondrial membrane potential, maintaining ATP production and improving the mitochondrial DNA (mtDNA) copy number. Pifredinone decreased tubular cell apoptosis by inhibiting the mitochondrial apoptotic signaling pathway. Pifredinone also reduced oxidative stress by enhancing manganese superoxide dismutase (Mn-SOD) and inhibiting intracellular reactive oxygen species (ROS) generation, which suggested that the anti-oxidant effects occurred at least partially via the mitochondrial pathway.

**Conclusions:** Pifredinone may be effective in earlier stages of CKD prior to the onset of renal fibrosis because this drug protected mitochondria in renal proximal tubular cells, to exert its anti-fibrotic effect.
SP111  
IN EARLY ACUTE KIDNEY INJURY, INDOXYL SULFATE IMPAIRS ENDOTHELIAL PROGENITOR CELLS – MODULATION BY STATIN
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Introduction and Aims: Renal ischemia rapidly mobilizes endothelial progenitor cells (EPCs), which provides renoprotection in acute kidney injury (AKI). Indoxyl sulfate (IS) is a protein-binding uric acid toxin with a potential role in endothelial injury. Methods: AKI patients in the present study were consecutively enrolled when AKI was diagnosed. A certain number of early EPCs were allowed to grow continuously into colonies of late EPCs. Peripheral blood cells were used to evaluate the percentage of CD34+/KDR+ peripheral mononuclear cells by flow cytometry. Donor transgenic Tie2-GFP mice were used for evaluation of EPC mobilization.

Results: In forty-one consecutive patients (26 male; age, 70.1 ± 14.1 years) diagnosed with AKI according to the AKIN criteria were enrolled. The AKI patients had higher serum IS levels than patients with normal kidney function (1.35 ± 0.94 X10⁻⁴M vs 0.02 ± 0.02 X10⁻⁴M, p<0.01). IS levels were negatively correlated to the number of double-labeled (CD34+/KDR+) circulating EPCs (<0.001). After IS stimulation, the cells displayed decreased expression of phosphorylated endothelial nitric oxide synthase, vascular cell adhesion molecule-1, increased reactive oxygen species, decreased proliferative capacity, increased senescence and autophagy, as well as decreased migration and angiogenesis. These effects of IS on EPCs were reversed by atorvastatin. Further, exogenous administration of IS significantly reduced EPC number and attenuated angiogenesis. These effects of IS on EPCs were reversed by atorvastatin.

Conclusions: Our results are the first to demonstrate that circulating IS is elevated in AKI and has direct effects on EPCs via nitric oxide-dependent mechanisms both in vitro and in vivo. Targeting the IS-mediated pathways by nitric oxide-releasing statins such as atorvastatin may preempt disordered vascular wall pathology, and represent a novel EPC-rescued approach to impaired neovascularization after AKI.

SP112  
EARLY RENAL HISTOPATHOLOGICAL AND FUNCTIONAL CHANGES IN STAR FRUIT INDUCED ACUTE OXALATE NEPHROPATHY
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Introduction and Aims: The intake of star fruit (Averrhoa carambola), which contains high oxalate concentrations, may cause acute kidney injury by the precipitation of oxalate crystals. The aim of this research is to evaluate early histopathological and functional changes in acute nephropathy induced by the ingestion of star fruit juice. Methods: Three groups of Wistar rats were treated (gavage), after 15-hour fasting and deprivation of water intake, with 4ml per 100g of body weight of one of the following solutions: group SF - pure star fruit juice (oxalate concentration: 4.7mg/mL); group C - saline solution (control); group OX - oxalate solution (concentration: 4.7mg/mL with similar pH and osmolality). After 24 hours, the following studies were performed: renal function (glomerular filtration rate by inulin clearance - GFR, fractional excretion of sodium - FENA, fractional excretion of potassium - FEK, and urine osmolality - Osm), histopathological (acute tubular necrosis - ATN and oxalate crystals), and immunohistochemical (proliferating cell nuclear antigen - PCNA and macrophage - ED1+). Statistical analyses were carried out using the Kruskal-Wallis test.

Results: The results of the functional studies are shown in Table 1. The immunohistochemical results represent the measurements in the inner strip of the outer medulla, where there was a higher concentration of lesions. The histopathological analysis showed moderate to severe ATN in groups SF and OX. Moreover, through polarized view, these two groups showed intratubular deposition of oxalate crystals (mild to severe). Conclusions: Typical histopathological and functional changes of ATN were present 24 hours after the administration of star fruit juice. This ATN can be attributed to intratubular deposition of oxalate crystals. Likewise, there was a reproduction of this nephropathy, although less severe, in the group treated only with oxalate solution.

Table 1. Median (percentiles 25%, 75%) of functional and immunohistochemical studies. *p<0.05 Group SF vs. Group C, **p<0.05 Group SF vs. Group OX, ***p<0.05 Group C vs. Group OX.

<table>
<thead>
<tr>
<th></th>
<th>Group SF (n=9)</th>
<th>Group C (n=7)</th>
<th>Group OX (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GFR (mL/min)</td>
<td>0.15 (0.09; 0.29)*</td>
<td>0.61 (0.59; 0.65)</td>
<td>0.39 (0.29; 0.67)</td>
</tr>
<tr>
<td>FENA (%)</td>
<td>0.70 (0.26; 1.06)*</td>
<td>0.08 (0.05; 0.28)</td>
<td>0.26 (0.22; 0.30)</td>
</tr>
<tr>
<td>FEK (%)</td>
<td>19.74 (15.40; 31.25)*</td>
<td>4.19 (3.54; 4.93)</td>
<td>7.40 (5.72; 8.90)</td>
</tr>
<tr>
<td>U_ox (mOsm/kg H2O)</td>
<td>613 (500; 741)***</td>
<td>1543 (1424; 1670)***</td>
<td>846 (631; 1073)***</td>
</tr>
<tr>
<td>PCNA (No. of positive/</td>
<td>32.8 (29.45; 35.57)**</td>
<td>0.2 (0.07; 0.61)</td>
<td>0.31 (0.23; 1.53)</td>
</tr>
<tr>
<td>ED1+ (No. of positive/</td>
<td>12.2 (9.5; 17.9)*</td>
<td>3.2 (1.9; 4.4)**</td>
<td>9.4 (5.6; 14.6)**</td>
</tr>
</tbody>
</table>
**SP114** RENAL FUNCTION DURING SEPSIS SYNDROMES: ROLE OF CAROTID BODY CHEMORECEPTORS

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Introduction and Aims: The carotid body, the main peripheral chemoreceptor, modulates the autonomic nervous system response under stress conditions like sepsis. The influence of carotid body on renal function is not known. The aim of the present study was to test whether the sepsis-like syndrome could modify the renal function in absence of different pathways from carotid body.

Methods: We evaluated serum creatinine (CRE), blood urea nitrogen (BUN) and physiological parameters 90 min after intraperitoneal (IP) administration of 15 mg/kg of lypopolysaccharide (LPS) or saline. Experiments were performed in male Sprague-Dawley rats anesthetized with sodium pentobarbitone (60 mg/kg IP), in control conditions (SHAM surgery) and after bilateral carotid neurotomy (BCN).

Results: In SHAM group, LPS significantly increased respiratory rate (RR) (73±6 to 102±6/min), heart rate (HR) (387±35 to 47±24/min), respiratory minute volume (V̇E) (81±12 to 111±13 mL/min) and decreased systolic blood pressure (P S) (67±13 mmHg), without inducing changes in neither CRE (saline, 0.66±0.14; LPS, 0.61±0.14 mg/dL), nor BUN (saline, 21.3±6; LPS, 19.4±9 mg/dL). LPS also increased plasma levels of epinephrine (31±15 to 41±22 pg/dL), cortisol (0.5±0.4 to 1.6±0.9 ng/mL), and TNF-α (0.5±0.4 to 1.2±0.1 ng/mL). BCN blunted the LPS response on RR (74±7 to 62±4/min), V̇E (73±7 to 63±9 mL/min), and enhanced both, the increase on HR (394±22 to 497±22/min) and the fall on P S (110±10 to 63±9 mmHg). Besides, LPS administration increased CRE (saline, 0.56±0.1; LPS, 0.98±0.1 mg/dL) and BUN (saline, 16.6±2.9; LPS, 25.1±6.3 mg/dL) and BCN prior to endotoxic suppressed LPS-induced cortisol increase (0.6±0.4 to 0.3±0.1 ng/mL), but enhanced the increase of epinephrine (28±4 to 265±200 pg/dL) and TNF-α (0.4±0.3 to 3.3±2.2 ng/mL).

Conclusions: Our results suggest that carotid body chemoreceptors might contribute to regulation of renal function during sepsis, through a communication network, including neural, humoral, and cytokine components.

**SP115** TEMPORAL ATTENUATES RENAL INJURY VIA PI3K – Akt – FoxOs MODULATION IN MICE WITH UNILATERAL URETERAL OBSTRUCTION

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1Internal Medicine The Catholic University of Korea Seoul Republic of Korea

Introduction and Aims: Oxidative stress contributes to the pathogenesis of chronic kidney disease. Phosphatidylinositol 3-kinase (PI3K), serine/threonine protein kinase B/Akt, and Forkhead box O (FoxO) transcription factors control oxidative stress and apoptosis. This study investigated whether tempo, an anti-oxidant, protects against renal injury by modulating PI3K-Akt-FoxO signalling.

Methods: Mice received unilateral ureteral obstruction (UUO) surgery with or without administration of tempol. We evaluated renal damage and expression of PI3K, Akt, FoxO3α and their target molecules, superoxide dismutase (SOD2), catalase, Bax, and Bcl-2 in the obstructed kidneys on days 3, 7, and 14.

Results: Collagen deposition and F4/80 macrophage infiltration were significantly lower in the obstructed kidneys of tempo-treated mice compared with those control mice on days 7 and 14. The expression of PI3K, phosphorylated Akt, and phosphorylated FoxO3α decreased markedly in the obstructed kidneys of the tempo-treated mice on days 7 and 14. Tempo increased the expression of SOD2 and catalase, which was followed by decreased production of hydrogen peroxide and lipid peroxidation. Significantly less apoptosis, a lower ratio of Bax to Bcl-2 expression, and fewer apoptotic cells in TUNEL staining were observed in the obstructed kidneys of tempol-treated mice.

Conclusions: The results show that tempo attenuates oxidative stress, inflammation, and fibrosis by modulating PI3K-Akt-FoxO3α signalling in the kidneys of mice with UUO.

**SP116** INTRAVENOUS POLYCLONAL IMMUNOGLOBULINS STIMULATE ERYTHROPOIESIS IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Introduction and Aims: The action of immunoglobulins on the erythroblasts’ erythroid receptor involved in the modulation of response to erythropoietin, in normal and pathological conditions, has shown a new system of positive regulation of erythropoiesis. Using these data as a starting point, we wanted to study the response of bone marrow to intravenous bolus administration of high doses of polyclonal immunoglobulins in patients with chronic kidney disease (CKD) stage III and IV.

Methods: Ten patients affected by CKD and/or by autoimmune diseases have been treated with infusion of polyclonal immunoglobulins (0.200 g/kg of body weight), and serum erythropoietin, CD34 as an early marker of erythropoiesis, Hb and reticulocytes were assessed (at the time intervals T0 and T1). The following day they have undergone the same infusion, blood sampling for the same assays, and also subcutaneous administration of erythropoietin alpha 4000 IU (at the times T2 and T3). Results: The administration of immunoglobulins has pointed out a statistically significant increase in the erythropoietin and CD34 levels. At the end of the two boli, erythropoietin values increased up to 85%. Serum erythropoietin significantly increased after administration of polyclonal immunoglobulins (Ig) in all CKD patients. After the administration of polyclonal immunoglobulins, the percentage of CD34 increased in a statistically significant manner in our patients with CKD, as to show a prompt response to erythropoiesis.

Conclusions: Our study demonstrates that the infusion of polyclonal immunoglobulins increases the levels of serum erythropoietin and CD34 right from its first administration. The treatment with polyclonal immunoglobulins and erythropoietin alpha increases CD34 production in a statistically significant manner. These data seem to suggest a new therapy for anaemia in patients with CKD. In conclusion, immunoglobulins behave as ‘enhancers of erythropoiesis’, acting in cooperation with erythropoietin in promoting erythropoiesis.

**SP117** POSSIBLE NEW UTILITY OF VDBP PROTEIN AS BIOMARKER OF CHRONIC PREDISPOSITION TO ACUTE KIDNEY INJURY

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1Unidad de Toxicología and Unidad de Fisiopatología Renal and Cardiovascular, Universidad de Salamanca Salamanca Spain, 2IIBSAL Salamanca Spain, 3IESCYL Soria Spain, 4Unidad de Investigación Hospital Universitario de Salamanca Salamanca Spain

Introduction and Aims: In the last years, the new concept of predisposition to acquire acute kidney injury (AKI) is emerging. This concept was observed in our group when experimental animals exposed to an absolutely subnephrotoxic acute treatment with
certain drugs (e.g. gentamicin and cisplatin) developed AKI when they were treated with a second insult with another drug, while control animals exposed to the same second drug experienced no toxicity. On these grounds, we decide to study if chronic exposure to nephrotoxics might induce this predisposition to acute kidney injury and investigate how to detect this condition by the search of predisposition biomarkers.

**Methods:** To this end, rats (Sprague-Dawley) were treated with a subtoxic dosage of the experimental nephrotoxin urea nitrate (UN, 5.4 g/L) in the drinking water for 22 weeks, or plain water (as control). After 11 or 21 weeks both groups were exposed to subtoxic regime of gentamicin during 7 days. Renal function was monitored by means of serum creatinine, serum urea, proteinuria, N-acetyl-beta-D-glucosaminidase and lactate dehydrogenase excretion measurement. After and before gentamicin treatment a subset of rats were sacrificed and their kidneys used for histology. With the purpose of identifying biomarker of predisposition, proteomic studies were performed before gentamicin administration at week 21.

**Results:** Chronic administration of UN in drinking water during 11 or 21 weeks did not modify renal function or renal tissue integrity, as revealed by serum and urine biochemical parameters and histology. However, when rats exposed to UN during 21 weeks where challenged with low doses of a second potentially nephrotoxic insult, gentamicin, they developed an overt renal failure as shown by an increase in serum creatinine, and urine protein excretion. These alterations were not observed in the control group nor in the UN group at 11 weeks. Using a proteomic analysis, VDBP was detected as a potential biomarker in the urine of predisposed animals at 21 weeks, which was validated by Western blot. Urinary excretion of VDBP was statistically higher than the exposed group. At 11 weeks.

**Conclusions:** Our results suggest that chronic exposure to UN, at doses that apparently does not produce damage, predispose to acute kidney injury. The protein VDBP appears increased in urine of predisposed animals at 21 weeks but not at 11 weeks means that this increase is associated with hidden injury but not with the exposition to uranium. VDBP protein might be potentially used as marker of chronic predisposition to ARF. This new diagnostic tool might help to reduce AKI incidence and severity, and also the associated sanitary and socioeconomic costs.

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**SP120**

**VITAMIN D DEFICIENCY AGGRAVATES TENOFIVIR INDUCED METABOLIC SYNDROME AND RENAL FAILURE**

Daniele Canale, Ana Carolina de Bragança, Janaina Gonçalves, Maria Heloisa M. Shimizu, Rildo A. Volpini, Lucia Andrade, Antonio Carlos Seguro

**Nephrology University of São Paulo School of Medicine São Paulo Brazil**

**Introduction and Aims:** Vitamin D deficiency (VDD) is highly prevalent among HIV infected individuals. Tenofivir disoproxil fumarate (TDF), a widely used component of antiretroviral regimens for HIV treatment, has been associated with comorbidities, some of which have been attributed to renal toxicity and metabolic syndrome. The aim of the study was to investigate the effect of VDD on TDF treated rats.

**Methods:** Wistar rats were randomly divided into four groups: control (C, n = 9), receiving a standard diet for 60 days; VDD (n = 6), receiving a free-vitamin D diet for 60 days; TDF (n = 9), receiving a standard diet for 60 days with the addition of TDF (50 mg/kg food) for the last 30 days. We measured insulin clearance (GFR, mL/min/100g), blood pressure (BP, mmHg), renal blood flow and calculated renal vascular resistance (RVR, mmHg/ml/min/m²); serum levels of 25-hydroxyvitamin D (25(OH)D, ng/mL), cholesterol (mg/dL) and triglycerides (mg/dL); urinary sodium excretion (UV Na,mEq/24h) and the endogenous antioxidant, serum glutathione (μM/mL). Renal tissue was immunoblotted for angiotensin II (AII), endothelial nitric oxide synthase (eNOS) and immunoblotted for angiotensin II (AII), endothelial nitric oxide synthase (eNOS) and immunoblotted for angiotensin II (AII), endothelial nitric oxide synthase (eNOS) and immunoblotted for angiotensin II (AII), endothelial nitric oxide synthase (eNOS) and immunoblotted for angiotensin II (AII), endothelial nitric oxide synthase (eNOS) and immunoblotted for angiotensin II (AII)

**Conclusions:** Chronic administration of Tenofivir leads to a decrease in glomerular filtration rate, increase in blood pressure, renal tissue angiotensin II and oxidative stress. VDD association has a protective effect attributable to lower levels of lipid peroxidation and higher levels of glutathione. These findings have significant clinical implications for renal protection against Tenofivir nephrotoxicity.

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**SP120 Table 1.** Hemodynamic and biochemical parameters

<table>
<thead>
<tr>
<th></th>
<th>GFR</th>
<th>BP</th>
<th>RVR</th>
<th>serum UV Na</th>
<th>cholesterol</th>
<th>triglycerides</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>0.88±0.04</td>
<td>117±3</td>
<td>19.8±6</td>
<td>0.63±0.50</td>
<td>39±1</td>
<td>17±4</td>
</tr>
<tr>
<td>VDD</td>
<td>0.61±0.06</td>
<td>127±4</td>
<td>21.1±6</td>
<td>0.52±0.03</td>
<td>53±4</td>
<td>34±5</td>
</tr>
<tr>
<td>TDF</td>
<td>0.63±0.04</td>
<td>134±3</td>
<td>24.1±5</td>
<td>0.55±0.06</td>
<td>54±3</td>
<td>59±5</td>
</tr>
<tr>
<td>VDD+TDF</td>
<td>0.45±0.04</td>
<td>148±5</td>
<td>26.9±1</td>
<td>0.32±0.05</td>
<td>80±7</td>
<td>74±13</td>
</tr>
</tbody>
</table>

a, p<0.05; b, p<0.01; c, p<0.001 vs. control d, p<0.05; e, p<0.01 vs. Tenofivir

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**SP119**

**PROTECTIVE EFFECT OF N-ACETYLCYSTEINE ON CHRONIC TENOFIVIR NEPHROTOXICITY IN RATS**

Maria H.M. Shimizu, Daniele Canale, Ana C. de Bragança, Lucia Andrade, Weverton M. Luchi and Antonio C. Seguro

**Nephrology School of Medicine - University of São Paulo São Paulo Brazil**

**Introduction and Aims:** Tenofivir is an effective drug for HIV infection and chronic hepatitis B. This antiretroviral drug is associated to chronic kidney disease and increased oxidative stress. N-acetylcycteine (NAC) has been shown to be a potent antioxidant by increasing glutathione levels. Previous study from our laboratory demonstrated that NAC attenuates the progression of chronic renal failure in rats submitted to 5/6 nephrectomy (Kidney Int 2005;68:2208-17). The aim of this study was to evaluate the effect of chronic use of tenofivir on renal function and oxidative stress in rats, and a possible protector effect of the association of N-acetylcycteine (NAC) against Tenofivir nephrotoxicity.

**Methods:** Three groups of 2-month old male Wistar rats were studied: 1- control (n=7); 2- Tenofivir (50 mg/kg diet, n=10); 3- Tenofivir (50 mg/Kg diet) + NAC (600 mg/L drinking water, n=10). The rats were monitored during 4 months, after which clearance studies were performed. Twelve hours prior to clearance studies, the animals were housed in metabolic cages to collect 24h urine volume. The rats were anesthetized to measured intrulineulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinulinuin
Results: Vitamin D levels were similar in C (15.4±1 ng/mL) and TDF (14.8±1.3 ng/mL) groups and <1.5 ng/mL in VDD groups. Body weight, water intake and food ingestion were not different among the 4 groups. Treatment with TDF led to impaired renal function, hypertension, higher RVR and dyslipidemia. Administration of TDF also increased protein expression of AII and VDR. Association of TDF and VDD exacerbates TDF nephrotoxicity, as well as metabolic syndrome. Furthermore, VDD + TDF group showed urinary sodium retention. The increased VDR protein expression in TDF groups may represent a compensatory effect to decrease renal injury.

Conclusions: VDD aggravates renovascular effects and TDF-induced renal failure at least in part due to the involvement of renin-angiotensin-aldosterone system. Therefore, the assessment of vitamin D is important in HIV patients receiving TDF. (FAPESP,CNPq).

SP121 THE 5/6 NEPHRECTOMIZED RAT AS A GOOD MODEL TO STUDY CHRONIC KIDNEY DISEASE

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Introduction and Aims: Chronic kidney disease (CKD) is, usually, associated with anemia, hypertension, dyslipidemia and inflammation. Animal models of CKD/anemia have been widely used as a tool to study physiological, pathophysiological and pharmacological aspects of this disease. Most of these studies have been focused on specific tissue or cell changes and few studies perform a more global evaluation, to understand the interactions between the most important players in anemia of CKD. In that way, we studied a rat model of CKD induced by 5/6 nephrectomy, focusing on anemia, iron metabolism, inflammation, lipid profile, kidney dysfunction and histomorphological damage.

Methods: Two groups (n=7) of male Wistar rats (280 g), were studied during 12 wks: Sham – surgery without kidney reduction; CRF – subjected to (5/6) nephrectomy. At wks 0, 3, 6, 9 and 12, renal function and hematological data was assessed in blood. Body weight, blood pressure and heart rate were also measured. At the 12th week, blood and tissues were collected. Iron metabolism, inflammation, lipid profile, tissues trophy indexes and histomorphological kidney analysis, as well as liver gene expression of iron related gene expression, by RT-qPCR, were evaluated.

Results: Severe CRF group showed, at the 3rd week, a significant and sustained increase for creatinine (p<0.001) and urea (p<0.001) and anemia. At the end of the protocol, hypertension and dyslipidaemia were present in CRF rats, when compared with sham animals. Concerning to the iron related gene expression in the liver, we found a reduction in Hamp, TRP1, TRP2, HIV, HFE, TMPRSS, EPOR and DMT1 gene expression. Regarding kidney tissue, CRF rats showed hypertrophy and structural damage. The most prevalent and evident lesions were: a) glomerular: mesangial expansion and thickening of Bowman capsule; b) tubulointerstitial: presence of hyaline cylinders, irregularity of tubular basement membranes, tubular dilatation and IFTA; c) vascular: arteriolar hyalinosis and arterioloesclerosis.

Conclusions: This rat model of CKD induced by 5/6 nephrectomy shows that anemia triggers several changes in the expression of iron related genes to overcome anemia, and leads to functional and structural kidney damage, as occurs in a wide percentage of CKD patients. Thus, this rat model provides a good tool to study chronic kidney disease. Acknowledgement: FCT (PTDC/SAU-TOX/114253/2009, SFRH/BD/61020/2009 and PEST-C/SAU/031282/2011) and COMPETE.
LAB METHODS / BIOMARKERS

COMPARISON OF ATHEROMATOUS DISEASE IN HIGH RISK POPULATIONS REVEALS A DISTINCT ASSOCIATION OF RISK FACTORS AMONG PATIENT POPULATIONS AND A STRIKING RELEVANCE FOR GLYCEMIC CONTROL IN DIABETIC NEPHROTIC SYNDROME

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Introduction and Aims: Patients with Chronic Kidney Disease (CKD) and/or Diabetes are at a high risk for cardiovascular (CV) disease. Improved outcomes require a better understanding of specific risk factors that distinctly modulate the incidence of atheromatous disease. Herein, we compared the distinct and combined impact of CKD and of diabetes (DM) on the development of atheromatous disease, and prevalent risk factors per condition.

Methods: Cross sectional study in 2088 asymptomatic patients categorized as: 1) General Population (2 CV risk factors, no DM, estimated glomerular filtration rate (eGFR) >60 ml/min); 2) CKD no DM; 3) DM, eGFR<60 ml/min, proteinuria>300 mg/dl; 4) Established diabetic nephropathy (DN). Carotid ultrasound of left and right carotid arteries evaluated intima-media thickness (IMT) in the common, bulb, internal and external carotid. Carotid plaque (CP) was defined as IMT>1.5mm. Multivariate Logistic Regression analysis examined the variables independently associated with the presence of CP, including glycosylated haemoglobin (HbA1c) in diabetic patients.

Results: Table 1 shows the percent of patients with CP among the 4 populations of patients categorized by age. Table 2 shows the results of the multivariate analyses. There is a distinct association between classical risk factors and CP among the 4 subpopulation of patients. In DN, age and Triglycerides are the only classical risk factors independently associated with CP. Also, exclusively in DN, HbA1c emerges as a main risk factor independently associated with the presence of carotid plaques.

Conclusions: Our findings confirm the high prevalence of atheromatous disease in asymptotic high CV risk patients with a distinct association of risk factors among patient populations. Importantly, in diabetic nephropathy, HbA1c emerges as a main risk factor independently associated with the presence of carotid plaques.

SP122

<table>
<thead>
<tr>
<th>2 CV Risk Factor</th>
<th>CKD no DM (n = 1315)</th>
<th>DM no CKD (n = 552)</th>
<th>DM no CKD (n = 110)</th>
<th>DN (n = 111)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;52 y</td>
<td>28.2 %</td>
<td>16.4 %</td>
<td>28.6 %</td>
<td>37.5 %</td>
</tr>
<tr>
<td>52-60 y</td>
<td>53.9 %</td>
<td>53.4 %</td>
<td>86.4 %</td>
<td>65.6 %</td>
</tr>
<tr>
<td>61-66 y</td>
<td>62.5 %</td>
<td>72.3 %</td>
<td>70 %</td>
<td>72.2 %</td>
</tr>
<tr>
<td>&gt;67 y</td>
<td>75.8 %</td>
<td>83.3 %</td>
<td>90.5 %</td>
<td>80.5 %</td>
</tr>
</tbody>
</table>

SP123

PREDICTIVE VALUE OF TRADITIONAL AND NOVEL RISK FACTORS FOR CARDIOVASCULAR DISEASE AND END STAGE RENAL DISEASE IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Introduction and Aims: Up to 25% of mild to moderate chronic kidney disease (CKD) patients die from cardiovascular (CV) disease before entering dialysis, whereas control of CKD progression risk factors remains a bet to be won by nephrologists. The predictive value of traditional and novel risk factors is important because the identification of «the best predictor» is of obvious importance for risk stratification in CKD patients. Mortality and non-fatal CV events (myocardial ischemia, stroke and peripheral vascular event) along with initiation of dialysis were the major end points.

Methods: Two hundred thirty consecutive CKD outpatients of stages 1-4 (52% men) with mean age 65±12 years were prospectively followed up to 3 years. Patients lost of FU (17.5%) were excluded. Estimated glomerular filtration rate (eGFR, MDRD-6 variables) was 52.4±28.7 ml/min at recruitment. Demographic, somatometric, clinical characteristics, routine laboratory parameters and specific inflammatory markers, along with drug therapy were assessed at study entry. Echocardiograms were undertaken and left ventricular mass index (LVMI) was calculated. Cox regression, proportional hazard models were used to determine factors that best predicted the occurrence of a CV event/death or initiation of dialysis. Models included traditional and novel risk factors: sex, age, smoking, body mass index, mean BP, diabetes mellitus (DM), CV disease history, eGFR, uric acid (UPR, mg/dl), serum cholesterol, albumin (sAlb), uric acid and phosphorus, Hb, fibrinogen, CRP, IL-6, TNF-α, ICAM-1, VCAM-1 and LVMI.

Results: During the follow up 31 (16%) CV events and 7 CV deaths (3%) occurred with a mean time to the event of 21±12.5 months. Twenty one (11%) patients started dialysis in a mean time of 20±9 months. The statistically important predictive factors for the CV outcome were: DM (RR: 0.455, 95%CI: 0.22-0.932, p=0.03), sAlb (RR: 0.296, 95%CI: 0.113-0.773, p=0.013), LVMI (RR: 1.0, 95% CI: 1.009-1.001, p=0.021) and VCAM-1 (RR: 1.007 95% CI: 1.001-1.003, p=0.026). For the renal outcome significant factors were: eGFR (RR: 0.894, 95%CI: 0.844-0.947, p<0.001), UPR (RR: 1.005, 95% CI: 1.002-1.007, p<0.001). A limitation of our study was the relatively small number of patients.

Conclusions: The predictive value of traditional risk factors resulted to be superior to that of novel risk factors with regards to CV disease and end stage renal disease in long term CKD 1-4 stage patients.

SP124

CAROTID INTIMA-MEDIA THICKNESS AND PLAQUES ARE INDEPENDENTLY ASSOCIATED WITH RATE OF RENAL FUNCTION DECLINE IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Introduction and Aims: Increased carotid intima-media thickness (cIMT) and the presence of plaques are surrogate markers of systemic atherosclerosis and closely associated with adverse cardiovascular outcomes. Whether cIMT and plaques are related to renal decline rate and progression to dialysis remains to be determined in chronic kidney disease (CKD) patients.

Methods: This longitudinal observational study enrolled 413 CKD stage 3 and 4 patients. All patients performed carotid ultrasonography at their first visit to nephrology. We classified patients into CKD stage 3a, 3b and 4 based on estimated glomerular filtration rate (eGFR), and the decline of renal function was measured by eGFR slope. The renal endpoint was defined as commencement of dialysis.

Results: Mean age was 69.7 years and mean eGFR slope was -1.90 ± 1.08 ml/min/1.73 m²/yr. The cIMT values and plaque prevalence was significantly elevated with increasing severity of CKD stages (p<0.001). During the 2.5-year follow-up, 11.4% started dialysis therapy. Patients with cIMT ≥1.0 mm had a worse dialysis-free survival than those with cIMT <1.0 mm [hazard ratio 2.17, 95% confidence interval (CI) 1.21 to 3.68, p=0.006]. Statistically significant variables associated with more rapid renal progression rate were diabetes mellitus, wide pulse pressure, lower baseline eGFR, lower albumin, greater proteinuria, and increased cIMT and the presence of carotid plaque.
SP125 THE EFFECTS OF THE CKD-MBD (CHRONIC KIDNEY DISEASE-MINERAL AND BONE DYSREGULATION) PARAMETERS ON LEFT VENTRICULAR (LV) GEOMETRY IN PRE-DIALYSIS CKD

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Introduction and Aims: The biochemical parameters of CKD-MBD such serum phosphorus (P), Ca, iPTH (intact parathyroid hormone), and FGF (fibroblast growth factor)-23 have been reported to have strong effects on the mortality of CKD patients. Left ventricular hypertrophy has also known to be a strong risk factor for the death of CKD patients. Hence we investigated the effects of the parameters of CKD-MBD on the LV geometry in pre-dialysis CKD.

Methods: KNOW-CKD is an on-going, prospective, university hospital based observational cohort study under the sponsorship of Korean Center for Disease Control and Prevention. Cross-sectional analysis of echocardiography data and other clinical data was performed in 1231 participants of KNOW-CKD. LV muscle indexed (LVMI) from left ventricle was measured. With Portabl compact digital recorder Mobil-O-Graph NG (I.E.M GmbH Stolberg Germany) device arterial stiffness parameters, pulse wave velocity (PWV) and augmentation index (AI) were measured. With the use of monoclonal antibodies: the capture antibody, anti-dpMGP, is coated onto a microtitre plate

Results: The number of patients with CKD 1 & 2, CKD 3, and CKD 4 & 5 was 310 (25.8%), 489 (40.7%) and 402 (33.5%) persons respectively and LVMI increased along with progression of CKD (87±24, 90 ±24, 121±28, 3.9±3.8) mg/m2 in each group, (p<0.001). Along with the progression of CKD stage, the frequency of normal LV geometry decreased and those of eccentric and concentric LVH increased (normal; 43.2%, eccentric LVH; 21.7%, concentric remodeling; 13.6%, concentric LVH; 21.4% in CKD 4 & 5). Linear regression models showed that LVMI was positively associated with FGF23 (β=0.014, p<0.001). The relationship was pronounced in patients with proteinuria ≥ 0.2g/day (r=0.025, p<0.001). Multivariable analysis fully adjusted by age, sex, FGF23, and other significant variables in univariate analysis revealed that age, female, systolic blood pressure (SBP), body mass index (BMI), eGFR < 30ml/ 1.73m2 were risk factors for eccentric and concentric LVH, respectively. Among the parameters of CKD-MBD, serum Ca was related to eccentric and concentric LVH.

Conclusions: Along with the progression of CKD stage, LVMI and frequency of eccentric and concentric LVH increased. Although serum FGF23 level was positively related to LVMI in CKD patients, and more prominently in presence of proteinuria, serum FGF23 was not independent risk factor for LVH in our cohort. Serum calcium was related to eccentric and concentric LVH in Korean CKD patients.

SP126 ARTERIAL STIFFNESS IN PATIENTS WITH DECREASED RENAL MASS

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Introduction and Aims: In the presence of hypoplastic kidney or a residue of kidney after nephrectomy some compensatory alterations take place. In this study, we aimed to investigate whether any alteration take place in arterial stiffness in patients with decreased renal mass and if alteration is present to evaluate the relation of this alteration with renal functions and ambulatory blood pressure.

Methods: One hundred and thirty five patients who had one sided nephrectomy due to different causes or with congenital single kidney (mean age 43.4±8.5) and 44 healthy volunteers (mean age 43.2 ±8.5) were included. Patients with diabetes mellitus, with hypertension, obesity, smoking, arterial hypertension, diabetes mellitus, lipid profile and non-traditional (serum calcium, phosphate, C-reactive protein – CRP) risk factors were also assessed. Two groups were defined based on a AACS cut-off > 5.5 AACS<5 (n=37) and AACS≥5 (n=40). This value was obtained by ROC curve analysis considering the reported cut-off for RRI=0.7 (area under the curve 0.69 [0.56-0.81], p<0.001). Spearman test was used for correlations.

Results: Vascular nephropathies (50%), diabetic nephropathy (26%) and primary glomerulonephritis (8%) were the main causes of CKD. The eGFR was similar in the two groups (30.2 [28-35.2] vs. 33.7 [30.3-39]). Patients with AACS≥5 were older (71.8 [68.7-84.8] vs. 66.7 [64-69.5], p=0.006), had higher serum cholesterol (193 [175-211] vs. 167 [160-182], p=0.006), and more pronounced inflammation (CRP: 6 [4-12] vs. 3 [2-7], p=0.01). No other investigated CV risk factors differed between the two groups.

Lower ABI (0.92 [0.84-1.0] vs. 1.08 [1.04-1.21], p=0.001) and higher IMT (0.08 [0.08-0.09] vs. 0.07 [0.07-0.08], p=0.06), but similar CAVI were found in AACS≥5 group. Moreover, AACS was negatively correlated with ABI (r= -0.51, p<0.001) and positively with IMT (r=0.27, p=0.01), underlining the relationship of AACS with the extent of atherosclerosis in other territories rather than with arterial stiffness. RRI was significantly higher in subjects with AACS≥5 (0.73 [0.70-0.75] vs. 0.68 [0.64-0.69], p<0.001), and showed a significant direct correlation with AACS (r=0.35, p<0.001).

Conclusions: Assessment of AACS could predict advanced atherosclerosis, since it was associated with carotid plaques (IMT) and vascular artery disease (ABI). Hence important, AACS could be used as a fast, available and inexpensive tool for estimation of RRI and consequently of the intrarenal vascular status, but further research is warranted.

SP127 IS ABDOMINAL AORTIC CALCIFICATION RELATED TO RENAL RESISTIVE INDEX?

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1Gabriel Stefan ‘Caroll Davila’ University of Medicine and Pharmacy Bucharest Romania, 2Dr Carol Davila Hospital of Nephrology Bucharest Romania, 3Delta Hospital Bucharest Romania

Introduction and Aims: In chronic kidney disease (CKD), abdominal aorta calcification (AAC) is frequent and correlates with cardiovascular (CV) risk. Renal resistive index (RRI) predicts both renal and CV outcome. Therefore, we aimed to evaluate the relationship between AAC and RRI in non-dialysis CKD patients.

Methods: This cross-sectional, single-center study prospectively enrolled 77 clinically stable CKD patients (49% male, 70 [65-73] years, eGFR 33.5 [30.1-36.9] ml/min) with a positive history for systemic atherosclerosis. Exclusion criteria were end-stage renal disease, obstructive nephropathy and valvular heart disease. RRI and carotid intima-media thickness (IMT) were assessed by Doppler sonography. AAC were measured on a plain on lateral lumbar X-ray (Kaupilla score - AACs), carotid-ankle vascular index (CAVI) and ankle-brachial index (ABI) were measured.

Results: There was no significant difference between study and control group with regard to age, gender, body mass index, abdominal sympathetic (116±10 and 113±10, p=0.088) and diastolic (73±9 and 72±10, p=0.146) blood pressure. Among the arterial stiffness parameters of the cases, PWV value was significantly higher compared to controls (6.72±1.1 vs 6.29±0.75, p=0.018). Although augmentation index (AI) of cases was higher than control group, it did not statistically differ, it was 55±13.2, p=0.187. In correlation analysis, there was correlation between PWV and age, blood pressure (BP), GFR, calcium and uric acid levels. Also there was correlation between AI and age, BMI, pulse pressure, hemoglobin value and GFR. In Liner regression analysis, there was correlation between PWV and age and AI (r=0.34, p=0.001) in 24 hours mean systolic BP (SP125=0.349, p=0.000), and between AI and age (β=0.314, p=0.001) and hemoglobin values (β=0.2-0.3, p=0.026).

Conclusions: Arterial stiffness increases in cases with renal mass loss. In these cases arterial stiffness increase is related to age, mean systolic blood pressure and hemoglobin level.

SP128 DEVELOPMENT OF A NOVEL ELISA TEST KIT FOR THE DETECTION OF DESPHOSPHO-UNCARBOXYLATED MATRIX GLA PROTEIN

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Introduction and Aims: Matrix Gla-protein (MGP) is regarded as the strongest inhibitor of vascular calcification and produced by many cells, including vascular smooth muscle cells. MGP can undergo gamma-glutamte carboxylation (vitamin K dependent step) and then phosphorylation. Circulating desphospho-uncarboxylated (dpcMGP) reflects the amount of uncarboxylated and microcarboxylated MGP produced in the arterial vessel wall and is a direct marker for the vascular vitamin K status. In CKD patients high levels of circulating dp-uc MGP have been associated with calcification and overall mortality risk. The purpose of this study is to develop an ELISA for the accurate detection of dp-uc MGP.

Methods: The ELISA measures dp-ucMGP in plasma samples by use of two monoclonal antibodies: the capture antibody, anti-dpMGP, is coated onto a microtitre plate and the detection antibody, anti-ucMGP, is biotinylated. Standards, controls and

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samples (neat or diluted) are added to the microtitre plate followed by the addition of the biotinylated antibody and incubated overnight. The plate is washed and incubated with enzyme labelled avidin before a second wash step and the addition of a chromogenic substrate. The absorbance of the stopped reaction is read at 450-650nm with an optical density range of 0.2 to 0.8. The average absorbance of samples spiked with synthetic material is 0.210. 

**Conclusions:** The newly developed ELISA to a research in house ELISA shows the assay to be fully comparable with a slope of 0.755, intercept of 50.8 and R² of 0.860. The assay shows a positive relationship between increasing dp-ucMGP levels and progressing CKD stage with the color intensity directly proportional to the concentrations of dp-ucMGP.

**Introduction and Aims:** Fibroblast growth factor 23 (FGF23) is a regulator of mineral and bone metabolism which was discovered in the early 21st century. A number of studies reported the association of high levels of FGF23 with cardiovascular disease (CVD) and mortality in patients with chronic kidney disease (CKD), however they still have controversies. Thus, we aimed to elucidate the association of FGF23 with the presence of coronary artery calcification and its prognostic value in patients with moderate and advanced stage CKD.

**Methods:** Serum FGF23 levels in patients with CKD stage 3 to 5 and 25 age and sex matched controls were measured by using ELISA. We made routine biochemistry and assessed coronary calcification by multi-slice spiral computed tomography (MSCT) within the CKD patients. The relationship between FGF23 and the presence of coronary artery calcification were studied. The occurrence of cardiovascular events and deaths was recorded over 22±3 months.

**Results:** Serum FGF23 levels in CKD patients were significantly higher than those in healthy controls (P=0.01). The concentrations of FGF23 were positively related with duration of dialysis (r=0.288, P=0.007), serum calcium (r=0.377, P<0.001), serum phosphorus (r=0.576, P<0.001), calcium and phosphorus product (r=0.659, P<0.001), PTH (r=-0.331, P<0.001) and CRP (r=0.286, P=0.001) levels, and negatively related with hemoglobin (r=-0.302, P=0.004), 25(OH)D (r=-0.207, P=0.007) and 1,25(OH)2D (r=-0.187, P=0.023) levels. Serum FGF23 levels were significantly associated with coronary artery calcification score (CACS) (r=0.177, P=0.034). During the follow-up, 19 cardiovascular events (12.7%) and 6 deaths (6%) were registered. Patients were stratified to two groups by median FGF23 level (675.8pg/ml). The Kaplan-Meier survival curves showed that patients with FGF23 levels <675.8pg/ml had significantly higher cardiovascular event incidence rate (P=0.01) and all-cause mortality (P=0.05) than patients with FGF23 levels above the cut-off. Cox regression analysis showed that FGF23≥675.8pg/ml (HR=5.334, 95%CI: 1.111-24.26, P=0.05) and severe coronary artery calcification (CACS≥400) (HR=4.445, 95%CI: 1.554-12.717, P=0.01) were independent risk factors for cardiovascular events in CKD patients, while FGF23 levels (HR=5.334, 95%CI: 1.167-10.704, P=0.05) and severe coronary artery calcification (CACS≥400) (HR=7.918, 95%CI: 1.790-32.770, P=0.01) were independent risk factors for all-cause mortality in CKD patients.

**Conclusions:** Serum FGF23 levels in patients with moderate and advanced stage CKD were significantly higher than normal population. Serum FGF23 levels may be associated with coronary artery calcification and adverse clinical outcomes in patients with moderate and advanced stage CKD.

**Introduction and Aims:** Hypertension and poor Quality of Life (QOL) are 2 common conditions highly prevalent among hemodialysis (HD) patients. Provision of individualized nutritional counseling has shown to improve these 2 components. The aim of this study is to measure the effect of advanced individualized nutrition education given to HD by renal dietitian on serum phosphorus (P) and QOL.

**Methods:** The study is a randomized controlled trial with a post design. Patients (n=300) were recruited from 6 HD units in Lebanon. Each HD unit was divided to half as per the HD shift and assigned to the 2 study groups: experimental or control. Patients in the experimental group received nutritional education of 2 hours per month for 6 months by dedicated renal dietitian. Both study groups continued to receive the routine dietetic care by hospital dietitian. Outcome Measures : Serum P (mg/dl) and QOL measured by SF-36 questionnaire.

**Results:** Serum P in the experimental group dropped significantly from 5.6±1.55 mg/dl to 5.0±1.51 mg/dl, no significant change was seen in the control group. As for QOL, at baseline, study participants reported to have 48-75% of full health. Post intervention only 2 components of QOL changed, they significantly dropped from better to worse: social functioning (experimental: 85.19±27.68 to 56.44±32.26, Control:85.64±28.79 to 57.77±32.96) and bodily pain (experimental: 76.85±29.57 to 56.62±36.65, Control: 77.7±27.44 to 61.22±33.71).

**Conclusions:** The educational intervention proved to be effective in improving serum P in Lebanese HD patients, but it was not effective on QOL parameters. Among the problems we faced in collecting QOL from patients was that most did not like to complain about their health, and instead thanked God for their current situation. Our findings suggest the need for developing a culturally sensitive QOL instrument that would be able to detect QOL in religious and oriental cultures.

**Introduction and Aims:** Of life is a 3-year randomized study in Lebanese HD patients aged 18 years or older receiving thrice weekly maintenance HD to measure the effect of an educational intervention on serum P and QOL. The intervention only 2 components of QOL changed, they significantly dropped from better to worse: social functioning (experimental: 85.19±27.68 to 56.44±32.26, Control:85.64±28.79 to 57.77±32.96) and bodily pain (experimental: 76.85±29.57 to 56.62±36.65, Control: 77.7±27.44 to 61.22±33.71).

**Conclusions:** The educational intervention proved to be effective in improving serum P in Lebanese HD patients, but it was not effective on QOL parameters. Among the problems we faced in collecting QOL from patients was that most did not like to complain about their health, and instead thanked God for their current situation. Our findings suggest the need for developing a culturally sensitive QOL instrument that would be able to detect QOL in religious and oriental cultures.
Methods: We collected urine sample data from electronic medical records that were submitted simultaneously for urine chemistry and dipstick test. Urine samples were collected from adult (Age 16-98) patients. Six thousand nine hundred forty one random urine samples were tested for PCR and urine dipstick, and 3,874 samples for ACR and dipstick.

Results: The median values of PCR and UCR were higher in samples of high grade DP and low SG. When DP 2+ (100 mg/dl) and over or 1+ (30 mg/dl) with SG ≤ 0.100 or trace with ≤ 0.005 were used as selection criteria, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for detection of overt Proteinuria (PCR ≥ 500 mg/g) were 89.6%, 87.7%, 85.9% and 89.8% respectively. When more than trace was used, the sensitivity, specificity, PPV and NPV for detection of microalbuminuria (ACR ≥ 30mg/g) were 60.2%, 86.6%, 85.6% and 62.0% respectively. With negative results, especially if SG levels were lower, there were many microalbuminuria cases.

Conclusions: Combination of DP and SG value is more useful to estimate PCR and to detect overt proteinuria cases than DP only.
Results: 137 patients were included in the analysis. TI fibrosis was graded 1 in 16 patients, 2 in 52 patients, 3 in 37 patients, 4 in 32 patients. A1m/creat was significantly different among groups than A1m/albumin. Statistically significant differences of A1m/creatinine were found between grade 0-1 versus grade 3-4 (p<0.002), grade 4 versus grade 1 (p<0.0005), and grade 4 versus grade 2 (p=0.01). Using the ROC analysis we found that the discriminating power of a A1m/creatinine was good between grade 4 versus grade 1 with the sensitivity 78.1% and specificity 82.6% (AUC 0.795, cutoff = 28 mg/mmol), and between grade 4 versus grade 1+2 with the sensitivity 71.9% and specificity 68.9% (AUC 0.718, cutoff = 46.07 mg/mmol).

Conclusions: We confirmed our results of our small pilot study, that urinary A1m is strongly associated with the grade of TI fibrosis. A1m/creatinine can be used as a non-invasive marker, which is particularly useful to identify patients with a high degree of renal tubulointerstitial fibrosis.

SP138 ROLE OF THE FUNCTIONAL TOLL-LIKE RECEPTOR-9 PROMOTER POLYMORPHISM (-1237T/C) IN THE INCREASED RISK OF END-STAGE RENAL DISEASE: A CASE-CONTROL STUDY

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1Department of Medicine Cardinal Tien Hospital, Fu-Jen Catholic University New Taipei City Taiwan Republic of China, 2School of Public Health National Defense Medical Center Taipei Taiwan Republic of China

Introduction and Aims: Inflammation is a universal response to infectious and noninfectious triggers in the kidney that may progress to end stage renal disease (ESRD). Toll-like receptor 9 (TLR-9), a receptor for CpG DNA, is involved in activation of immune cells in renal diseases and may contribute to chronic inflammatory disease progression. Previous studies indicated that -1237T/C confers regulatory effects on TLR-9 transcription. To date, the effect of TLR-9 polymorphisms on ESRD remains unknown. Therefore we investigated the predictive value of TLR-9 gene polymorphisms and further functional study on ESRD in a Han Chinese population.

Methods: We performed a case-control study and genotyped (-1237T/C, -1486T/C polymorphisms) in 750 ESRD patients and 450 controls analysed by real-time PCR assays. Plasma concentrations of interleukin-6 (IL-6) were determined by ELISA. A luciferase reporter assay and real-time PCR were used to test modulation of TLR-9.

Results: A significant association between -1237T/C in TLR-9 and ESRD was identified. The frequency of TLR-9 polymorphism haplotype “TCA” was 27.8% in the ESRD patients compared with 34.6% in the controls (OR = 0.73, 95% CI = 0.60-0.88, p= 0.001). In contrast, haplotype TTA and CCA were more common in the ESRD patients (6.5% and 2.5%, respectively) than in the controls (1.9% and 0.6%, respectively) (OR = 3.47 and 4.45, 95% CI = 2.02-5.97 and 1.70-11.67, p < 0.001 and < 0.001, respectively). ESRD patients carrying -1237TC had a higher mean plasma IL-6 level when compared with -1237TT (p<0.001). The TLR-9 transcriptional activity of the variant -1237CC allele is higher than the -1237TT allele. In vitro studies demonstrate that -1237T/C may be involved in the development of ESRD through transcriptional modulation of TLR-9.

Conclusions: We found that single nucleotide polymorphisms of the TLR-9 gene, especially -1237T/C, were significantly associated with ESRD in the Chinese population. The functional study showed that -1237T/C may be involved in the development of ESRD through transcriptional modulation of TLR-9. It could provide a new insight into the role of TLR-9 in disease that has the potential to provide new avenues for treatment and to also identify individuals at risk.

SP139 IDENTIFICATION OF COMBINED URINARY MRNA BIOMARKERS FOR RENAL FIBROSIS IN IGA NEPHROPATHY WITH PCR ARRAY

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Introduction and Aims: Immunoglobulin A nephropathy (IgAN) is the most common form of primary glomerulonephritis worldwide. Here we reported an application of real-time quantitative PCR (RT-PCR) array in profiling new urinary biomarkers of IgAN.

Methods: 32 biopsy-proven IgAN patients and 6 healthy controls (HF) were enrolled in this study with complete clinical data. To evaluate progression of IgAN, patients were divided into four groups based on the semiquantitatively graded tubulointerstitial fibrosis area (%): none (5%, n=7), mild (6-25%, n=11), moderate (26-50%, n=7), and severe (>50%, n=5). Urinary cell pellet was collected from each study participant and the total RNA were extracted and identified from the urinary sediment. The PCR array contains 89 renal fibrosis related genes, 4 housekeeping genes and 3 quality controls and its performance was evaluated. The relative expression of each gene between IgAN patients and healthy controls (HC) was examined and the data was treated with ΔΔC method. Correlation between differentially expressed mRNA and clinical parameters and the ROC-curve analysis of differentially expressed mRNAs were also determined. Linear discriminant analysis was used to weight those differentially expressed mRNAs and derive composite biomarkers which make superb performance for RF diagnosis to the single gene.

Results: The array we fabricated displayed high sensitivity, specificity, and repeatability. Compared with healthy controls, a total of 20 mRNAs varied significantly in IgAN patients (>2-fold) (p<0.05). They are podocyte markers, renin angiotensin system related, EMT markers, tubular injury markers, cytokines, signal pathway related, and apoptosis related, respectively. Among these 20 differentially expressed mRNAs, 6 ones (ACE, CD71, PODXL, CCL5, VIM, TIMP) were positively correlated with both serum creatinine and fibrosis area (%), and negatively correlated with eGFR (P<0.05).ROC-curve analysis show 5 mRNAs (ACE, CD71, PODXL, CCL5, VIM) out of 6 were effectively able to differentiate RF and non RF subjects (p<0.05), with calculated area under the curve (AUC) above 0.7(p<0.05). Linear discriminant analysis was used to weight variables and derive composite biomarkers that identified the level of RF based on urinary mRNA level of ACE, CD71, PODXL, CCL5, and VIM. The developed biomarkers included ACE, CD71, and CCL5 as the independent variables. The composite biomarker showed sensitivity and specificity of 82% and 90%. The positive predictive value and negative predictive value was 95% and 70%, respectively.

Conclusions: This study demonstrated that target mRNA array might serve as a high-throughput and sensitive tool for detecting mRNA expression in urinary sediment. The composite of urinary mRNA established in this study might serve as a novel biomarker for RF of IgAN.
of the disease are primordial towards an improved disease management. To attain this goal there is a clear need for novel biomarkers. In recent years, the so-called omics approach emerged as a powerful tool for biomarker discovery. The objective of this work was to perform a proof-of-concept metabolite study for CKD.

**Methods:** Serum samples from CKD patients at stage 3 (n = 20), at stage 5 on hemodialysis (n = 19) and from healthy controls (n = 20) were monitored on a holistic metabonomics platform combining reversed-phase liquid chromatography coupled to high-resolution mass spectrometry (LC-Q-TOF MS) in both negative and positive ionization mode and gas chromatography coupled to quadrupole mass spectrometry (GC-MS). The methodological validity was ensured by use of quality control (QC) samples in the analytical setup, and by a thorough data analysis strategy involving principal component analysis (PCA) and orthogonal projections to latent structures-discriminant analysis (OPLS-DA) for class comparison.

**Results:** A substantial portion of the serum metabolome was covered. Ninety-six metabolites were identified. Forty-five metabolites were already known in the context of CKD (6 downregulated and 39 upregulated) while 51 metabolites were yet unknown (16 downregulated and 35 upregulated). Of the latter, 5 metabolites were found to be significantly increased (fold change ≥ 5) at CKD stage 3 compared to control. These metabolites were the sulfate and glucuronide conjugate of 3-hydroxyhippuric acid or 2-hydroxyhippuric acid (salicyluric acid) (p < 0.001), hydroxypyridine (p < 0.00005), urinary hipuroate (p < 0.00005) and a hexose based tetrasccharide (C_{12}H_{23}O_{12}, p < 0.0005).

**Conclusions:** Further targeted analysis in an increased study population will be performed to validate and quantify these novel, potential biomarkers across all CKD stages.

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**Abstracts**

**Nephrology Dialysis Transplantation**

**SP140 MASS SPECTROMETRY- AND ANTIBODY-BASED PROTEOMICS OF THE HUMAN KIDNEY AND URINE**

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**Introduction and Aims:** Functions of the kidney and nephron segments are obituary known, however, the precise details have not been clarified. Pathophysiological mechanisms of human kidney diseases have also not been disclosed yet. Proteomics is a powerful tool to analyze tissues or urine to understand the functions, protein interactions (pathways) and pathophysiology.

**Methods:** Normal parts of tissues (cortex, medulla and glomerulus) were obtained from non-kidney organ donors due to renal cancers. Urine samples were also collected from healthy volunteers. Proteins were separated by gel electrophoresis and peptides were prepared by in-gel tryptic digestion for mass spectrometry (MS). Sections of nephron segments were taken by laser-microdissection from normal human kidney biopsies. nephron segments were taken by laser-microdissection from normal human kidney biopsies. Microdissection of each segment (proximal, distal tubules and collecting duct, respectively). Glomerular sections were also collected from kidney biopsy samples of kidney disease patients (membranous nephropathy, IgA nephropathy and others). The peptides were prepared by direct digestion of these sections with trypsin (On-Site Direct Digestion) method for MS. Antibody (Ab)-based analysis of human tissues have been carried out in the Human Protein Atlas (HPA) project and more than a half of human proteins have been localized in the human body and in the kidney by immunohistochemistry (IHC).

**Results:** MS identified more than a thousand proteins with high confidence in each component of the normal human kidney. The Ab-based proteomics disclosed thousands of proteins in the kidneys. Comparison of the MS-based and Ab-based glomerulus protein discovery and expression profiles, both proteins were also identified by MS or Ab, were detected by both MS- and Ab-based methods. About a half of urine proteins identified by MS were also found in human plasma proteins. Urine proteins, which were not plasma proteins, were localized in the kidney and other urinary tract by looking at the HPA IHC images. The localization of urine proteins were summarized in a human urine proteome database. By MS analysis of human glomerular sections of each kidney biopsy samples, approximately a thousand proteins were identified and were further analyzed by bioinformatics to understand pathophysiology of kidney diseases.

**Conclusions:** Proteomic analyses of human kidney tissues and urine provided function- and disease-related information. These data were combined in a kidney and urine proteome database for public use.

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**SP141 INFLUENCE OF CYP3A5, CYP2C8 AND ABCB1 POLYMORPHISMS ON TACROLIMUS-INDUCED NEPHROTOXICITY IN LIVER TRANSPLANT RECIPIENTS**

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**Introduction and Aims:** The nephrotoxicity of calcinurin inhibitors (CNI) remains a serious concern after solid organ transplantation. The aim of this study is to investigate the risk factors of worsening renal function by tolvaptan in NDCKD patients with CHF.

**Methods:** A total of 136 living donor liver transplant recipients (107 males and 29 females) and 150 healthy controls (120 males and 30 females) were enrolled in this study. All the recipients had normal renal function (normal Cystatin C and normal kidney micro-albumin) before transplantation and received Tac-induced immunosuppressive regime (Tac+MMF+ prednisone) afterwards. CYP3A5, CYP2C8 and ABCB1 SNPs were assessed by polymerase chain reaction (PCR) and high-resolution melting curve analysis (HRM analysis). The trough concentrations of Tac were measured by enzyme-multiplied immunoassay technique (EMIT). We also detected serum Cystatin C (Cys-C) and urine microproteins including α1 microglobulin (α1M), microalbumin (MA), transferring (TRU) and IgG (IgG) among 136 allo-liver recipients to evaluate whether they have early renal injury and the probable location of the renal lesion.

**Results:** We could clearly distinguish three genotypes of CYP3A5 and ABCB1, while only two genotypes of CYP2C8 were identified in 136 recipients included. The genotype frequencies of the recipients did not show significant deviation from the Hardy-Weinberg equilibrium (P>0.05). The levels of cystatin C as well as all the four urine micro-proteins in the recipient group were significantly higher than those in the control group (P<0.05). There was a significant difference in TRU concentration instead of other three microproteins among patients with different CYP3A5 genotypes (P<0.05). The concentrations of α1M and Cys-C in recipients with CYP2C8*31 were significantly higher than that in those with CYP2C8*1 allele (P<0.05). Regarding MDR1 SNPs C3435T and C2673T, no significant difference was found In Cys-C and urine microproteins among patients with different genotypes.

**Conclusions:** CYP2C8*3 and CYP3A5*3 might have predictive value on the risk of Tac-induced nephrotoxicity. CYP3A5*3 was associated with the risk of early glomerular injury, while CYP2C8*31 was associated with the risk of early tubulointerstitial injury. ABCB1 genotypes (both C3435T and C2673T) were irrelevant to the Tac-induced nephrotoxicity in liver transplant recipients.

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**SP142 THE RISK FACTORS OF WORSENING RENAL FUNCTION BY VASOPRESSIN RECEPTOR 2 ANTAGONIST (TOLVAPTAN) IN NON-DIALYSIS CHRONIC KIDNEY DISEASE PATIENTS WITH CHRONIC HEART FAILURE**

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**Introduction and Aims:** Tolvaptan is a selective vasopressin receptor 2 antagonist and dose-dependent drug used to treat chronic heart failure (CHF) as diuretics. It is known that tolvaptan increases excretion of excess fluids and improves blood sodium levels in patients with heart failure without affecting renal function compared to conventional diuretics. It is possible that tolvaptan increases renal excretion of sodium especially in non-dialysis chronic kidney disease (NDCKD) patients, and few studies examined the risk of worsening renal function about tolvaptan. The aim of this study is to investigate the risk factors of worsening renal function by tolvaptan in NDCKD patients with CHF.

**Methods:** We administrated tolvaptan (Doses 10.7±3.9mg) for 120 NDCKD patients (male/female: 7/4, 72.8±11.9 years old, estimated glomerular filtration rate (eGFR), 42.3±21.8 ml/min/1.73m^2) with CHF in admission. Those of all patients have already treated conventional diuretics. The patients who changed the dose of conventional diuretics in observation period were excluded. The following data were collected from the electric record at baseline: age, sex, presence of diabetes, blood pressure, urine output, body weight, eGFR, serum sodium concentration, hemoglobin, serum albumin, serum bicarbonate, brain natriuretic peptide (BNP), and cardiac ejection fraction (C29). We defined reduction of eGFR in duration from administration of tolvaptan to discharge as worsening renal function (WRF), and statistical analysis was used by logistic regression models.

**Results:** 3% patients (36.7%) developed the WRF. In univariate analysis, age (Odds ratio 1.43, 95%CI 1.11-1.85, p<0.003), serum albumin (0.87, 0.78-0.93, p=0.02), urine output (0.047, 0.01-0.99, p=0.008), bicarbonate (0.92, 0.80-0.97, p=0.03), and cardiac ejection fraction (0.68, 0.55-0.84, p=0.008) were associated with WRF. In multivariate analysis, age (1.16, 1.06-1.31, P<0.002), serum albumin (0.91, 0.83-0.95, P=0.03), cardiac ejection fraction (0.88, 0.72-0.93, P=0.01) were remained significant after adjusted for age, eGFR, serum albumin, urine output, and bicarbonate. It suggests that diuresis by tolvaptan in condition of low serum albumin and cardiac ejection fraction causes decrease of renal plasma flow especially in NDCKD and lead to WRF.

**Conclusions:** Age, serum albumin, and cardiac ejection fraction were independent risk factors of WRF by tolvaptan in NDCKD patients with CHF.
BARIATRIC SURGERY IN OBESE PATIENTS IS ASSOCIATED WITH REDUCTION OF ALBUMINURIA AND CARDIOVASCULAR RISK FACTORS

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Introduction and Aims: Obesity is a health problem with epidemic proportions and has been shown to be associated with chronic kidney disease and albuminuria. Extreme obesity (body mass index [BMI] > or =40 kg/m2) is associated with cardiovascular disease, type 2 diabetes, dyslipidemia, and hypertension. Bariatric surgery (BS) is an effective means of achieving long-term weight loss. Improvement in albuminuria has also been reported. The objective was to evaluate, at a weight control center in a community hospital setting, the effect of weight loss after BS on blood pressure (BP), renal parameters and cardiovascular risk markers.

Methods: We performed a prospective study in 71 obese adults who had undergone gastric bypass surgery. Clinical and laboratorial data were evaluated at baseline and 1, 6 and 12 months after surgery.

Results: Our cohort of 71 patients had a mean age of 46.1±11.4 years, 84.7% female and 76.3% caucasian, with a mean BMI of 44.5±5.3 (33-73.7) kg/m2. At baseline 55.6% had BP > or =140/90mmHg, and 45.8% had type 2 diabetes. During the 10.4±5.3 months of follow-up (postoperative), a decrease occurred in body weight (14.2±5.6 kg/m2 to 40.6±12 kg/m2; p<0.0001), excess body weight (113.6±19.5 kg to 78.9±13.5 kg; p<0.0001), systolic BP (134±23.9 to 116±11.5 mmHg; p=0.01), diastolic BP (81±13.2 to 67±4.9 mmHg; p<0.04), total cholesterol (182±36.9 to 169±20.4 mg/dl; p=0.04), triglycerides (163±66.6 to 97.7±44.9 mg/dl; p<0.0001), hypotensive medication (1.3±1.4 to 0.4±0.8; p<0.001), oral antidiabetics (0.9±1.2 to 0.3±0.6; p=0.0001) and dyslipidemic medication (0.6±0.7 to 0.5±0.4; p<0.0001). Five from the twelve patients treated with insulin stopped this medication. The majority (53.3%) of the patients with significant preoperative albuminuria lowered their albumin excretion levels (urinary albumin excretion rate [UACr] as the mean of three 24-hour urines) to normal range (UACr<150 mg/24h) after BS, and 65.7% of obesity-related diabetics normalised their levels of HbA1c (p<0.0001) and 75.8% of obesity-related diabetics normalised their levels of HbA1c (p<0.0001).

Conclusions: In this study of obese patients submitted to BS there was a significant reduction in UACr during the follow-up time. There was also an association between higher percentage of weight reduction (> 18%) and higher UACr reduction at 6 months (p=0.007, Exp(B): 3.0, CI.0.41-74), even when adjusted for age, diabetes mellitus and hypertension.
all study subjects, eGFR was positively correlated with ADC (r=-0.55, p<0.05) and negatively correlated with A1MG (r=-0.68, p<0.05). On the other hand, there were no significant correlations between eGFR and levels of NAG, B2MG or urinary protein. ADC was negatively correlated with A1MG (r=-0.34, p<0.05), but not with NAG, B2MG or urinary protein. We could follow up 24 patients for more than 6 months (720 days on average). In the longitudinal analyses of their data, change in eGFR during follow-up period (delta-eGFR, ml/min/1.73 m²) was negatively correlated with urinary protein (r=-0.69) and with A1MG (r=-0.60, p<0.05). However, correlation between delta-eGFR and ADC did not reach statistical significance (r=0.36, p=0.09).

Conclusions: Declined ADC in MRI indicates reduction in GFR. Of urinary markers examined in the present study (NAG, A1MG, B2MG, urinary protein), only A1MG is useful for detection of declining GFR. In prediction of renal prognosis, A1MG and urinary protein levels appear to be better markers than ADC.

**SP147**
A SIMPLE SCORING ALGORITHM USING SERUM FREE LIGHT CHAINS FOR THE RISK ASSESSMENT OF PROGRESSION OF CHRONIC KIDNEY DISEASE
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**Introduction and Aims:** There is a major need for accurate risk stratification for patients with stage 4 CKD. Although 30% of patients progress to end-stage kidney disease (ESKD) as defined by a requirement for renal replacement therapy (RRT), the majority do not. Here we propose an algorithm utilising polyclonal combined serum free light chains (cFLC; KFLC + AFLC), as a marker of kidney function and adaptive immunity, in combination with routinely measured laboratory data to optimise the identification of those at no risk of progression to ESKD within 12 months.

**Methods:** Baseline sera from 561 stage 4 CKD patients (University Hospital Birmingham [UHB] n=201, Chronic Renal Insufficiency Standards Implementation Study [CRISIS] n=205 and Renal Insufficiency in Secondary Care [RIISC] n=155) had FLC measured using the Freelee™ assay (The Binding Site Group Ltd, UK). Results were used in combination with other laboratory assessments to develop the model (initially in UHB and validated in CRISIS and RIISC).

**Results:** The UHB population (median follow up 1483 days [range 22-2906]), cFLC levels were associated with reduced time to ESKD (HR=1.015, 95% CI 1.007-1.012, p<0.001). During this period 60 patients progressed to RRT. Univariate analysis identified 7 risk factors (including cFLC, ACR, phosphate and eGFR) being associated with progression to RRT. An algorithm comprising cFLC>120mg/L, eGFR>20ml/min/1.73m², ACR>30mg/mmol, and phosphate>1.4mmol/L was developed. By 12 months 7/201 patients progressed to RRT, 5/201 (25%) patients were negative for all risk factors and none progressed to RRT. A further 61 patients were positive for 1 risk factor, a single patient from this group progressed at 361 days. Individually, each variable had a poorer discrimination than the collective value. In the validation populations, 51/205 (25%) (CRISIS) and 36/155 (23%) (RIISC) patients had 0 risk factors and 0 patients progressed to ESKD. 68/205 (33%) and 51/155 (33%) patients had 1 risk factor respectively, of which 4 progressed to ESKD. Combining the 3 datasets, the algorithm identified 138/561 (25%) patients with no risk factors, with no patients with stage 4 CKD; although 30% of patients progress to end-stage kidney disease.

**Conclusions:** An algorithm for the risk stratification of stage 4 CKD that includes cFLC identifies patients at no and very low risk of progression to ESKD in the subsequent 12 month period. This approach has major potential benefits, both for patients and the costs of health care in stage 4 CKD.

**SP148**
PLASMA PTH LEVELS MEASURED WITH THE 3RD GENERATION 1-84 PTH ASSAY IN PATIENTS WITH DIFFERENT STAGES OF CHRONIC KIDNEY DISEASE
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**Introduction and Aims:** Previous guidelines derived from studies that used the Allegro intact PTH assay, which measures both the full 1-84 PTH molecule as well as the 7-84 PTH inactive fragment, recommended that patients with different chronic kidney disease (CKD) stages should be managed in order to maintain plasma PTH within a given range, which was fixed between 150 and 300 pg/ml in CKD stage 5 patients. Several methods of intact PTH assay are available and a wide inter-method variability in the PTH results has been shown and opposite therapeutic attitudes may be reached in a single patient depending on the PTH assay used. A new 3rd generation PTH assay, which measures only the full length molecule, is currently available. Aim of the present study was to define PTH ranges using this assay in patients with different stages of CKD.

**Methods:** A series of 141 patients (65 females and 76 males, age 21-89 yr) with CKD stage 3-5 followed in a tertiary care center were enrolled in the study. Patients were classified according to the estimated GFR (eGFR, stage 3: n=46, stage 4: n=42; stage 5: n=53). Plasma PTH was measured using the 3rd generation LIASON® 1-84 PTH assay (DiaSorin; normal range 5-40 pg/ml). Serum bone specific alkaline phosphatase (BASP; normal range 16-22 ng/ml), serum C-terminal telopeptide (S-CTx; normal range 0.7-1.43 ng/ml) and 25OH vitamin D (25OH; normal range 4-64 ng/ml) were also measured. Finally, in a subgroup of patients (n=80) plasma intact PTH was measured using the 2nd generation LIASON® N-tact™PTH (Diaisorin).

**Results:** Plasma 1-84 PTH was increased in the majority (72%) of our patients and there was a significant negative correlation with the eGFR (r=-0.46, P<0.001). Conversely, a significantly positive correlation was found between plasma 1-84 PTH and BASP (r=0.23, P=0.008) and S-CTx (r=0.31, P=0.001), and no correlation with serum 25OH and age. A significantly high positive correlation was found between plasma 3rd generation 1-84 PTH and intact 2nd generation PTH concentrations (r=0.94, P<0.0001). The table summarises our data for the whole group of patients and the patients divided according to the different CKD classes. Results are expressed as means±SD.

**Conclusions:** The plasma PTH levels, measured by the 3rd generation 1-84 PTH assay, nicely segregate patients with different stages of CKD and could provide a reference point for managements of CKD patients across the various stages of CKD.

**SP149**
THIRD GENERATION BIO-INTACT PTH ASSAYS PRODUCE RESULTS WHICH ARE BETTER CORRELATED WITH BIOCHEMICAL AND SKELETAL PARAMETERS IN CKD PATIENTS THAN DO SECOND-GENERATION INTACT PTH ASSAYS – NOW IS IT TIME TO MOVE ON AND CHANGE OVER?
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**Introduction and Aims:** As – and CKD becomes more severe, PTH levels in the blood increase. As well as PTH (1-84), PTH (7-84) – and many other fragments of PTH – accumulate in the bloodstream of patients with severe CKD, particularly those receiving dialysis. Using traditional assays, even ‘intact PTH’ assays, the presence of PTH (7-84) typically leads to an overestimation of concentrations of biologically active full-length PTH, further compounded by the longer half-life of these fragments. True ‘biointact’ PTH assays are now available for use. We wanted to compare analytical data from the second generation (Roche Diagnostics, Basel) intact PTH assays with Roche Elecsys EDTO-plasma biointact PTH (1-84) (Roche Diagnostics, Basel) assays using CKD and dialysis cohorts - splitting blood samples to record PTH concentrations in parallel.

**Methods:** Serum calcium, phosphate, creatinine, bone specific alkaline phosphatase (BAP), Tartrate-resistant acid phosphatase-5b (TRACP-5b) were determined in 79 healthy ambulant CKD (stage 2-4) patients. Bone mineral density (BMD) was determined by DXA scan at the fore-arm (FARM), lumbar spine (LS), femoral neck (FN) and total hip (TH). PTH was analysed by both the second and third generation PTH assays. The relationship between the 2 PTH assays with the biochemical parameters and BMD was compared.

**Results:** 79 healthy ambulant CKD (stage 2-4) patients - 41M, 38F, mean±SD age of 53±15 years. Inter and intra-assay CVs were - 2% for both PTH assays at mean concentrations of 41, 105, 131 pg/ml. The results from the two assays were closely correlated (r=0.958, p<0.001). The intact (second generation) PTH concentration was significantly higher 79[55] pg/ml compared to biointact (third generation) PTH 68 [49] pg/ml (p<0.001). Bland-Altman plot revealed a significant average bias of -18%. Only the biointact PTH assay showed any significant correlation with serum calcium concentrations (r = 0.26, p<0.05) and phosphate (r=0.25, p<0.05). BMD was better correlated to biointact PTH than with intact PTH, especially at the FARM and LS (Z score FARM r = -0.33, p<0.009 cf r = 0.26, p<0.004; 15 : r=0.34, p=0.006 cf r = 0.29, p=0.02).

**Conclusions:** PTH and calcium concentrations are normally very tightly coupled. The inability of intact PTH assays to show a correlation with simultaneous plasma calcium, or phosphate, concentrations suggests that what is most biologically relevant. The improved correlations between plasma PTH (but only when measured by the biointact assay) and bone mineral density also point to more relevant functional
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Abstracts

1H-NMR PROFILING OF URINARY METABOLITES FOR A BETTER CHARACTERIZATION OF KIDNEY INJURIES: A PILOT STUDY
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Introduction and Aims: Proton-Nuclear Magnetic Resonance (1H-NMR) based characterization of small molecules, including metabolites, in body fluids is a promising method to detect biomarkers and to drive hypothesis.

Methods: We undertook a pilot study to generate the urinary metabolic profiles of patients with various kidney diseases. In this monocentric prospective study, 24 consecutive patients who underwent a diagnosis kidney biopsy were recruited and provided an urinary sample for biochemical and NMR analysis. The NMR experiments were run at 500.13 MHz for 1H on a Bruker AVANCE 500 spectrometer. Each NMR spectrum was reduced to 170 variables (buckets), obtained by integrating spectral regions of equal width (0.04 ppm). We applied a principal component analysis (PCA) to identify groups of patients based on their urinary profiles.

Results: The PC discriminated two groups of patients, and explained 77% of the variability. All patients in one group (A) had a diagnosis of glomerular nephropathy, whereas all but one the other patients (group B) had a tubular and/or interstitial injury. Subsequently, the patients were assigned within group A or group B, and a supervised method (Partial Least Squares Discriminant Analysis) was used to test whether some variables (buckets) would separate the two groups. The model obtained has highlighted discriminating variables; most of them localized between the 8 and 8.3 ppm part of the spectrum. Two buckets (on 170) with the minimal variance could effectively separate groups A and B. Small molecules that provide a signal within this part of the spectrum are aromatic molecules, including nucleic acids (adenine, ATP, ...

Conclusions: Our results suggest that 1H-NMR-based detection of urinary nuclear acids could discriminate patients with glomerular injury vs. tubular injury. Since nuclear acids signal promote tubular inflammation through purinergic receptors, our findings provide a new hypothesis regarding the negative impact of proteinuria on tubulointerstitial inflammation and fibrosis.

ASYMMETRIC DIMETHYLARGININE CONTRIBUTES TO THE KIDNEY FUNCTION DECREASE VIA AGGRAVATION OF VASCULAR REMODELING IN OBESE PATIENTS WITH CKD I-IIla
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Introduction and Aims: Asymmetric dimethylarginine (ADMA) is well known endogenous inhibitor of all types of NO-synthases. Endothelial dysfunction caused by elevated plasma ADMA leads to vascular alteration. Thickening of intima-media complex in early markers of atherosclerotic remodeling is one of the main mechanisms in damage of kidney in obesity which is a trigger of metabolic, hemodynamic and inflammatory disturbances. Aim of our study was to define role of ADMA and vascular remodeling in the progression of early stage CKD in obese patients.

Methods: 86 obese patients (64M, 22F) were included in the study (age 44±11 yrs, BMI 33.5±6.3 kg/m²). Exclusion criteria were CKD IIIb-V, albuminuria >2 g/day, hematuria, glomerulonephritis, severe hypertension, coronary heart disease, brain insult, autoimmune diseases et al. GFR was estimated by MDRD equation. All patients were tested on common biochemical features of blood and urine including hematuria, C-peptide, ADMA (by ELISA), urinary albumin excretion (UAE), Intima-media thickness (IMT) of common carotid artery was measured by duplex ultrasonography.

Results: CKD I-IIla was at 27 (31%) patients. CKD individuals had higher BMI and waist circumference as well as increased level of insulin, C-peptide, HOMA-index which were linked to UAE rate. Patients with CKD I-IIla had elevated plasma ADMA (0.770±0.19 umol/l vs. 0.584±0.10, p=0.048), vs. CKD II 0.61±0.13, p=0.071). We found significant correlations between ADMA and IMT (r=0.43, ADMA and high density lipoproteins (HDL) level (r=0.52). IMT correlated with eGFR (r=0.38). Independently from plasma ADMA, serum uric acid (SUa) and blood pressure level were linked to IMT as well (r=0.41 and r=0.45, respectively). Using of multiple linear regression analysis we found prognostic factors of eGFR decline in obese patients (p<0.003, R²=0.64, standard estimation error 15): insulin (13.3±6.5 uM/l; b = 1.52±0.040), HOMA-index (3.3±1.7; b = -1.31±0.09), SUa (421±100 umol/l; b = 0.46; p=0.038).

Conclusions: In obese patients progression of early stage CKD is tightly associated with endothelial dysfunction and vascular remodeling. We detected that ADMA can contribute kidney function decrease mainly via aggravation of dyslipidemia and vascular alteration. Additional factors influencing on thickening of intima-media complex were elevation of serum uric acid and blood pressure.

HbA1c IS AN INDEPENDENT RISK FACTOR FOR MORTALITY BUT NOT FOR END STAGE RENAL DISEASE IN NON DIABETIC CKD POPULATION
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Introduction and Aims: Glycated hemoglobin (HbA1c) is used as a diagnostic test for diabetes (DM) with an usual threshold of 6.5%. The association between HbA1c and progression for end-stage renal disease (ESRD) and mortality has been demonstrated in the diabetic population. The aim of this study was to examine the association between HbA1c and these endpoints in a non diabetic chronic kidney disease (CKD) population.

Methods: In the NephroTest cohort study, we measured glomerular filtration rate (mGFR) by Cr-EDTA clearance and Hba1c in 1162 adult patients with non-diagnosis CKD stages 1 to 5 and no DM (HbA1c value> 6.5%, fasting glycemia<7 mmol/L, absence of known DM or hypoglycemic treatment). Deaths and ESRD (initiation of renal replacement therapy) were retrieved using national registries. Cox models were used to estimate hazard ratio (HR) of ESRD and mortality according to Hba1c [as a continuous and a categorical variable using tertile cut-off (<5.2, 5.2-5.6, ≥5.7), with adjustment for mGFR, age, gender, race, BMI, elevated blood pressure, history of cardiovascular disease, smoking, albuminuria, ARBs and ACE inhibitors and center.

Results: Mean age was 56.6±16.0 years with a mean BMI of 25.4±4.6; 66% were men, 12.8% black. The mean mGFR and HbA1c at inclusion were respectively 42.1±19.8 ml/min/1.73 m² and 5.4±0.5%. HbA1c values were significantly associated with age, BMI, systolic blood pressure, mGFR, albuminemia, fasting blood glucose, insulineemia and orosomucoid. The risk of ESRD was significantly decreased in patients with intermediate value of HbA1c even after adjusting for initial mGFR (middle tertile HR 0.95 (0.90-0.99); compared to the lowest tertile). After adjustment for all other risk factors, HbA1c level was no more associated with a better renal survival in this group [HR=0.670 (0.43,1.04)]. Morality HR was associated with higher HbA1c levels yet not a categorical variables: for each increase of 1% in HbA1c HR=1.95 (1.31,2.91). After adjustment for similar risk factors, the HR associated with HbA1c remained significant (HR=1.69 (1.10-2.59)). Consistent results were found when analysis was restricted to mortality before ESRD.
Conclusions: In a CKD cohort, HbA1c within normal range in non diabetic patients is associated with ESRD occurrence and mortality. The later persists even after adjustment for known risk factors. Since HbA1c is correlated with insulinemia and oxsomucoid, various hypothesis including metabolic or inflammatory pathway must be explore to better understand these results.

Introduction and Aims: Increased homocysteine (hCys) level is considered as an independent risk factor for cardiovascular complications in end stage renal disease (ESRD) patients. The aim of this study was to determine the effects of Zinc supplementation on serum hCys level in ESRD patients.

Methods: One hundred ESRD patients with Zinc deficiency were enrolled in this prospective, randomized, double blind study. They were randomly subdivided into two groups and supplemented with 50 mg/day Zinc (Zinc treated group) or placebo (placebo treated group) for 6 weeks. Fasting plasma hCys and Zinc levels were measured before treatment, and 43 days after the start of the study. An enzyme immunoassay (EIA) was used to measure total bCys. Serum plasma zinc level was measured with atomic absorption method. The data were analyzed using the SPSS 15.0 and p < 0.05 was considered significant.

Results: Serum zinc levels increased significantly in Zinc treated group (56.9±13.9 μg/dl; p < 0.0001). There was no significant change in Zinc levels in the placebo-treated group. Serum hCys levels were also significantly reduced in the Zinc treated group (17.1±4.4 μmol/L versus 13.20 ± 3.7 μmol/L; p<0.0001), while no significant change was observed in the placebo group. Mean percentage reduction of hCys was 21.5±18.3 in the Zinc treated group compared to 1.2±16.1 in placebo group (p<0.0001). Mean percentage reduction of hCys level positively related with baseline hCys (r=0.251; P<0.001), plasma Zinc level at 43 days (r=0.446; P<0.0001) and mean percentage increase of Zinc (r=0.327; P>0.001).

Conclusions: Zinc supplementation leads to a reduction in serum hCys level in ESRD patients with Zinc deficiency.

Introduction and Aims: Renal dysfunction is one of the most important comorbidities associated with congestive heart failure (CHF) complicating acute myocardial infarction (AMI). However, the clinical course and treatment of patients with CHF are not well established, especially in patients with concomitant renal dysfunction. This study aimed to examine the influence of renal dysfunction on clinical outcomes in patients with CHF complicating AMI.

Methods: We performed a retrospective analysis of the prospective Korean Acute Myocardial Infarction Registry data to assess the treatments and clinical outcomes of patients with CHF (Killip classes II or III) complicated by AMI in the presence or absence of renal dysfunction. The main outcome measures were the major adverse cardiac events (MACEs) and mortality rates during the 1-year follow-up period.

Results: Of 13,498 patients with AMI, 2769 (20.5%) had CHF on admission. Compared to CHF patients with preserved renal function, patients with renal dysfunction were older; more often female; and had a higher prevalence of hypertension, diabetes, dyslipidemia, and multivessel disease. Patients with renal dysfunction were less likely to receive aspirin, beta-blockers, statins, and angiotensin-converting enzyme (ACE) inhibitors, but were more likely to receive diuretics, calcium channel blockers (CCBs), and angiotensin II receptor blockers (ARBs) during hospitalization or at discharge. Furthermore, renal dysfunction was associated with increased in-hospital mortality and MACEs both at 1 month and at 1 year after discharge. In patients with renal dysfunction, in-hospital use of aspirin, beta-blockers, ACE inhibitors, or ARBs and statins, which had been prescribed at discharge, significantly reduced the 1-year mortality rates with 1-year mortality in both groups.

Conclusions: Patients with CHF complicating AMI, which is accompanied with renal dysfunction, are at higher risk for adverse cardiovascular outcomes than patients without renal dysfunction. However, they receive fewer medications proven to reduce mortality rates.

Introduction and Aims: The increasing prevalence of obesity, especially in the Western world is associated with the risk to develop renal disease or accelerate the progression of renal disease. Adequate estimation of renal function in obese is thus essential. Recently, CKD-EPI formula was recommended as the most reliable method to estimate GFR, but this formula was not validated in patients with extreme variations of weight, and especially in obese patients.In this study, we measured GFR in obese patients and compared the performance of creatinine-derived equations with measured GFR indexed or not to body surface area (BSA) and using either real or ideal body weight (BW).

Methods: A total of 218 obese patients were included (126 men [57.8 %] aged 17 to 87 years). They all had nephropathy of various origins and were selected according to the criteria body mass index (BMI) ≥ 30 kg/m². The mean BMI was 34.8 ±4.6 kg/m² (30 to 67). Twenty-three patients have a BMI > 40. We determined GFR with creatinine-derived equations, MDRD and CKD-EPI formulas (eGFRMDRD and eGFRCKD-EPI) (enzymatic assay of serum creatinine standardized to IDMS). These formulas were compared to the gold standard method insulin clearance not indexed to BSA (mGFR mL/min) or indexed with BSA either with actual body weight (BW) (mGFRreal mL/min/1.73m²) or ideal BW (mGFRideal mL/min/1.73m²). The ideal weight was determined by Lorentz formula. The BSA was determined by Dubois and Dubois formula.

Results: mGFRreal (51.8 ± 24.2) was significantly lower (p < 0.01) than mGFRideal (61.9 ± 28.3) or mGFR not indexed to BSA (60.2±28.0). eGFRMDRD and eGFRCKD-EPI were respectively 57.3±27 and 60.6±28.0. They were not statistically different. There was no significant difference between creatinine-derived formulas and mGFR not indexed to BSA or mGFRideal. But mgFRideal was significantly lower than the formulas (p < 0.01). Bias are accurate and shown in the following table.

Conclusions: As nephron mass depends on lean mass rather than fat mass, GFR in obese patients should be indexed to BSA using ideal BW. Since there was no difference between CKD-EPI formula and mGFRideal measured by inulin clearance and the performance of this formula was better than MDRD in terms of accuracy and bias, we recommend the use of CKD-EPI in obese patients.

Introduction and Aims: Malnutrition is common in patients with end-stage kidney disease on hemodialysis, and is associated with poor outcome. A number of studies have documented malnutrition as a powerful predictor of morbidity, mortality and an
increased hospitalization rate in ESRD. It is recognized that no single alternative objective test is able to determine the overall nutritional status in ESKD patients. Several methods of nutritional risk evaluation are known: the Subjective Global Assessment (SGA), the Malnutrition-Inflammation-Score (MIS), the Objective Score of Nutrition on Dialysis (OSND). We have developed a new score, Integrative Clinical Nutrition Dialysis Score (ICNDS). The score is based solely on biochemical parameters routinely taken monthly from HD patients, as well as their weight change, in order to assess nutrition status and detect deterioration as early as possible, thus preventing further complications.

Methods: In an attempt to develop a simple nutritional status score of HD patients, we used laboratory tests parameters, routinely taken monthly starting dialysis session: Albumin, Creatinine, Urea, Cholesterol, CRP, Kt/V and the patient’s Weight change. Each of the above parameters was given a scoring value of 1-5. A score of five for each parameter value close to the NKF-K/DOQI Nutrition Guideline Recommendations, and a lower score for sub-optimal values. Scoring results for all parameters were summed each month and a final result, a number between 0-100, was given for each patient. A higher score indicates a tendency towards a good nutritional status, a lower score represents malnutrition.

Results: In 63 patients, score results were significantly correlated with nutrition evaluation by the SGA within the same month (r=0.82, P<0.01). In 179 patients, followed for 31 months, baseline score emerged as a significant inverse predictor of mortality and hospitalization frequency: For every unit increase in baseline score, death odds as well as hospitalization frequency were significantly decreased (mortality: HR=0.929, 95% CI 0.88-0.974, p=0.002; hospitalization frequency: HR=0.977, 95% CI 0.972-0.981, p<0.0001). A unit increase of slope at beginning of study significantly reduced mortality and hospitalization risk (mortality: HR=0.485, 95% CI 0.726-0.881, p<0.0001). A threshold score level of 75 was found to be a significant outcome: Score greater or equal to 75 significantly reduced mortality. Worsening nutrition status over time indicated by both score and slope significantly increased death hazard.

Conclusions: We have developed a convenient tool to address the need of a monthly routine follow up of nutrition status and identification of nutritional deterioration at its beginning. The Model provides for a high resolution of various nutrition status and their prognosis.

### SP158 ESTIMATION OF THE PREVALENCE OF CKD IN HEALTHY SUBJECTS BY FOUR DIFFERENT EQUATIONS

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Introduction and Aims: To calculate the prevalence of CKD in a sample of healthy Spanish individuals, we compared the 24h creatinine clearance rate corrected by body surface area (CCr), Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, Cockroft-Gault formula corrected by body surface area (CG), the abbreviated Modification of Diet in Renal Disease (MDRD) equation and the Mayo Quantic (MQ) formula to determine glomerular filtration rate (GFR) in patients from a nephrology consultation.

Methods: 1067 healthy patients were enrolled in the present study. Patients were casually instructed about the 24h urine output collection by the same nurse. GFR was estimated using five methods: CCr, CKD-EPI, CG, MDRD and MQ equations. The statistical analysis was performed using SPSS Statistics 19.

Results: Figure 1 summarizes the % of individuals with GFR <60 ml/min according to the different equations: Figure 2 represents the correlation between Scr, CCr and the eGFR equations. We found a positive correlation (p=0.03) between urinary Na, Mg, P and Ca and GFR measured by all equations, and a negative correlation (p=0.02) between all equations and SCr, serum glucose and age.

Conclusions: The prevalence of CKD in the Spanish population is 6.8%, according to the results of the EPIRCE study. In our sample the percentage of patients classified as CKD varies widely depending on the method of evaluation used. CCr provides the highest average eGFR value, probably due to mistakes in the 24h urine recollection, followed by MQ equation, CG-BSA, CKD-EPI and MDRD. These differences are statistically significant (p<0.001). GFR equations are a useful tool in clinical practice, although they should be carefully considered, especially in patients with extreme weights or age. MQ equation seems the most precise equation to assess GFR in healthy patients, although neither method has an accuracy of 100%.

### SP159 NOVEL METABOLITES ASSOCIATE WITH IMPAIRED KIDNEY FUNCTION AND KIDNEY FUNCTION DECLINE IN THE GENERAL POPULATION

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Introduction and Aims: Small molecules are extensively metabolized and cleared by the kidney and may also play a role in the pathophysiology of chronic kidney disease (CKD).

Methods: Here we applied an untargeted metabolomics approach (GC/MS and LC/MS/MS assays by Metabolon) to measure the serum concentrations of a broad spectrum of more than 400 known and unknown molecules in the general population-based KORA study (maximal n=1735). Metabolites were then related in linear or logistic regression analyses to both eGFR estimated from serum creatinine or cystatin C cross-sectionally, as well as to annual eGFR change based on serum creatinine change over a mean of 7 years, all adjusted for known kidney disease risk factors.

Results: Significant cross-sectional associations with both creatinine- and cystatin C-based eGFR were identified for 114 metabolites accounting for multiple testing. Published cross-sectional associations of serum acylcarnitines with lower eGFR were confirmed. Most remarkably, higher serum concentrations of c-glycosyltryptophan were associated cross-sectionally with lower eGFR (P< 8.9 x 10^-89 for creatinine-based eGFR; P< 1.0 x 10^-39 for cystatin C-based eGFR) and presence of CKD (eGFR < 60 ml/min/1.73 m^2; P= 1.1 x 10^-25). It was also associated with longitudinal kidney function decline even after adjustment for baseline kidney disease risk factors and creatinine-based eGFR (P< 8.7 x 10^-10). The pair-wise Pearson correlation between serum c-glycosyltryptophan and creatinine-based and cystatin C-based eGFR was -0.61 and -0.71, respectively. Serum c-glycosyltryptophan has previously been described as associated with insulin clearance in smaller studies of humans and rats.

Conclusions: In the general population, serum c-glycosyltryptophan was associated with kidney function impairment measured by cross-sectional eGFR, as well as...
longitudinal eGFR decline. Further studies are needed to validate the observed associations externally and clarify the identity of all discovered molecules.

**SP160** NEUTROPHILS ACTIVATION CORRELATES WITH INSULIN RESISTANCE IN END-STAGE RENAL DISEASE (ESRD) PATIENTS

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**Introduction and Aims:** Insulin resistance is often associated with chronic kidney disease, especially in ESRD patients requiring maintenance dialysis. During extracorporeal circulation at the time of hemodialysis procedure, activation of various cells takes place, including chronic activation of neutrophils. In consequence, concentration of plasma leucocyte elastase/alpha 1 protease inhibitor complex (HLE/alpha1PI) increases in plasma. The endothelial dysfunction related to repeated hemodialysis procedures may additionally exacerbate insulin resistance.

**Methods:** Fasting pre-dialysis blood samples were collected from 68 patients with ESRD, 29 women and 39 men, aged 60 +/- 12 years, treated with maintenance hemodialysis for median period of 60 (IQR: 36-100) months using reprocessed polysulphone dialyzers and low molecular weight heparin as anticoagulant. Patients with diabetes and acute inflammation were excluded. Control samples were collected from 35 healthy sex and age matched subjects. The concentrations of HLE/alpha1PI and insulin was measured by ELISA, CRP by nephelometry and glucose by routine method. Homeostasis model assessment index of insulin resistance (HOMA-IR) was calculated as [fasting glucose concentration (mmol/L) x fasting insulin concentration (mU/L)]/22.5.

**Results:** The concentration of HLE/alpha1PI in studied group was 50.81 +/-16.50 ng/mL and was significantly higher than in controls (37.20 +/- 1.36 ng/mL; p<0.001). HLE/alpha1PI significantly correlated with insulin level (R=0.32; p=0.02) and HOMA-IR (R=0.35; p=0.009). In multiple models, these correlations were independent of CRP concentration as a marker of inflammation.

**Conclusions:** Chronic neutrophil activation in ESRD is connected with insulin resistance independently on chronic inflammation. The consequence of insulin resistance expressed as increased insulin level and HOMA-IR are glucose metabolism disturbances and the increase of cardiovascular morbidity.

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**SP161** RENAL FUNCTION, SUBCLINICAL ATHEROSCLEROSIS AND C1 METABOLISM IN APPARENTLY HEALTHY SUBJECTS

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**Introduction and Aims:** Although homocysteine has been proposed as a cardiovascular risk factor, no interventional trial on homocysteine lowering in CKD patients demonstrated clinical benefit. Recent evidence suggested that the homocysteine metabolite S-Adenosylhomocysteine (SAH) is a better marker for cardiovascular disease. Additionally, an association between elevated SAH and early CKD has been shown in preliminary studies. Of note, these studies estimated PRECLINICAL DATA

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**SP162** BIOMARKERS OF TISSUE REMODELING, TISSUE INJURY RESPONSE AND INFLAMMATION IN CHRONIC KIDNEY DISEASE (CKD): CLINICAL AND PRECLINICAL DATA

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**Introduction and Aims:** Biomarkers apart from proteinuria, serum creatinine or cystatin C, which correlate with CKD grade and which have the potential to indicate earlier and predictively progression of CKD are demanded for selecting therapy regimes that fit best to attenuate loss of kidney function in CKD patients. Biomarkers reflecting in particular renal tissue remodeling and renal tissue injury response have been analyzed to identify biomarkers of prognostic value.

**Methods:** In a translational approach, circulating tissue remodeling biomarkers (e.g. osteopontin, tenasin C (C-domain and B-domain), MMP2, MMP9), tissue injury biomarkers (NGAL, cystatin C, H-FABP) and inflammatory markers (e.g. MCP1, calprotectin, MPO, CRP) were determined in comprehensively characterized CKD patients (n=125, NT-CVD Study) and compared to matching controls (n=84). Respective plasma proteins and mRNA were measured in renal cortex obtained from chronically pressure and volume overloaded rodents with gradually increasing loss of renal function (DOCA hyperaldosteronism: SHR-SP).

**Results:** Biomarkers of tissue remodeling and tissue injury correlated highly significant with loss of renal function as defined by eGFR. Plasma cystatin C levels differentiated the four groups: controls (0.73 +/- 0.23 μg/mL, n=84), CKD1 (1.1 +/- 0.34 μg/mL, n=55), CKD4 (2.4 +/- 0.79 μg/mL, n=17), CKD5 (3.71 +/- 0.99 μg/mL, n=52) by p<0.001 for each group comparison. Similar differentiations of CKD grade groups were measured for other tissue injury markers like NGAL (controls: 61 +/- 21 ng/mL, CKD3: 93 +/- 49 ng/mL, CKD4: 267 +/- 118 ng/mL, CKD5: 587 +/- 351 ng/mL) or H-FABP. Likewise, tissue remodeling markers osteopontin (controls: 7.4 +/- 25 ng/mL, CKD3: 9 +/- 32 ng/mL, CKD4: 151.1 +/- 93.1 ng/mL, CKD5: 303.7 +/- 124.8 ng/mL), tenasin C or TIMP1 showed a similar grade of significance in correlating with severity of CKD. In sharp contrast, serum markers indicating inflammatory processes like myeloperoxidase (MPO), C-reactive protein (CRP) or MCP1 do not reach levels of significance to discriminate the CKD groups (p=0.05). A similar biomarker pattern was seen in plasma and mRNA expression in renal cortex obtained from rodent models of chronic renal impairment (DOCA hyperaldosteronism; SHR-SP).

**Conclusions:** Tissue remodeling biomarkers are being highly elevated in CKD patients and these markers differentiate severity of CKD significantly even at small group-sizes (n=20). In sharp contrast, inflammatory markers lack this relationship in clinical and preclinical samples. Further investigations are ongoing by monitoring the longitudinal course of these tissue remodeling markers in CKD patients (NT-CVD study) to evaluate the predictivity of these markers for disease progression.

**SP163** LECITHIN:CHOLESTEROL ACYRTANSFERASE (LCAT) ACTIVITY IN CHRONIC KIDNEY DISEASE

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**Introduction and Aims:** The LCAT activities have been shown to decrease in ESRD, the corresponding plasma LCAT activities at the different CKD stages, however, are not known. The aim of this study was to determine whether LCAT activities also decrease in mild to moderate renal dysfunction groups.

**Methods:** The study included 186 patients whose plasma LCAT activities were measured by enzymatic method from 2011 to 2012 at a single center. Other parameters relate to lipid profile, including apolipoprotein A-I, apolipoprotein B, and lipoprotein (a) were also evaluated in an observational cross-sectional study. We calculated glomerular filtration rate (GFR) by CKD-EPI equation.

**Results:** The mean of plasma LCAT activities among all individuals was 65.34 ±1.64 (U/mL/hr/7°C). The LCAT activities at each CKD stage 1-5 were 77.49 ± 3.22, 77.34 ± 4.18, 65.59 ± 3.52, 60.05 ± 3.89, and 55.44 ± 2.45, respectively (U/mL/hr/7°C). The present data showed that more advanced CKD stages tend to have lower LCAT activities, correlated with lower HDL cholesterol level, although it did not have statistical significance. In more advanced CKD stages, plasma apoA-I level significantly decreased, while apoB, and Lp(a) showed no differences. Multivariate regression analysis demonstrated that plasma LCAT activities were associated positively with estimated GFR (β=0.233, p=0.012), and negatively with age (β=-0.282, p=0.002), as well as with the interaction between LCAT activities and the amount of microalbuminuria (β=0.289, p=0.001), independent of diabetes, hypertension and BMI.

**Conclusions:** The plasma LCAT activities decreased at more advanced CKD stages, even after adjustment for other confounder factors. The present results support that plasma LCAT activity is as potential therapeutic target for dyslipidemia in CKD.
SURVIVAL ON LOW-PROTEIN DIETS: RESULTS OF A MULTIPLE CHOICE APPROACH

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Introduction and Aims: Concerns on the long-term safety of low-protein diets limit their diffusion in Nephrology. The aim of this discussion on the first "moment" to start attention switched from slowing of the kidney function decline to the effects of delaying dialysis on survival. The aim of the study was to analyse survival in a cohort of patients treated by low-protein diets, followed in the same setting in December 2007-September 2012, with regard to baseline clinical conditions and low-protein diet chosen.

Methods: Two main diets were offered, both at 0.6 g/Kg/day of proteins: a simplified low-protein supplemented diet (LPD-KA supplementation: Ketosteril 1/10 Kg) and a low-protein diet employing "arotiche" commercial food (LPD-AFC). Survival analysis was performed according to Kaplan Meier; multivariate analysis employed Cox model. The analysis took into consideration the period on the diet (up to dialysis start), or alternatively 1 year after the start of dialysis or the discontinuation of follow-up.

Results: 285 patients started a LPD (167 LPD-KA and 118 LPD-AFC); the two groups were non homogeneous for age (median age LPD-KA: 68, LPD-AFC: 74 years (p<0.0001) and GFR at start (LPD-KA: 18.8; LPD-AFC: 22.9 mL/min;p=0.0008); prevalence of comorbidity was high in both (68%, 94%) in line with the European population starting dialysis. No significant difference in patient survival was observed according to the diet (607 patient years; 254 on LPD-KA and 254 on LPD-AFC); patient survival was significantly influenced by age and comorbidity, not by gender or baseline GFR. Survival equivalence was confirmed prolonging follow-up up to one year after dialysis start or discontinuation. As for "renal survival" a significant advantage of LPD-AFC was found in univariate analysis; the effect is lost if the combined outcome of death-start of dialysis is analysed, underlining the differences between the two populations and suggesting a substantial equivalence between the two diets. Mortality rates were 4 per 100 patient years on LPD-KA and 7 per 100 patient years on LPD-AFC, without differences after adjustment for age. The study was finally analyzed with mortality on dialysis, as reported on 3 Registries (Italy, France, USRDS), both comparing the age-adjusted rates and finding no significant difference.

Conclusions: Our data support the safety of LPDs, suggesting that the patients do not have a survival disadvantage as compared to dialysis and may on the contrary have an advantage. The substantial equivalence between treatments supports the policy of allowing patients choosing the preferred diet option.

ENDOTHELIAL DYSFUNCTION IN CARDIORENOAL SYNDROME

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Introduction and Aims: In cardiorenal syndrome endothelial dysfunction (ED) promotes the pathological process and influences its course. This study investigates the features of the development of ED in cardiorenal syndrome.

Methods: We observed 48 patients (27 female and 21 male) aged 42-68 years (average age 54 ± 7.3 years). The cause of chronic kidney disease (CKD) in 18 cases was diabetic nephropathy, in 12 - chronic glomerulonephritis, in 8 - ischemic renal disease, in 7 - cholesterol nephropathy, in 3 - lupus nephritis, and in 2 - polycystic kidney disease. In 14 cases was determined the 2nd stage of CKD, in 16 - 3rd and in 18 - the 4th stage of CKD. All patients had 1-3 stages of heart failure (according to the NYHA). Functional state of endothelium was determined by the method of D.Celermajer (1992) by measuring the diameter of the brachial artery diameter. In healthy people, the application of nitroglycerin and reactive hyperemia. Discovered disorders were more pronounced in patients with cardiorenal syndrome compared to those without it. With increasing stage of CKD, increases the degree of endothelial dysfunction, which can be explained by the increase of arterial hypertension, dyslipidemia, conductive to the development of atherosclerosis.

Results: Along with the clinical picture of renal and heart failure, hypertension, we observed hypoalbuminemia, hyperuricemia, dyslipidemia. The diameter of the brachial artery in patients with CKD was 4.41 ± 0.76 mm, which did not differ much from that of the control group (4.3 ± 0.78). In healthy people, after the application of nitroglycerin artery diameter increased by 10.23%, and the measurements were not significantly different from those obtained from patients (an increase by 10.21%). Along with this, endothelium dependent vasodilation in healthy people increased by 13.4 ± 0.99%, while the increase in examined patients was only 6.7 ± 0.6%. Discovered dysfunctions were more pronounced in patients with cardiorenal syndrome compared to those without it. With the increase of CKD stage, we noted an increase in the degree of endothelial dysfunction, which can be explained by the increase of arterial hypertension, dyslipidemia, contributing to the development of atherosclerosis and impaired calcium-phosphorus metabolism.

Conclusions: In CKD the occurrence of complications in the cardiovascular system, the primary pathogenetic role belongs to the endothelial dysfunction that may occur due to metabolic disorders. On the other hand, the decrease in the level of relaxing, and the increase in the concentration of pressor agents in the body and decrease in sensitivity to vasodilator stimuli also contribute to endothelial dysfunction. Endothelial dysfunction can be considered the main pathogenetic mechanism for the development of cardiorenal syndrome.

CIRCULATING ANGIOTENSIN-CONVERTING ENZYME 2 IN PATIENTS WITHOUT HISTORY OF CARDIOVASCULAR DISEASE

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Introduction and Aims: Circulating ACE2 activity is increased in patients with cardiovascular (CV) disease and in experimental models of diabetes mellitus (DM). However, it has not been previously studied in patients with Chronic Kidney Disease (CKD) without history of CV disease.

Methods: A total population of 834 patients without history of CV disease from the NEFRONA study was analyzed. Patients were distributed into two groups: non-dialysis CKD stage 3-5 patients (CKD3-5,n=288) and patients on dialysis (CKD5D,n=546) (haemodialysis or peritoneal dialysis). Variables analyzed were: gender, age, DM, dyslipidemia, hypertension, glycemic, renal, nutritional and lipidaemia profiles, phosphorous-calcium metabolism and treatment with ACE inhibitors or angiotensin II receptor blockers (ARBs). Circulating ACE2 activity was measured using a modified fluorometric assay for plasma samples.

Results: On patients dialysis had higher levels of ACE2 activity compared to CKD3-5 patients (38.46±1.32RFU/l/hour vs 28.22±1.13,p<0.05). Similar differences were observed when patients treated with ACE inhibitors were removed from the analysis. Assessing only CKD3-5, an increased ACE2 activity was observed in men compared to women (31.88±1.58 vs 22.8±1.41,p<0.05), DM patients (33.49±2.11 vs 26.32±1.25, p<0.05) and with dyslipidemia patients (29.8±1.32 vs 26.31±2.19,p<0.05). In concordance, limiting the analyses to CKD5D, ACE2 activity was increased in men (45.5±2.6 vs 27.7±1.37,p<0.05) and in those with dyslipidemia (42.58±2.84 vs 33.93±1.30, p<0.05). A direct correlation between age and ACE2 activity (p<0.05) was found in both CKD3-5 and CKD5D patients, but only in CKD3-5 patients HBAlc directly correlated with ACE2 activity (p<0.05). By multiple regression analysis, male gender, advanced age and DM were independent predictors of circulating ACE2 activity in CKD3-5 patients. Predictors in CKD5D patients were male gender, age and ARBs treatment, but not DM (Table). When all patients were included in the model, male gender, older age, ARBs treatment and CKD5D were predictors of elevated circulating ACE2.

Conclusions: In CKD patients without history of CV disease, old age and male gender are significant predictors for elevated circulating ACE2 activity. Independent additional predictors are DM in CKD stages 3-5 and treatment with ARBs in CKD5D. Increased circulating ACE2 activity in CKD might indicate the CKD patients at risk for developing CV disease.

PSYCHOLOGICAL EVALUATION OF CKD PATIENTS. ASSOCIATION OF DEPRESSION AND STRESS WITH RENAL FUNCTION

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Introduction and Aims: Depression and psychological stress are both associated with adverse health outcomes, like hypertension and cardiovascular disease. Prevalence of depression in CKD reaches 20% of patients, even before initiation of dialysis. Increased
psychosocial stressors have been linked with an augmented rate of renal function decline. However, the direct impact of psychological stress and depression on renal function has not yet been investigated.

Methods: 41 patients (23 M and 18 F) with CKD stage 2-4 (mean age 73±6 years) were enrolled in the study. Participants were receiving optimal therapy and had controlled levels of blood pressure and plasma glucose concentration. Hospital Anxiety Depression Scale (HADS) was used to evaluate stress and depression. Estimated GFR was calculated using MDRD formula, at the time of the psychological evaluation (eGFR2) and 12 months before (eGFR1).

Results: Psychological evaluation was normal in 16 (40%) individuals. Psychological disorder was present in 25 (60%) participants. 15 suffered from both depression and stress, while 5 experienced either stress or depression. A major chronic stressor, such as loss of a child, was present in 20 participants. Patients with normal HADS measurement for stress improved their renal function, compared to the stressed ones (eGFR1=42.8±18 vs eGFR2=48.3±17, p=0.006). Absence of depression, using HADS scale, led to similar results (eGFR1=46.6±16 vs eGFR2=45.8±17, p=0.1). Patients suffering from both stress and depression had a significant eGFR decline (eGFR1=43±18 vs eGFR2=39.8±15, p<0.1). HADS measurements for stress and depression were positively correlated with the rate of CKD progression (HADS stress: r=0.5, p=0.001, depression: r=0.4, p=0.01).

Conclusions: Psychological disorders seem to be a common, though under diagnosed problem in CKD patients. In the present study, normal values for stress and depression in HADS scale were associated with eGFR increase, while affected individuals presented an augmented rate of renal function decline. These results suggest a possible relationship between psychological disorders and CKD progression. Further investigation is warranted into factors that mediate this relationship and its potential clinical consequences.

WHAT ARE THE MAJOR FACTORS TO DETERMINE SERUM CREATININE IN HEALTHY POPULATION?

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Introduction and Aims: Measurement of serum creatinine (Cr_S) concentration is essential to estimate glomerular filtration rate (GFR) as in GFR-Epi. Understanding the factors which influence the concentration of Cr_S is important to reduce error in estimating GFR. The aim of the study was to investigate relationship of Cr_S and body composition measured using whole body bioimpedance method in a healthy population.

Methods: A group of healthy subjects with absence of hypertension and renal disease were studied. Body weight, blood pressure, serum and urine creatinine were measured. Whole body bioimpedance (Hydra4200, Xitron Technologies) measurement was performed with a supine position. Extracellular and intracellular resistances were measured with a supine position. Extracellular and intracellular resistances were measured (wECV) and wICV. Fluid volume were estimated using a Xitron program. Linear regression analysis was performed to find correlations of Cr_s to wECV, and wICV. A multiple linear regression model (Cr model) was used to analyze relationship between Cr_s and wECV, wICV, and age.

Conclusion: A group of healthy subjects with absence of hypertension and renal disease were studied. Body weight, blood pressure, serum and urine creatinine were measured. Whole body bioimpedance (Hydra4200, Xitron Technologies) measurement was performed with a supine position. Extracellular and intracellular resistances were measured (wECV) and wICV. Fluid volume were estimated using a Xitron program. Linear regression analysis was performed to find correlations of Cr_s to wECV, and wICV. A multiple linear regression model (Cr model) was used to analyze relationship between Cr_s and wECV, wICV, and age.

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Abstracts

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Ion VT technique AAS

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eopper for the successive determination in the solid phase by using visual test technique. The interface interaction has been investigated. The modified silica demonstrates significant color change from bright orange to dark purple due to interaction with Cu(II) ions. The standard color scale range is 0.50-7.50 μg per sample Cu(II), sample volume - 4.0 mL, time of analysis is 5 min. Blood collection from 39 patients with end stage renal failure was carried out before the first HD session of the week.

Results: The data was compared to the results obtained using standard atomic-absorption spectroscopy technique (AAS). The data obtained are listed in Table. Average concentration of Cu(II) in serum of HD patients (n=39, P=0.951) Data obtained follows normal distribution. Paired t-test showed no significant (α=0.05) difference between results obtained by two methods (texp=1.476, tcrit(α/2)=0.025, F=37)-2.026. Accuracy and precision of the results are satisfactory.

Conclusions: Due to its simplicity and reliability the visual test technique on the base of modified silica can be used for the analysis of multiple biological samples providing valuable analytical information. The developed visual test technique can be recommended for the rapid Cu(II) determination in serum in the clinic laboratories.

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EXPRESSION PATTERN OF CALPONIN IN THE CAPSULAR EPITHELIUM AND PERIGLOMERULAR AREA OF HUMAN KIDNEY IS RELATED TO THE DEVELOPMENT OF GLOMERULOSCLEROSIS

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Introduction and Aims: Progressive glomerulosclerosis lead to a common histological and functional end point referred to as end-stage renal disease. We previously have reported that periglomerular calponin expression in two chronic nephropathy rat models, puromycin aminonucleoside nephropathy and subtotal nephrectomy. In present study, we examined correlation between calponin immunoreactivity in the periglomerular area and development of glomerulosclerosis using specimens obtained (KT, n=9) from the recipients at the time of kidney transplantation, and normal specimens (NS, n=4) from normal portions of kidney segments from patients undergoing nephrectomy for a renal tumor.

Methods: Analysis was performed on two serial 5-μm paraffin sections stained with periodic acid-Schiff (PAS) and calponin-specific antibody respectively. The degree of glomerulosclerosis was assessed on a blinded basis by determining the sclerotic damage to glomeruli, and were graded as follows: G0, no changes; G1+ injury involved <25% damage to the glomeruli; G2+, 25%-50%; G3+, 50%-75%; and G4+, 75%-100% damage. Data were represented as percentage of damaged glomeruli showing any level of injury (scale G0 to G4+). Periglomerular coverage with calponin-positivity were graded as follows: C0+, no calponin-positivity in periglomerular area, C1+, <30%, C2+, 30-80%, C3+, >80%. All the periglomerular calponin was detected in myofibroblast and glomerular parietal epithelium.

Results: In NS, most glomeruli (>95%; G0) showed no sclerotic damage, calponin-positivity at its periglomerular area (>7%; C0). In KT, results was as follows: glomerulosclerotic index; G0+ (14%), G1+ (49%), G2+ (24%), G3+ (9%), and G4+ (4%); calponin index; C0+ (57%), C1+ (24%), C2+ (10%), and C3+ (9%).

Conclusions: These results suggested that calponin-positive myofibroblasts and glomerular parietal epithelium may play a key role in the development of glomerulosclerosis. (This research was supported by Basic Science Research Program through the National Research Foundation of Korea(NRF) funded by the Ministry of Education, Science and Technology(20110002683).

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ADVANCES IN KIDNEY FOCAL LESIONS-USE OF CONTRAST ENHANCED ULTRASONOGRAPHY

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Introduction and Aims: Kidney focal lesions are frequent. Although CT scan and MRI are widely used, ultrasonography is noninvasive and repeatable, but can be improved using contrast-enhanced ultrasonography (CEUS). It has few side effects and can be safely used in chronic kidney disease.

Methods: We used CEUS in ten patients with different kidney focal lesions: three atypical cysts, three benign lesions and four malignant lesions, one of them for monitoring the treatment. Patients were examined with an ultrasound device with contrast soft application. 2.6 ml of contrast agent SonoVue was injected intravenously in bolus. The vascular pattern within the kidney lesion was recorded immediately after injection for three minutes.

Results: From all lesions, six appeared benign in standard, Doppler and CT scan examination before contrast: three cysts and three angiolipomas. After contrast US the diagnosis was confirmed in all ten cases, and the results were confirmed by histopathology. All three cysts showed fine echogenic signal of the wall that appeared highly vascular in CEUS and RRC was confirmed. The histology of kidney tumors was renal cell carcinoma (RRC). CEUS had a specificity of 100% and sensitivity of 100%, with a PPV of 100. RRC are vascular tumors and can be easily detected by CEUS, in cases when color Doppler has lower sensitivity. In the atypical cysts there was a vascular signal inside the cyst and the histopathology revealed malignancy. The benign lesions were angiolipomas and they were confirmed by the similar pattern of vascularization as the normal kidney cortical parenchyma. The three malign lesions were characterized by the rapid wash-out phenomena. One malig lesion was a metastasis from renal cell carcinoma and it was monitored after 6 months of treatment.

Conclusions: CEUS is a noninvasive, harmless, high tech investigation of kidney focal lesion, with an excellent positive predictive value and can be performed also in kidney failure.

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SODIUM BICARBONATE THERAPY OF THE METABOLIC ACIDOSIS OF CHRONIC KIDNEY DISEASE

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Introduction and Aims: The prevalence of metabolic acidosis increases with declining renal function. The authors in this study investigated correcting metabolic acidosis in chronic kidney disease (CKD) patients may preserve renal function and improve nutritional parameters.

Methods: We assigned 49 adult patients with creatinine clearance (CrCl) 15-60 ml/min and serum bicarbonate 16-20 mmol/L, to either supplementation with oral sodium bicarbonate (the bicarbonate group, n=25) or standard care (the control group, n=24) for 12 months. At the primary end points CrCl, proteinuria, and serum creatinine...
showed changed, and at the secondary end points body weight, lean body mass (LBM), mid-arm muscle circumference (MAMC) and serum albumin showed changed.

Results: Compared with the control group, the bicarbonate group was improved in GCI (+7.19 vs -3.47ml/min/yr, p<0.05) (Figure 1), nutritional parameters, body weight (+3.0 vs -1.0kg, p=0.05), LBM (+1.0 vs -2.8kg, p<0.05), and MAMC (+1.1 vs -0.34cm, p<0.05).

Conclusions: Correcting metabolic acidosis (via bicarbonate supplementation) may preserve renal function and improve nutritional parameters in CKD patients.

Introduction and Aims: Urinary synaptopodin excretion is increased in diabetic kidney disease compared with glomerulonephritis, and it showed significant correlation with serum creatinine elevation in glomerulonephritis. We suggest that urinary synaptopodin level can be a predictor of glomerular damage regardless of urinary albumin excretion.

Introduction and Aims: Measurement of the protein content of a timed 24 hour urine collection is the definitive method of establishing the presence of abnormal proteinuria, however, the urine collection is cumbersome. The spot urine protein to creatinine (p/c) ratio seems to be a reliable diagnostic tool for urine protein measurement. Our aim is to evaluate the spot urine p/c ratio compared to 24-h urine total protein excretion in different proteinuria ranges.

Methods: Observational, cross-sectional study of 1179 consecutive paired determinations of 24-h urine total protein excretion and the spot urine p/c ratio in renal patients. The strength of the correlation was determined by calculating the intraclass correlation coefficient (ICC) and the Spearman correlation coefficient (SCC).

Results: Among all groups, the ICC was 0.749 (CI 95% 0.660-0.809) and the SCC was r=0.8 (p<0.01). As shown in the table, there is an excellent significant correlation between the spot urine p/c ratio and 24-hour urine total protein excretion when proteinuria was more than 300 mg/24 hours. This correlation decreased when it was more than 3500 mg. When patients were stratified according to eGFR, the correlations between the spot urine p/c ratio compared to 24-h urine total protein excretion were similar between groups.

Conclusions: In summary, a strong correlation is observed between spot urine p/c ratio and 24-h urine total protein excretion when the level of proteinuria is less than 3500 mg/day. In our experience, there is not enough correlation between spot urine p/c ratio and 24-h urine total protein excretion in nephrotic range proteinuria.

Introduction and Aims: Women with CKD increasingly choose to undergo the challenges of pregnancy, but very few tools are available to counteract the effects of the hyperfiltration of pregnancy; experience with low protein diets in CKD in pregnancy is limited. Hence, we report the results obtained in pregnant women with severe CKD treated by supplemented vegan low protein diets, focusing on intrauterine fetal development and on subsequent children growth.

Methods: Diet group: CKD stages 3b and 4, or stage 3a in the presence of kidney transplantation, type 1 diabetes, collagen disease and/or proteinuria >1 g in the first trimester, or nephrotic later on. Controls: CKD stage 3a not included either for stable, less severe disease, or for late referral, cultural or linguistic barriers, other low protein diets, eating disorders, patient’s choice. Diet: vegan, low-protein (0.6-0.7 g/Kg/day) with amino and chetoacid supplementation,1-3 free meals/week. Compliance, side effects, biochemical data recorded at least twice monthly. All mothers delivered in the same trimester, or nephrotic later on. Controls: CKD stage 3a not included either for stable, less severe disease, or for late referral, cultural or linguistic barriers, other low protein diets, eating disorders, patient’s choice. Diet: vegan, low-protein (0.6-0.7 g/Kg/day) with amino and chetoacid supplementation.
Center. Small for gestational age (SGA) babies were defined as gestational-age adjusted <10 percentile.

Results: Out of over 350 CKD pregnancies referred between 2000 and 2012, 21 cases were treated by the diet (median age 33 yrs (26-40), sCr 1.3 mg/dl (0.5-3.2), proteinuria 2.5 gr/24h (0.2-6.3); 8/21 diabetes-3/21 kidney graft-3/21 interstitial glomerular diseases-10/21 interstitial or malformative). In the diet group, 1 pregnancy was terminated (patient's choice); 1 was a twin pregnancy; 19 singletons babies were delivered. 1 twin, affected by great vessel transposition died after neonatal heart surgery. In the control group 14 singletons were delivered. In the diet group, in spite of pre-term delivery in 20/21 cases, 4/9 singletons were SGA (2 <5thcentile, 2 5-10thcentile). Conversely in the control group, with additional and safe tool in the management of selected pregnant CKD patients, with a risk of SGA at least comparable (and potentially lower) than controls, and a good auxologic profile in the long term.

Conclusions: Our report suggests considering vegetarian supplemented diets as an alternative and safe management of selected pregnant CKD patients with a risk of SGA at least comparable (and potentially lower) than controls, and a good auxologic profile in the long term.

Introduction and Aims: Chronic kidney disease (CKD) results in hypertriglyceridemia which is largely due to impaired clearance of triglyceride-rich lipoproteins occasioned by down-regulation of lipoprotein lipase and VLDL receptor in the skeletal muscle and adipose tissue and of hepatic lipase and LDL receptor-related protein (LRP) in the liver. However information on the effects of CKD and niacin administration on fatty acid metabolism in the liver is limited and was investigated here.

Methods: Expression of molecules involved in fatty acid metabolism in the liver were determined in untreated CKD (5/6 nephrectomized), niacin-treated CKD (50 mg/Kg/day in drinking water for 12 weeks) and control rats.

ASSOCIATION OF SERUM CYTOKINE PROFILES WITH TACROLIMUS-INDUCED CHRONIC NEPHROTOXICITY IN CHINESE LIVER TRANSPLANT RECIPIENTS

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Introduction and Aims: Calcineurin inhibitors (CNI) associated chronic nephrotoxicity has become a serious problem which threatens the prognosis of liver transplant recipients. This study was aimed to find out the relationship between serum cytokines, chemokines and chronic tacrolimus (Tac) induced nephrotoxicity. We detected the posttransplant serum inflammatory cytokines and chemokines levels in liver transplant recipients to illuminate the correlations of inflammatory cytokines or chemokines with the chronic renal injury.

Methods: A total of 136 living donor liver transplant recipients (107 males and 29 females) and 150 healthy controls (120 males and 30 females) were enrolled in this study. All the recipients had normal Cystatin C (Cys-C) and normal urine microalbumin before transplantation and received Tac-based immunosuppressive regime (Tac+MMF+ prednisone) afterwards. A human 10-plex antibody bead kit (BioSource, Camarillo, CA) was used to measure the levels of 10 cytokines and chemokines with the chronic renal injury.

Results: The levels of IL-6L-10, IFN-γ, IP-10 and MCP-1 in the recipients’ group were significantly higher than those in the control group (P<0.05), while the levels of IL-8 was onthoexcitory (P<0.05). In early renal damage group (Cys-C>12.5 mg/L), the concentration of IP-10 was much higher compared to the group with normal renal function (Cys-C<12.5 mg/L), whereas the concentration of MCP-1 in early renal damage group was lower than the group with normal renal function. The concentration of IP-10 in the group with tubulointerstitial injury (eGFR>12.5 mg/L) was much higher compared to the group without such injury (eGFR<12.5 mg/L).

Conclusions: IP10 may be the important cytokine leading to chronic CNI-induced nephrotoxicity, especially the tubulointerstitial injury. Allo-liver recipients with high serum IP10 posttransplant levels might develop severe chronic CNI-induced nephrotoxicity due to increased immune activation.

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HOW THE PATIENT KINETICS HAS ALTERED AFTER THE IMPLEMENTATION OF eGFR IN A NEPHROLOGY OUTPATIENT CLINIC

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Introduction and Aims: Implementation of estimated GFR (eGFR) in the general medicine has massively changed the renal clinics. Those changes might include not only the expansion of the renal patient numbers but also an increase in number of patients sent back to general practitioners. This study was done in order to clarify whether the patient management burden had been changed according to their renal function, before and after the eGFR measurement implementation.

Methods: Two 6-month periods (from Jan 1 to Jun 30), in years 2005 and 2010, i.e. before and after the nationwide implementation of eGFR, were chosen for the analysis. All the new visits to a certified nephrologist in the Hospital were included and the medical charts were reviewed to find out the background clinical status and the disposition of each patient 2 years after the initial visit. Patients already on maintenance dialysis due to ESRD at the initial visit or those with no renal disease were excluded from the analysis.

Results: In 2005 and 2010, 115 and 117 new patients were included in the analysis, respectively. Although the total number of new visits appeared close, the details in 2010 differed from those in 2005 in many aspects. New patients with eGFR between 15 and 45 mL/min/1.73m2 nearly doubled (35.2% in 2005 vs 64.8% in 2010, P<0.001). After the nephrologist’s initial evaluation, more patient were asked to be followed in the original non-nephrology clinic (9.6% vs 28.2%, P<0.001). The patients who continued to be followed in the renal clinic had significantly lower eGFR (median, 56.7 vs 33.8 mL/min/1.73m2, P=0.016, Mann-Whitney); within 2 years, those with baseline eGFR between 15 and 45 mL/min/1.73m2 were more likely to be sent back to non-nephrologists (9.6 vs 29.8% of all the followed patients, P<0.001), due to the overwhelming renal clinic. Dropout patients (14.4% in 2005 and 26.2% in 2010) had significantly lower eGFR in 2010 (median, 79.0 vs 35.0 mL/min/1.73m2, P=0.015, Mann-Whitney).

Conclusions: Implementation of eGFR has resulted in ‘backflow’ of more severe renal patients to non-nephrologists.

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BODY COMPOSITION IN HEALTHY SUBJECTS AND PATIENTS IN EARLY STAGES OF CHRONIC KIDNEY DISEASE

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Introduction and Aims: Fluid balance and body composition are maintained in patients with chronic kidney disease (CKD) until glomerular filtration rate (GFR) falls below 15 ml/min. The aim of this study was to evaluate whether body composition differs in healthy subjects and patients with moderate loss of kidney function.
Methods: Subjects older than 40 years without previous diagnosis of diabetes, cardiovascular and chronic kidney disease were selected. Calf, segmental and whole body bioimpedance spectroscopy (BIS) were performed using Hydra 4200. Extracellular (ECV), intracellular (ICV) fluid volume, total body water (TBW=ECV+ICV), and skinfold thickness were measured. Serum albumin, BMI, and whole body bioimpedance were performed using Hydra 4200.42. Whole body ECV/ICV and TBW/ICV were calculated. Blood pressure, serum creatinine and albumin were measured, eGFR was estimated using the CKD-EPIC equation and calculated aMDRD for staging and classification; plus basic renal parameters with diagnosis and weight, waist circumference, SBP, DBP, serum creatinine with eGFR calculation by eGFR. All procedures were conducted according to manufacturers instructions (dedicated electrodes, measurements sites, positions etc). Total body water (TBW), extracellular water (ECV), intracellular water (ICV) and BCM were measured. We strictly followed the procedure and used the Fluid Management Tool® software. All patients with moderate or severe loss of kidney function fluid distribution and muscle mass is altered. These finding suggests that loss of skeletal muscle mass might be an early event in the progression of CKD. ECV volume in the calf is already validated for corporal fluid composition and lower SMM in the leg. These finding suggests that loss of skeletal muscle mass is altered. Our results show an increased fractional ECV distribution and muscle mass is altered. This suggests that skeletal muscle mass might be an early event in the progression of CKD.

Conclusions: Already in subjects with moderate loss of kidney function fluid distribution and muscle mass is altered. Our results show a significant stepwise decreasing ICV volume in the calf is unaffected in CKD stages 1 and 2. ECV volume in the calf is already validated for corporal fluid composition and lower SMM in the leg. These finding suggests that loss of skeletal muscle mass might be an early event in the progression of CKD. ECV volume in the calf is unaffected in CKD stages 1 and 2.

Introduction and Aims: Bioelectrical impedance analysis (BIA) is an affordable, non-invasive and fast alternative method to assess body composition. The purpose of this study was to compare two different tetrapolar bioimpedance (BIA) devices for estimating body fluid volumes and body cell mass (BCM) in clinical setting among patients with kidney failure.

Methods: All double measurement were performed by multi-frequency and single-frequency BIA analyzers, a Body Composition Monitor BCM (Fresenius Medical Care, Germany) and BIA-101 (Akern, Italy), respectively. All procedures were conducted according to manufacturers instructions (dedicated electrodes, measurements sites, positions etc). Total body water (TBW), extracellular water (ECV), intracellular water (ICV) and BCM were measured. The primary objective was to implement the body composition monitoring in renal patients with significant chronic renal failure: CKD-EPI 54.58 ± 34.59, MDRD 2 (4 variables) 47.36 ± 28.35, Iohexol GFR 47.24 ± 34.05, Bjornsson 67.54 ± 45.25, Jelliffe 1 54.42 ± 36.56 and Jelliffe 2 61.04 ± 40.20.

Results: In general measurement of ICW and BCM were similar (19 ± 18.6; p = 0.87; and 24.8 ± 20.7; p = 0.08) in two devices. The Akern device gives higher mean estimates of TBW and ECV compared to the Fresenius device (41 ± 19.8 vs 35.8, p < 0.04 and 22 ± 17.2; p < 0.001, respectively). A comparison of results from patients with BMI ≥ 25 vs BMI < 25 revealed significant discrepancy measurement between both BIA devices. Namely in group with BMI ≥ 25 (n = 16) acceptable correlations were obtained in TBW (r = 0.99; p < 0.01), ICV (0.95; p < 0.01), BCM (0.84; p < 0.01), ECV (0.81; p < 0.05), but in group with BMI ≥ 25 (n = 20) huge discrepancy (poor correlations) in TBW (r = 0.54; p > 0.05), ICW (0.32; p = 0.30), BCM (0.15; p = 0.55), ECV (0.81; p < 0.01) were found. In those patients (BMI<25) the Akern device gives significantly higher mean estimates of TBW (45.9 ± 40.1; p = 0.03), ECW (24 ± 19.2; p = 0.01) and BCM (28 ± 23; p = 0.05) than Fresenius device.

Conclusions: Since estimates of TBW, ICW BCM by the present BIA devices do not differ in patients with BMI < 25, they might be interchangeable. This does not hold true for overweight/obese renal patients. Because both BIA devices could over/under estimate BCM in obese patients an effort to reduce the bias (electrodes repositioning) and finally comparison to gold standard should be undertaken.

SP187

APPLICABILITY OF A DIFFERENT ESTIMATION EQUATION OF GLOMERULAR FILTRATION RATE IN TURKEY

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Introduction and Aims: We aimed to investigate the performance of various creatinine based glomerular filtration rate estimation equations that were widely used in clinical practice in Turkey and calculate a correction coefficient to obtain a better independent of the aetiology of the CKD.

Conclusions: The BCM with FMT is a utility tool in all CKD patients whatever the diagnosis; it allows the detection of over- and under-hydration with precise quantitation of W excess or deficit in P at different eGFR staging. The procedure takes only 10 min in a clinic and was superior to a senior clinician. We recommend to implement the body composition monitoring in renal patients with significant chronic renal failure: CKD-3 to 5.
estimate using the isotope dilution mass spectrometry (IDMS)-traceable Modification of the Diet in Renal Disease (MDRD) formula.

Methods: This cross-sectional study included adult (>18 years) outpatients and in patients with chronic kidney disease as well as healthy volunteers. Iohexol clearance was measured and the precisions and bias of the various estimation equations were calculated. A correction coefficient for the IDMS-traceable MDRD was also calculated.

Results: A total of 229 (113 male/116 female; mean age 53.9±14.4 years) subjects were examined. A median iohexol clearance of 39.21 mL/min/1.73 m² (range: 6.01-168.47 mL/min/1.73 m²) was found. We found that the Cockcroft-Gault, Mauer, Byrnsen and Gates formulae overestimated the mean GFR by more than 10 mL/min. The MDRD 2 equation overestimated the GFR by 11 mL/min/1.73 m². The largest and smallest bias and random errors were recorded with the Mawer and MDRD 2 formulae, respectively. The best precision and accuracy was also obtained with the MDRD 2 formula. Bias and random error for the IDMS-traceable MDRD equation were 11.33±8.97 mL/min/1.73 m² and 14.21 mL/min/1.73 m², respectively. There was a good agreement between iohexol-measured GFR and corrected MDRD, especially in patients with GFR<60 mL/min/1.73 m².

Conclusions: MDRD formula seems to provide the best estimates. To obtain the best agreement with iohexol clearance, a correction factor of 0.804 must be introduced to IDMS-traceable MDRD equation for our study population.

**SP189**

## CKD PREVENTION IN PATIENTS WITH CAUDA EQUINA SYNDROME, USING ALTERNATIVE THERAPEUTIC METHODS

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Introduction and Aims: Cauda equina syndrome (CES) is a severe complication of lumbar spinal disorders. It is known that CES represents one of the most important causes of repeated acute pyelonephritis that cause chronic pyelonephritis, and then CKD. The aim of this study was to evaluate if electrotherapy and hydrotherapy therapy with natural factors (mud) help in reducing acute pyelonephritis episodes in these patients.

Methods: We conducted a prospective study on 48 patients with CES and repeated acute pyelonephritis. 30 of the patients had catheters à demeure. The age of the patients considered for the study was between 20 and 70. These patients underwent every 3 months, for 1 year, electrotherapy with medium frequency current (nemectron) lombosuprapubian applied with variable frequency (0-100 Hz), 20 minutes, 1 session/day, 20 days and overall mud bath at 37 degrees Celsius for 20 minutes, 1 session/day/20 days.

Results: In 65% of patients that underwent this recovery plan, the number of acute pyelonephritis episodes decreased during the follow up period, compared to the frequency of episodes before the beginning of treatment (p<0.0001). Out of those with catheters à demeure, 59% (p=0.0001) didn’t use them anymore. The number of pyelonephritis episodes was lower in patients aged between 20 and 50, compared to those aged 50-75 years (p=0.0001). There were no statistical significant differences between male and female sex in regards to the number of pyelonephritis episodes after treatment.

Conclusions: Applying alternative methods of treatment in the CES seems to have an effect in reducing the number of acute pyelonephritis episodes, as well as in reducing the permanent bladder catheterisation. Patients younger than 50 years seem to have a better response to treatment than those over 50 years. By reducing acute pyelonephritis episodes in these patients we help preventing chronic pyelonephritis and chronic kidney disease.

**SP189**

## THE CREATININE AND CYSTATIN C BASED CKD-EPI EQUATION IMPROVES RISK PREDICTION OF RENAL OUTCOME IN CKD PATIENTS

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Introduction and Aims: Plasma creatinine and cystatin C are markers used to estimate glomerular filtration rate (GFR). Cystatin C is less influenced by muscle mass or diet than creatinine. Recently, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) validated an equation which integrates creatinine and cystatin C to estimate GFR (i.e. the CKD-EPI creat-cys equation). We present the first comparison of the CKD-EPI creat-cys equation with the more established MDRD equation for prediction of renal outcome.

Methods: We recruited 420 CKD patients from our ongoing CARE FOR HOME study for the present subanalysis. Baseline creatinine and cystatin C were measured and then GFR estimated by the MDRD 4 and CKD-EPI creat-cys equations. Patients were classified to 2013 KDIGO CKD stages (stage 2: eGFR 60-90 mL/min/1.73 m²; stage 3a: eGFR 45-60 mL/min/1.73 m²; stage 3b: 30-45 mL/min/1.73 m²; stage 4: 15-30 mL/min/1.73 m²) by the MDRD equation and then re-classified by CKD-EPI creat-cys. Annual follow-ups were performed. The predefined renal outcome was either a 50% decrease in eGFR, or initiation of renal replacement therapy, or death from any cause.

Results: Out of 420 patients, CKD-EPI creat-cys re-classified 49 to a less advanced CKD stage than MDRD, 59 to a more advanced CKD stage, and 312 to the same stage. During a median follow-up of 2.4 ± 0.8 years 54 patients suffered a renal outcome event of whom 13 (24%) had been re-classified; 12 to a more advanced CKD stage and only 1 to a less advanced CKD stage. Among the remaining 366 patients not suffering an event, 47 had been re-classified to a more advanced and 48 to a less advanced CKD stage. The net re-classification improvement was 20.4% (95% Confidence interval: 9.1% to 34.3%) for patients with the subsequent outcome event, and 0.3% (-4.9% to 5.5%) for patients without the event.

Conclusions: Compared to the established MDRD 4 equation, the new CKD-EPI creat-cys equation allows better stratification of CKD patients for prediction of renal outcome. This finding is consistent with recent the 2013 KDIGO recommendation to use CKD-EPI to estimate GFR.

**SP190**

## VALIDATION OF A NEW STANDARDIZED CYSTATIN C TURBIDIMETRIC ASSAY: EVALUATION OF THE THREE NOVEL CKD-EPI EQUATIONS IN HYPERTENSIVE PATIENTS

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Introduction and Aims: The aim of this study was first to evaluate the analytical performances of a new standardized automated turbidimetric cystatin C assay using Diasys reagents (DiaSys Diagnostic Systems GmbH, Holzheim, Germany) on Olympus AU2700® analyzer (Olympus, Rungis, France). Furthermore, in order to evaluate the clinical relevance of the new function markers (enzymatic IDMS-traceable creatinine and standardized cystatin C) was assessed by comparison of estimated GFR (eGFR) equations with the renal function markers (enzymatic IDMS-traceable creatinine and standardized cystatin C).

Methods: We have studied imprecision, linearity, limit of detection and limit of quantification of this new immunoassay. Method comparison was assessed by comparing with results generated by the standardized Siemens- particle-enhanced nephelometric immunoassay. In order to evaluate the clinical relevance of this assay, estimated glomerular filtration rate (GFR) was calculated using MDRD, CKD-EPI creatinine, CKD-EPI cystatin C 2012 and CKD-EPI creatinine-cystatin C 2012 and compared to GFR measured using urinary clearance of 99mTc-DTPA in 100 hypertensive patients.

Methods: We have studied imprecision, linearity, limit of detection and limit of quantification of this new immunoassay. Method comparison was assessed by comparing with results generated by the standardized Siemens- particle-enhanced nephelometric immunoassay. In order to evaluate the clinical relevance of this assay, estimated glomerular filtration rate (GFR) was calculated using MDRD, CKD-EPI creatinine, CKD-EPI cystatin C 2012 and CKD-EPI creatinine-cystatin C 2012 and compared to GFR measured using urinary clearance of 99mTc-DTPA in 100 hypertensive patients.

Results: Cystatin C measurements using Diasys reagents have reliable analytical performances and is comparable to the standardized Siemens- PENIA method (bias of 0.01 mg/L). The mean measured GFR was 90.0±29.7 mL/min/1.73 m². Bias and accuracy of the three CKD-EPI equations were better than the MDRD. Both CKD-EPI creatinine-based and cystatin C-based formulae had similar bias, precision and accuracy. The combined creatinine-cystatin C equation was significantly more accurate and precise than the CKD-EPI creatinine equation, in particular for early stages of chronic kidney disease.

Conclusions: The use of cystatin C in a combined equation with creatinine could improve the accuracy of eGFR in patients with high GFR (stage 1) and served as a confirmatory test in patient monitoring.
**SP191**

**ESTIMATED GLOMERULAR FILTRATION RATE BASED ON SERUM CYSTATIN C PROVIDES PROGNOSTIC INFORMATION BEYOND ITS ROLE AS AN INDEX OF KIDNEY FUNCTION**

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**Introduction and Aims:** Cytoatin C elevation may reflect the wide spectrum of abnormalities including predisposition to cardiovascular disease (CVD), accompanying renal dysfunction. Clinical significance of estimated glomerular filtration rate based on serum cytoatin level (eGFRcy) in predicting adverse outcomes has not been tested in HIV subjects, comparing with eGFR based on serum creatinine (eGFRcr).

**Methods:** A 3.5-year prospective cohort study was conducted in 661 HIV-infected individuals (mean age, 46.4 ± 11.6 years old) to compare the ability to predict adverse outcomes between eGFRcy and eGFRcr. Adverse outcomes included all-cause mortality, CVD and a decrease in eGFR over 25% from baseline. The ability to predict incidence of adverse outcomes was evaluated using the area under the receiver operating characteristic curves (Au-ROC).

**Results:** Au-ROC for eGFRcy (0.604) was moderate yet significant (P = 0.0003), whereas one for eGFRcr (0.564) was not statistically significant (P = 0.0950).

**Conclusions:** The frequency of HIV individuals affected with renal dysfunction manifested a nearly 2.5-fold decrease, if it was assessed by eGFRcy, instead of eGFRcr. Furthermore, eGFRcy is likely superior to eGFRcr in predicting composite adverse outcomes among HIV-infected individuals.

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**SP192**

**MDRD VERSUS CKD-EPI EQUATIONS TO ESTIMATE GLOMERULAR FILTRATION RATE IN OBSE Patients**

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**Introduction and Aims:** Obesity is recognized as a risk factor both for the development and progression of chronic kidney disease (CKD). Estimating glomerular filtration rate (GFR) is thus especially important to follow these patients. We have tested the performances of two creatinine-based equations, namely the MDRD and CKD-EPI equations, in an obese population.

**Methods:** Patients with body mass index (BMI) higher than 30 kg/m² were included. The reference method for GFR measurement was 51Cr-EDTA (single injection method, two blood samples at 120 and 240 minutes). Serum creatinine was measured using the IDMS traceable compensated Jaffé method. When obese patients are considered, one important issue is the question of BSA indexation. In this work, we will present the result with non-indexed GFR. We calculated bias (defined as the mean difference between measured and estimated GFR), precision (defined as the SD around the bias) and accuracy 30% (defined as the percentage of estimations which are between ± 30% of measured GFR). Analyses were repeated in patients with measured GFR higher than 60 mL/min.

**Results:** The population included 93 patients (Liège, Belgium), 62 women and 31 males. Mean age was 51 ± 14 years and mean BMI was 41 ± 9 kg/m². Mean measured GFR was 94 ± 30 mL/min (11 patients had a GFR lower than 60 mL/min). In the global population, the bias was -1 and -6 mL/min for the MDRD and CKD-EPI equations respectively. Precision was 19 mL/min for both equations. Accuracy 30% was 80% for the MDRD and CKD-EPI equations, respectively (no significant difference). In patients with measured GFR higher than 60 mL/min, bias, precision and accuracy for the MDRD and CKD-EPI equations were: -12 and -6 mL/min, 20 and 20 mL/min, and 90 and 84%.

**Conclusions:** Both in the global and subgroup analyses, the CKD-EPI equation did not outperform the MDRD study equation. The performances of both equations were worse in patients with obesity. These two conclusions were still valid if indexed GFR was considered.

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**SP193**

**SHORT-TERM EFFECTS OF TOLVAPTAN ADDED TO FUROSEMIDE IN PATIENTS WITH CONGESTIVE HEART FAILURE AND ADVANCED STAGES OF CHRONIC KIDNEY DISEASE**

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**Introduction and Aims:** Increasing dose of furosemide (Furo) often leads to worsening renal function (WRF) in patients with Furo-resistant congestive heart failure (CHF), especially when complicated with advanced chronic kidney disease (CKD). Add-on use of tolvaptan (Tol), a novel V2 receptor antagonist, may give better control of excessive body fluid in CHF patients without increasing dose of Furo and WRF, however, it has been unclear whether it may give similar effect in advanced stages of CKD patients. This study aimed to clarify the efficacy of add-on Tol in patients with CHF and advanced stages of CKD.

**Methods:** 23 patients with CHF and CKD stage G3b-5 who showed insufficient control of excessive body fluid using 40-200 mg of oral Furo daily were included in this study. We assessed the changes of hemodynamic and renal functional parameters in 23 patients given fixed doses of Furo with add-on Tol (15 mg daily) for 1 week.

**Results:** Compared with the baseline, increasing of urine volume(UV, mL/d) in stages G3b, G4 and G5 were 696±1250(P=0.19), –381±736(P=0.87) and 678±474(P=0.05), respectively, which showed significant increment of UV in CKD stage 5 at the end of the study. Increment of serum creatinine levels(SAuCr, mg/dL) in each stage were 0.02±0.14(P=0.79), 0.48±0.7(P=0.05) and –0.11±0.44(P>0.53), respectively, showing no significant WRF except in stage 4. Changes in blood pressure(ABP, mmHg) were not statistically significant, and status of excessive body fluid improved clinically in each stage.

**Conclusions:** Without WRF and decreasing BP, add-on use of Tol not only showed apparent increase of UV, but improved clinical symptoms associated with excessive body-fluid status in patients with Furo-resistant CHF and advanced stages of CKD.

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**SP194**

**THE EFFICACY OF COLCHICINE TREATMENT IN RENAL AMYLOIDOSIS IN THE FRAMES OF FAMILIAL MEDITERRANEAN FEVER**

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**Introduction and Aims:** The main objective of the study was to assess the results of colchicicine treatment in renal amyloidosis in the frames of Familial Mediterranean Fever (FMF) depending on colchicicine daily dose and the stage of nephropathy in the beginning of the treatment.

**Methods:** We studied 41 FMF patients with amyloid nephotrophy. All patients were taking colchicicine: 18 patients began the treatment in proteinuric stage (I subgroup), 15 – in the stage of nephrotic syndrome (NS/ II subgroup), and 8 – in the stage of malial (creatinine level 116-300 mcmol/l) renal failure (RF/ III subgroup). The preparation dosage was adequate (1.8-2.0 mg/day) only in 11 of investigated patients (26,8%). The essential inclusion criterion for the participation in the study was the duration of colchicicine treatment not less than 3 consequent years.

**Results:** In I subgroup colchicicine efficacy, i.e. disappearance or decrease in intensity of proteinuria, was detected only in 3 adequately treated patients. In the rest 15 inadequately treated patients we detected persistence of proteinuria with increasing tendency – in 12, and increase in creatinine level – in 3 patients. 5 patients in II subgroup were treated adequately. In 3 of them colchicicine was efficient, however the rest 2 patient developed RF. In the majority (7) of inadequately treated patients in this subgroup (10 patients) colchicicine was not efficient, and 6 patients developed RF. Only in 3 of 10 inadequately treated patients we detected decrease in intensity of proteinuria. There were no cases of colchicicine efficacy in III subgroup regardless of preparation dosage.

**Conclusions:** Our investigation has shown that colchicicine in the most efficient in the terms of early prescription (proteinuric stage of amyloid nephotrophy) and in adequate dose. The efficacy of colchicicine tends to decrease in NS, and even full colchicicine dose is not able to prevent the progression of amyloidosis. In the stage of RF colchicicine treatment has no influence on the course of disease.
**SP195**  EXTRACELLULAR MATRIX PROTEIN FIBULIN-1 PLASMA LEVELS ARE ASSOCIATED WITH INCREASED CARDIOVASCULAR RISK IN CHRONIC KIDNEY DISEASE

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Introduction and Aims: Fibulin-1 is one of the few extracellular matrix proteins present in blood in high concentrations. We aimed to define the relationship between plasma fibulin-1 levels and risk markers of cardiovascular disease in patients with chronic kidney disease.

Methods: Plasma fibulin-1 was determined in patients with chronic kidney disease (n=32; median age, 63 years; inter-quartile range, 51 to 73 years). Serological biomarkers related to cardiovascular disease (fibrinogen, interleukin 6, C-reactive protein) were measured. Arterial application tonometry was used to determine central hemodynamic and arterial stiffness indices.

Results: We observed a positive correlation of fibulin-1 levels with age (r=0.38; p=0.033), glycated hemoglobin (r=-0.80; p=0.003), creatinine (r=0.35; p=0.045), and fibrinogen (r=0.39; p=0.027). There was a positive correlation between fibulin-1 and central pulse pressure (r=0.44; p=0.031) and central augmentation pressure (r=-0.55; p=0.001). In a multivariable regression model, diabetes, creatinine, fibrinogen and fibulin-1 were found to be independent variables associated with cardiovascular disease.

Conclusions: Fibulin-1 is an important biomarker for cardiovascular disease in chronic kidney disease patients.

**SP196**  INCIDENCE OF PROTEINURIA FOLLOWING GEMCITABINE ADMINISTRATION IS A LIKELY SIGN OF POOR OUTCOME FOR CANCER PATIENTS

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Introduction and Aims: Gemcitabine (Gem) is approved for treatment of a variety of cancers, including pancreatic and biliary carcinomas. Clinical experience suggests that Gem administration may be associated with the emergence of proteinuria. This study was undertaken to examine incidence of proteinuria following Gem administration, and an association of de novo proteinuria and mortality among Gem recipients.

Methods: A retrospective cohort study was conducted in 53 pancreatic or biliary cancer patients (27 men, mean age, 67 years) who received the first mono-therapy of Gem and who had never manifested proteinuria before it. Proteinuria was defined as dipstick test ≥ 1+, persistent in at least two consecutive examinations within six months following Gem administration. Cumulative mortality was analyzed by the Kaplan-Meier method, stratified by presence or absence of proteinuria. Multivariate Cox proportional hazards regression analysis was used to calculate hazard ratio (HR) with its 95% confidence interval (CI) for all-cause mortality, adjusted for age, gender, and stage of disease.

Results: Incidence of proteinuria was 20.7% (18 out of 53 patients), and totally 18 patients died during the follow-up period (mortality, 33.9%). Mean follow-up time after initiation of Gem was 453 ± 196 days. Cumulative mortality was significantly greater in patients who developed proteinuria than those who did not. In addition, the HR (95% CI) of incident proteinuria for mortality was 2.81 (1.09 - 6.78; P = 0.0335).

Conclusions: Proteinuria may be a harbinger of near-term death for cancer patients who received Gem treatment. Periodic monitoring of urinary protein is strongly recommended for frontline oncologists.

**SP197**  CONVERSION FROM ALLOPURINOL TO FEBUXOSTAT IS BENEFIT FOR CKD PATIENTS WITH HYPERURICEMIA

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Introduction and Aims: Hyperuricemia is known not only as a laboratory finding in chronic kidney disease (CKD), but also as one of major risk factors for both progresses in CKD and cardiovascular disease. In advanced CKD patients, xanthine oxidase inhibitor (XOI) such as allopurinol had been established for anti-hyperuricemic agent. However, allopurinol might be limited to use in advanced CKD patients due to severe side effects and pharmacological renal metabolism of this medicine. Febuxostat has been recently introduced as a novel XOI to reduce serum uric acid (sUA) markedly and safely. We investigated whether febuxostat potenitates to suppress the progression of kidney dysfunction in CKD individuals pre-treated with / without allopurinol.

Methods: 139 CKD patients (70+/-11 (SD) yo, M/F=107/32, diabetes: 30%) were subjected and administered 12.5+-5.4 (10 - 19)mg/day of febuxostat for 10+/-5.6 (3 - 19) months. Out of 139, 63 patients (OtoF group), administered 103+-45 (50 - 19) months. Out of 139, 63 patients (OtoF group) had not been treatment with any OXI. 76 patients (AtoF group), administered 103+-45 (50 - 200)mg/day of allopurinol previously, were converted to febuxostat (13.9+-11 mg/day). EGFR and sUA at -12, 6, 3, 1, 0, 1, 3, 6, 12 months after starting administration of febuxostat were applied to evaluate the time-dependent changes.

Results: At the start of febuxostat (0months), sUA and EGFR in all subjects were 24.4+-14 ml/min and 9.1+-3.3 mg/dl, respectively. At 12 months, sUA was significantly reduced to 7.0+-1.5 mg/dl (p<0.01). EGFR at 12 months was disclosed 25.5+-13 ml/min, with no significant change after administration of febuxostat. Before starting febuxostat, eGFR was decreased as -0.63+-0.8 ml/min/month. After initiating febuxostat, decline of eGFR was significantly diminished as 0.03+-0.8 ml/min/month. In both 0toF and AtoF groups, eGFR was showed stable during followed-up periods. There was no difference in changes of eGFR with the dose of febuxostat (10 vs 20mg/day), age (over 65yo), presence of diabetes.

Conclusions: In conclusion, treatment of hyperuricemia by XOI partially improved prognosis in CKD patients. Even in the patients already treated with allopurinol, conversion from allopurinol to febuxostat may be benefit for maintain kidney function through enhanced lowering sUA.
SP198  THE EFFECT OF ENVIRONMENTAL AND PATIENT HISTORY ON THE FORMATION OF RENAL STONE AND RELATED SERUM IONS LEVELS WITH REFERENCE TO URINARY TRACT INFECTIONS

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Introduction and Aims: As the prevalence of renal stone is different in males and females, some studies have focused on the possible roles of hormones including sex types and their receptors in renal calcium stone diseases. Environmental as well patient history, habits and habitats may also influence the formation of stones, ions metabolism and consequently urinary tract infections. The present study is an attempt to correlate between the relevant parameters including environmental as well patients criteria in relation to formation of renal stones, serum ion balances, hormones and possible urinary tract infections.

Methods: This study was conducted in Tikrit Teaching Hospital on 160 patients with post shockwave lithotripsy during 2012. The causative agents of urinary tract infections were identified. One hundred stones were collected and analysed. Blood samples were collected from patients for serum analysis of vitamin D, parathyroid and sex hormones, calcium, phosphorus, uric acid and magnesium. Types of diet, occupation, residence, drinking water, education and family history were recorded.

Results: Eighty four percent of the patients were infected with Gram-negative bacteria. The male to female ratio of infection was 2.1:Ca-oxalate was the predominant (85%). Which was either mixed or pure. More than a half of the urolithiasis patients had one or more metabolic abnormalities like hypercalcaemia and hyperuricaemia. Hypermagnesaemia related to hyperparathyroidism was recorded. Most of the patients used raw drinking waters without food restrictions. Almost 37% of the patients tested were having a history of renal stone. It was found a significant variations of serum ions with respect to sex hormones.

Conclusions: Increased incidence of renal stones among males was attributed to increased dietary protein intake which increases urinary excretion of phosphates and magnesium and reduced urinary citrate concentration. The recurrence rate among urolithiasis patients was almost 37% which indicates insufficient treatment of the underlying causes. Vitamin D, parathyroid and sex hormones were highly interrelated with ions metabolism, stone formation and urinary tract infections.

SP199  PREOPERATIVE MARKERS OF DECREASED KIDNEY FUNCTION AFTER SURGICAL TREATMENT OF NEPHROLITHIASIS

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Introduction and Aims: It is known, that patients with nephrolithiasis have the increased risk of development of the chronic kidney disease (CKD). Among risk factors of development of CKD in nephrolithiasis, it is possible to allocate the repeated operative interventions, accompanied by transient disturbances of microcirculation to the development of tubulointerstitial damage and endothelial dysfunction in nephrofibrosis outcome. Mediators of tubulointerstitial damage and nephrofibrosis participating in the cellular response can be used to predict the outcome of kidney damage in the surgical treatment of nephrolithiasis.

Methods: Examined 340 patients of nephrolithiasis. All patients underwent assessment of renal function by the formula MDRD; preoperative and 3 months after surgery using ELISA determined levels of some profibrotic cytokines (uIL-6, uIL-8, uMCP-1, uTGF-β) and mediators of endothelial dysfunction (VEGF, NO and ET-1) in urine and blood serum. The age of patients, body weight, anamnesis duration, salt composition of the stone, GFR, urea, serum creatinine also underwent the analysis.

Results: Based on the results of 57 intraoperative nephrobiopsy received during PCNL and open surgical treatment, revealed changes tubulointerstitial tissues of varying severity. The nonparametric correlation analysis on Spearman’s method showed a strong correlation (r ≥ 0.5) between of laboratory and morphometric parameters in patients with nephrolithiasis (p ≤ 0.05). Diameter of tubes correlated with concentration of IL-1 and IL-6 in urine (r=0.77; p=0.04), and also back correlated with the ET-1 level in blood serum (r=-0.78; p=0.006). Indicators such as uTGF-1 (r = -0.75; p = 0.026), uIL-6 (r = 0.77; p = 0.04) and VEGF (r = 0.77 p = 0.036) is directly dependent on elevation changes tubular epithelial cells (p ≤ 0.05). Infiltration of the renal parenchyma of the brain substance was correlated with the levels of TGF-β (r = 0.76; p = 0.02) and MCP-1 (r = 0.86; p = 0.02) in the urine, the concentration of NO in blood serum (r = 0.77; p = 0.036). Dimensions of the long axis of the glomerulus had a strong positive correlation with the concentration uIL-8 (r = 0.77; p = 0.036), and negatively with the concentration of VEGF in serum (r = -0.9; p = 0.013). Based on multivariate discriminant analysis and ROC-analysis (area under the curve of 0.70) to the factors predictive of the risk of decreased kidney function in postoperative period include increasing uTGF-β more than 498 pg / ml, VEGF more than 268 pg / ml, NO more than 15.1 mmol / l, and age older than 50 years.

Conclusions: Use of mediators nephrofibrosis as quantitative prognostic criteria risk of decreased kidney function after surgery in patients with nephrolithiasis can identify risk patients with a high probability of progression of CKD in the postoperative period, to choose the best algorithm for diagnostic and treatment interventions in these patients and to determine the appropriate target for renal protection therapy.
EPIDEMIOLOGY - RENAL OUTCOMES

SP200

TABUK FORMULA: A MODIFIED CKD-EPI FORMULA IMPROVES PREDICTING GFR IN SAUDI POPULATION

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1Internal Medicine School of Medicine, University of Tabuk Tabuk Saudi Arabia, 2Community Medicine School of Medicine, University of Tabuk Tabuk Saudi Arabia, 3Prince Sultan Kidney Center Tabuk Saudi Arabia, 4Physiology School of Medicine, University of Tabuk Tabuk Saudi Arabia

Introduction and Aims: Tabuk people has lower body mass index (BMI) and body surface area (BSA) than U.S. CKD-EPI formula was developed for estimation of GFR in Americans, but its accuracy in Tabuk people indicated adjustment of this formula is crucial. Aim: Is to adjust CKD-EPI formula and compare performance of tailored CKD-EPI formula (Tabuk formula) with the original CKD-EPI using isotopic GFR (iGFR) as a reference.

Methods: The study included 226 person, 69 diabetics; males 141, age 47±12 years, body weight 65±7 Kg, BSA 1.7±0.1 m²; BMI 23±3 Kg/m²; creatinine 2.5±1 mg/dl, BUN 34±15 mg/dl, iGFR 41±22 ml/min/1.73m ². As BMI in data provided by CKD-EPI was developed for estimation of GFR in Americans, but its accuracy in Tabuk people indicated adjustment of this formula is crucial. The aim was to improve accuracy of CKD-EPI formula by adding a corrective factor that is extracted from BMI of Tabuk people. So our suggested formula:

eGFR (ml/min/1.73m²) = (CKD-EPI) X (BMI)^1.066

Results: Tabuk formula gave the best performance as illustrated in tables below, considering error range between ±10%, ±30% and ±50%. Also, analysis by r² showed it is the best one for Tabuk people.

Conclusions: Tabuk formula represents a better estimation of GFR than original CKD-EPI and other published formulae so; it is the best one for monitoring kidney functions and could be applied in clinical practice in Tabuk area.

SP200 Table 1. iGFR and eGFR by Tabuk formula and other formula

<table>
<thead>
<tr>
<th></th>
<th>Mean Range Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>iGFR Tabuk formula (ml/min/1.73m²)</td>
<td>42±23 7-120 39</td>
</tr>
<tr>
<td>eGFR Tabuk formula (ml/min/1.73m²)</td>
<td>44±22 8-124 40</td>
</tr>
<tr>
<td>eGFR CKD-EPI (ml/min/1.73m²)</td>
<td>39±16 7-113 35</td>
</tr>
<tr>
<td>eGFR MDRD (ml/min/1.73m²)</td>
<td>40±18 8-116 37</td>
</tr>
<tr>
<td>eGFR Walser (ml/min/3m²)</td>
<td>37±17 3-97 3-97</td>
</tr>
<tr>
<td>eGFR Mayo Clinic (ml/min/1.73m²)</td>
<td>48±26 10-145 41</td>
</tr>
<tr>
<td>eGFR Nankivel (ml/min/1.73m²)</td>
<td>50±17 13-116 47</td>
</tr>
<tr>
<td>eGFR Cockroft-Gault (ml/min/1.73m²)</td>
<td>52±21 13-140 47</td>
</tr>
</tbody>
</table>

SP200 Table 2. % of prediction error in all formula

<table>
<thead>
<tr>
<th></th>
<th>within 10% within ±30% within ±50% R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tabuk formula</td>
<td>44 78 91 0.73</td>
</tr>
<tr>
<td>CKD-EPI</td>
<td>24 55 77 0.63</td>
</tr>
<tr>
<td>MDRD</td>
<td>20 51 71 0.58</td>
</tr>
<tr>
<td>Walser</td>
<td>19 49 70 0.58</td>
</tr>
<tr>
<td>Mayo Clinic</td>
<td>18 47 61 0.56</td>
</tr>
<tr>
<td>Nankivel</td>
<td>16 37 63 0.57</td>
</tr>
<tr>
<td>Cockroft-Gault</td>
<td>15 35 49 0.56</td>
</tr>
</tbody>
</table>

SP201

PROGRESSION OF CHRONIC KIDNEY DISEASE (CKD) IN THE RENAL RESEARCH INSTITUTE (RRI)-CKD STUDY

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Introduction and Aims: Understanding CKD progression is critical in designing optimum clinical management. There is little data from prospective cohort studies examining patterns and predictors of CKD progression. Our aim was to examine patterns and predictors of CKD progression. Our aim was to examine patterns and predictors of CKD progression in a prospective CKD cohort.

Methods: This study is a prospective observational study of adult patients with CKD Stage 3-5 conducted at 78 US nephrology clinics enrolled between 06/2000-01/2006. Data on demographic, comorbidity, laboratory, and medication were collected at all routine clinic visits. Glomerular filtration rate (GFR) was estimated using the 4-variable MDRD and CKD-EPI equations. CKD progression was assessed by eGFR change per year and time to ESRD. Multiple linear regressions were used to assess associations between eGFR slope and baseline characteristics. Rate of progression was analyzed using linear mixed models to predict eGFR over time and using all available data. Time to ESRD was analyzed via Cox survival models.

Results: 2,182 patients were enrolled in the study, mean age 63±15.65% white, 55% male, 47% diabetic, 52% hypertensive, 49% with a history of cardiovascular disease (CVD). Mean eGFR was 25±11 ml/min/1.73m², with the majority (77%) in CKD Stage 3 (28%) or 4 (49%) at enrollment. Patients were followed for a median of 2 years with an average of 4 follow-up clinic visits per year. There were 582 ESRD events and 184 deaths. GFR was either stable or 'improving' over time in 37%. Older age, higher CO₂ or serum albumin were associated with slower progression, while black race, male, diabetics, with history of CVD, higher systolic blood pressure and higher serum sodium were associated with steeper negative slope of eGFR decline. Figure displays adjusted eGFR slope estimates obtained from mixed model for patients with specific characteristics. Male sex, black race and DM were associated with a higher risk of ESRD, while older age, higher eGFR, higher serum albumin and use of ACEI or ARB was associated with a lower risk of ESRD. After adjustment for all factors noted above, a 10 ml/min/1.73m² higher eGFR was associated with a 74% lower risk of ESRD.
Conclusions: This prospective cohort of referred CKD patients likely typifies patterns of progression in US nephrology practices and identifies important modifiable risk factors for CKD progression and the outcome of ESRD.

Introduction and Aims: To expedite research in the field of chronic kidney disease (CKD), large scale, prospective, observational cohort studies with detailed phenotyping and long-term follow-up are mandatory and have the potential to generate novel hypotheses for future intervention trials. We report on the formation of a network of 5 cohorts comprising relevant patient subgroups including all age-groups, stages of CKD, overt proteinuria and comorbidities (diabetes mellitus and cardiovascular disease).

Methods: This initiative aims to conduct joint analyses of five prospective observational studies in the renal field (BIS, Berlin Initiative Study; CAD-REF, Coronary Artery Disease-Renal Failure-Registry; DIACORE, Diabetes Cohort; GCKD, German Chronic Kidney Disease Study and 4C, Cardiovascular Comorbidity in Children with CKD Study). To this end, prior to study start, 4 of the 5 prospective study cohorts defined core variables to be obtained by uniform data capturing. This includes analogue patient questionnaires, concordant standards for clinical measurements, a core laboratory for predefined blood and urine analyses and central event adjudication based on medical reports.

Results: Starting in 2009, participants are seen in the study clinics in 1-2 year intervals for a total follow-up duration of at least 4-10 years depending on each study’s protocol. At each follow-up visit, information is recorded on any incident micro- and macrovascular event, renal replacement therapy, cancer, hospital admission, and death. Furthermore, standardized clinical measurements are performed and blood and urine samples are taken, where possible, in a fasting state. Biomaterials are processed according to best pre-analytical methods for routine analyses in the core laboratory and samples are taken, where possible, in a fasting state. Biomaterials are processed for a total follow-up duration of at least 4-10 years depending on each study’s protocol.

Conclusions: The network of German Kidney Cohorts is establishing a prospective study cohort of 17,000 patients. This will expedite future research on factors involved in the initiation and progression of CKD and its complications.

Introduction and Aims: Accurate measurement of GFR is useful in many different clinical settings. Estimated GFR (eGFR) measurements, derived from manipulations of plasma creatinine concentrations in different ways, have become the cornerstone for screening for chronic kidney disease (but not without some controversy). Measured GFRs (mGFR) are done in fewer situations, but one still extant is the accurate measurement of renal function in people potentially able to donate a kidney. We wanted to see the level of agreement between these commonly-used formulae for eGFR and the mGFR in this group.

Methods: 508 people were evaluated between 2008 and 2012 for potential kidney donation by undertaking mGFR. mGFR was derived from 15C EDTA plasma creatinine clearance using blood samples taken at 2, 3 and 4 hours. The slope-intercept GFR was corrected for body surface area (BSA) using the Haycock formula and for the fast exponential using the Brochner-Mortensen equation. For each person with an mGFR and a contemporary plasma creatinine value we calculated the Cockcroft-Gault creatinine clearance, the 4-variable MDRD eGFR, and the CKD-Epi eGFR. We then explored the relationships between these different derived variables.

Results: The mean mGFR for this population was 92.0 +/- 14.1 ml/min (range 38.6 - 166.7). Age range was 21 to 84. Racial gender distribution was thus: White Female: 205; White Male: 193; Black Female: 32; Black Male: 28; Others Female: 27; Others Male: 22. Pearson correlation coefficients were poor between mGFR and MDRD eGFR (r=0.53), CG (r=0.54) and CKD-Epi (r=0.62). All very significant statistically, but, Bland-Altman plots showed very substantial bias: mGFR to MDRD bias -0.14 (SD 15.9), 95% limits -31 to +31 ml/min. mGFR to CG bias 21.3 (23.7), -25 to +67 ml/min. mGFR to CKD-Epi bias 12.2 (19.3), -25 to +50 ml/min.

Conclusions: The level of agreement between mGFR and all three sets of eGFR values was poor and thus eGFR was of no clinical utility in this setting. MDRD eGFR fared least badly under these circumstances. Use of mGFR of course remains an essential safeguard to ensure appropriate donation.

Introduction and Aims: Chronic kidney disease (CKD) is an irreversible and progressive disease and can lead to kidney failure (end-stage renal disease). Despite its prevalence, some physicians may be unfamiliar with the diagnosis and initial treatment of CKD. The Kidney Disease: Improving Global Outcomes (KDIGO) initiative developed goals: to distinguish CKD at its earliest stage; and understand what measures can be used to prevent its progression and associated complications. The objective of this research is to investigate the standard of care in CKD management including diagnosis, monitoring, co-management and referral patterns.

Methods: Data were drawn from the Adelphi Chronic Kidney Disease Specific Programme (DSP) conducted between September and December 2012. The DSP is an independent, real world, cross-sectional/prospective multinational survey. The data reflect current clinical practice, current symptoms, prevalence, and severity; physician and patient perspectives on CKD progression; and health status and its effect on patients’ daily working lives. Data were collected in France, Germany, Spain, and the UK via i) nephrologist and endocrinologist interviews, ii) patient record forms (PRFs) completed by participating physicians, and iii) matched patient self-completion forms. Eligible physicians provided detailed information for 8 consecutive patients who agreed to participate with CKD stage 3, stage 4 or stage 5 not on dialysis and 4 stage 5 patients on dialysis. Results: A total of 177 physicians participated, of which 157 were nephrologists and 107 were hospital-based. 95% of physicians indicated that MDRD (modification of diet in renal disease) was the most common method used to estimate GFR (glomerular filtration rate). Physicians estimated that of the patients they had managed in the previous 4 weeks, 8.1% were diagnosed at stage 1, 11.9% at stage 2, 22.1% at stage 3a, 21.6% at stage 3b, 20.7% at stage 4 and 15.7% at stage 5. Physicians indicated that 49.2% of their patients were referred by their PCP/family doctor, 14.7 by an
endocrinologist and 14.3% by a nephrologist. 6.1% of patients were referred to the nephrologist at stage 1, 10.5% at stage 2, 20.1% at stage 3a, 25.2% at stage 3b, 24.1% at stage 4 and 13.8% at stage 5. 48% of nephrologists suggested that patients should be referred when the GFRs fell between 45 and 59 ml/min/1.73m². Physicians specified that in 39.2% of cases the underlying cause of CKD was T2DM, 38.7% hypertension and 22% CV disease. 19% of physicians indicated that they usually discontinue angiotensin-converting enzyme inhibitor or angiotensin receptor blocker therapy to raise the GFR when a patient nears dialysis.

Conclusions: These findings indicate that while timely access to nephrologist and endocrinologist services are important for CKD patients, many are still being referred late to a specialist - in this analysis four out of ten are referred at Stage 4 or 5.

Introduction and Aims: We started the kidney early evaluation program in Japan (KEEP JAPAN) in 2006. This program is a cost-free chronic kidney disease (CKD): detection/triaging targeted for population with high risks of CKD that is a history of hypertension (HTN) or diabetes mellitus (DM), or family history of HTN, DM or CKD. The aim of this study was to report data from KEEP JAPAN and detect the relationship between a decline in eGFR and the lifestyle as risk factors.

Methods: Total of 4431 check-ups from the 1947 enrolled participants between August 2006 and December 2012 (Mean age, 55.8±16.5 years; male: female, 846: 1101). Of them, 2324 cases could be analyzed for one year changes of eGFR and ACR. The prevalence of CKD was analyzed with the results of the first check-up. CKD was defined with positive urine ACR (= or > 30 mg/gCr) and/or decreased eGFR (<60 ml/min/1.73m²) using Japanese equation because of the racial composition in Japanese population.

Results: CKD prevalence was 26.5% at the first check-up. Univariate analysis demonstrated that the history of DM (odds ratio (OR) 2.08, 95%CI 1.64 - 2.63), history of HTN (OR 4.46, 95%CI 3.58 - 5.56), history of cardiovascular disease (OR 2.08, 95% CI 1.63 - 2.66), older than 60 years of age (OR 4.88, 95%CI 3.92 - 6.09), obesity (OR 1.68, 95%CI 1.36 - 2.08) with blood pressure without DM or >130/85 mmHg in participants with DM, OR 2.40, 95%CI (1.96 - 2.96), were the significant risk factors for the prevalence of CKD. On the other hand, smoking, alcohol intake, having stress, daily exercise were not the significant risk factors for the prevalence of CKD. By yearly check-up, eGFR significantly declined with 0.6 ml/min/1.73m² (0.4%) per year but ACR did not significantly change. The decline of eGFR was significantly higher among participants who walked everyday more than 60 min (mean decline in eGFR: 1.25 ml/min/1.73m² vs. 0.52), and those who did not have a family doctor (1.14 ml/min/1.73m² vs. 0.44). Loss in weight tended to prevent the decline in eGFR (0.17 ml/min/1.73m² vs. 0.66). Furthermore, present smoking and alcohol intake may be a risk factor for the decline in eGFR (1.06 ml/min/1.73m² vs. 0.55 and 0.68 vs. 0.46, respectively).

Conclusions: It is demonstrated that obesity and high blood pressure are risk factors for prevalence of CKD. The corrections of lifestyle, especially the loss in weight, stopping smoking and alcohol intake and visiting family doctor are important for the prevention of decline in eGFR. However, too much exercise may accelerate the decline in eGFR among high risk population of CKD.

Introduction and Aims: Chronic kidney disease (CKD) is a major issue in public health. Its prevalence has been calculated using the creatinine-based equations such as the Modified Diet in Renal Disease (MDRD) study and Chronic Kidney Disease Epidemiology Collaboration study (CKD-EPI) equations for estimating glomerular filtration rate (GFR). Recently, new equations based either on cystatin C (CKD-EPI Cys) or both cystatin and creatinine (CKD-EPI mix) have been proposed by the CKD-EPI consortium. The aim of the study was to measure the difference in the prevalence of CKD, defined as estimated GFR below 60 ml/min/1.73 m², in a population using these different equations.

Methods: CKD screening is performed in the Province of Liège, Belgium. On a voluntary basis, people aged over 50 were invited to be screened. GFR was estimated by the four equations. CKD was defined as GFR < 60 mL/min/1.73 m². Serum creatinine was measured by the IMDS traceable compensated Jaffe method (Roche Diagnostics, Mannheim, Germany) on Modular apparatus. Cystatin C was measured by a particle-enhanced nephelometric immunoassay (PENIA) on the BNII nephelometer (Siemens Healthcare Diagnostics, Marburg, Germany).

Results: The population screened consisted of 4189 people (47% were men, mean age 63y ± 7y). The mean serum creatinine and plasma cystatin C levels were 0.88±0.21 mg/dl and 0.85±0.17 mg/L, respectively. The prevalence of CKD in this population using the MDRD, the CKD-EPI, the CKD-EPI Cys and the CKD-EPI mix equations was 13%, 9.8%, 4.7% and 3%, respectively. The prevalence of CKD is significantly higher with the creatinine-based (MDRD and the CKD-EPI) equations compared to the new cystatin C-based equations.

Conclusion: The present study has illustrated large discrepancies for the prevalence of CKD according to the biomarker used to estimate the GFR. Moving from strictly creatinine-based equations (MDRD or CKD-EPI) to cystatin C-based equations will decrease prevalence of CKD by half, which is highly significant from an epidemiological point of view. Additional studies are thus necessary before asserting we know the true prevalence of CKD in the general population.
Abstracts

**SP209**

**TWO NEW INSTRUMENTS TO MEASURE AUTOSOMAL POLYCYSTIC KIDNEY DISEASE (ADPKD) RELATED DISEASE BURDEN AND ADPKD-URINARY IMPACT SCALE (ADPKD-US)**

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1Otsuka Rockville MD United States, 2Covance San Diego CA United States, 3Department of Medicine UCLA Los Angeles CA United States, 4School of Medicine Emory University Atlanta GA United States, 5Tufts Medical Center Boston MA United States

**Introduction and Aims:** Patient-reported disease burden in ADPKD has not been sufficiently quantified. No instruments have been designed and validated specifically to measure ADPKD-related burden nor health-related quality of life (HRQoL). Based on extensive international qualitative research on patient disease impact, 2 patient-reported outcomes (PRO) instruments were developed:

- ADPKD-IS: captures overall disease impact on a 5-point response scale of 12 questions covering 3 domains (physical, fatigue, emotional)
- ADPKD-US: captures urinary impact on a 5-point response scale with 11 items covering 3 domains (daytime urinary urgency, daytime urinary frequency, nocturia).

Cross-sectional data from a sample of patients in the United States were analyzed to establish reliability and validity of both instruments.

**Methods:** US-English versions of ADPKD-IS and ADPKD-US were administered to 702 adults with CKD (CKD stages 1-5). Reliability and validity of both instruments were examined using confirmatory factor analysis (CFA) to ensure data fit with concepts patients noted as most important in qualitative research, item-response theory (IRT), and classical psychometrics at the item- and scale-level for each instrument/domain. Convergent validity correlations with the SF-12v2 and Brief Pain Inventory – Short Form (BPI-SF) were also examined.

**Results:** CFA confirmed a strong fit of ADPKD-IS and ADPKD-US items with their respective theoretical domains. Internal consistency for all domains ranged from the mid .80s to mid .90s. Finally, convergent validity of the ADPKD-IS and ADPKD-US domains with the SF-12 and BPI-SF domains were appropriately ranged from the mid .40s to mid .60s, and the magnitude of correlations supported interpretation of physical and emotional domains on the new instruments: for example, ADPKD-IS physical domain correlated well with the SF-12 Physical Component Summary (PCS) while the emotional domain correlated well with the SF-12 Mental Component Summary (MCS).

**Conclusions:** This study provides support for reliability and validity of both instruments based on cross-sectional data. The ADPKD-IS provides patient-endorsed and psychometrically strong measures of HRQoL for physical impact, fatigue, and emotional impact and the ADPKD-US provides reliable measures of urinary symptom impact on daytime urgency and frequency, and nocturia. Future research is required to evaluate stability of the instruments over time and their ability to detect true change in symptoms within an individual. Overall, these are encouraging results for ADPKD-specific measures of patient burden.

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**SP211**

**ASSOCIATION OF EXERCISE WITH PROTEINURIA IN A LARGE JAPANESE GENERAL POPULATION SAMPLE**

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1Department of Internal Medicine, Division of Kidney and Dialysis Hyogo Medical College Nishinomiya Hyogo Japan, 2Division of Nephrology and Genistic Medicine Osaka University Graduate School of Medicine Suita Osaka Japan, 3Steering Committee for the “Research on the Positioning of Chronic Kidney Disease in Specific Health Check and Guidance in Japan” Tokyo Japan

**Introduction and Aims:** Exercise habitant is well known to have favorable effect upon metabolic syndrome. And metabolic syndrome might cause proteinuria and CKD. But it remains unknown that exercise habitant have favorable effect upon proteinuria, although heavy exercise sometimes cause proteinuria. Aim of this study is to reveal the effect of exercise habitant upon proteinuria.

**Methods:** This study is cross-sectional cohort study. Subjects were 290213 persons who received the Specific Health Check and Guidance in Japan in Okinawa, Ibaraki, Miyagi,
Simone Warren, Peter Rutherford and Judith Van Den Bosch

Introduction and Aims: EDTA Best Practice Guidelines recommend that all patients should receive education about dialysis options in a structured program which covers all dialysis modalities. However many patients do not receive such education and home dialysis use remains substantially lower than in-centre dialysis in many countries. This study aimed to perform a literature review on the effect of dialysis options education on the patient’s modality choice, and more importantly, to identify effective educational methods and approaches.

Methods: PubMed literature searches (01/01/95- 08/10/12) with main search terms pre-dialysis, peritoneal dialysis, home dialysis, education, information and decision making were performed. 94 of 884 articles returning from the initial search had full text review as they potentially met inclusion criteria (adults, pre-dialysis or dialysis patients, details of education system included). In addition web searches engines were used to examine grey literature e.g. guidelines or experimental reports from CKD clinics. Articles were classified by study design and a detailed examination of educational process and outcomes performed.

Results: Only 30 out of the 94 studies met inclusion criteria - 21 with quasi-experimental design or observational studies, and 9 non-experimental (e.g. narrative review) studies. There were numerous methodological issues – lack of control group, no description of final dialysis choice and lack of detail of the educational process and content. 11 studies presented dialysis modality choice data and all showed an increase in homes dialysis choice vs control group or historical values. Descriptions of the educational process varied and included individual patient and group education, multidisciplinary intervention, varying duration and frequency of sessions, and variation in the roles of the educators (e.g. nurse as case manager). One of the few studies with a strong design, a randomized trial, showed that problem solving group sessions are an effective component of an educational program for enhancing the proportion of home-dialysis choice. The educational techniques and the required educator competencies are considered relevant for effectiveness although poorly defined or studied. There is some evidence from a study in which adult learning techniques were compared with conventional learning methods - the former resulting in a more effective programme (e.g. less infections, better compliance). Timing of education was seen as important but the studies did not allow firm conclusions to be reached over the timing of this start.

Conclusions: Educating patients about dialysis options is important to allow informed decision making but clinical evidence is lacking concerning effective educational methods and staff competencies. There is a need for a standardized approach built on best evidence (also from other clinical conditions) and existing knowledge on the evaluation of complex interventions to ensure good clinical outcomes and allow comparison between units as well as to formally test new educational interventions.

Methods: 205 pts (60.3±13y.) from three dialysis centers completed a battery of validated questionnaires Hospital Anxiety and Depression Scale (HADS), the Verbal Rating Scale (VRS) and Visual Analog Scale (VAS). Clinical and biochemical data (diabetes, obesity) were recorded.

Results: 130 HD patients (63.4%) suffered from chronic pain. Patients with pain (VRS/VAS >1 for >3 months) were on longer maintenance dialysis, showed higher level of PTH, had more depressive symptoms than those without pain (p<0.001). In 6-year period 96 (45.8%) patients died. The most common cause of death was cardiac in 44 (45.8%) patients. In stepwise regression analysis highly depressed patients (>6 points in HADS-D) exhibited a higher mortality (P=0.016), independent of age, diabetes, cardiovascular disease, CRP and albumin level.

Conclusions: Chronic pain, although frequent among HD patients did not lower survival. Depressive symptoms are an important predictor for all-cause mortality in HD patients, with the relationship independent of the nutritional or inflammatory status.
**Abstracts**

**SP215**

**A NOVEL APPROACH TO MANAGING CHRONIC KIDNEY DISEASE: REMOTE MONITORING**

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**Introduction and Aims:** Chronic kidney disease (CKD) is common affecting 5-7% of worldwide & 5-10% of UK & 11.6% of US population with its frequency increasing with age. With an ageing population, the burden of CKD on the healthcare budgets, is increasing and therefore new sustainable service models are required to enable delivery of good quality care to CKD.

**Aim:** Evaluate the impact of a remote, community-based disease management program (DMP) for patients with advanced CKD on disease progression, patient satisfaction and environmental outcomes.

**Methods:** A pilot program was initiated between our hospital (tertiary referral centre) & our local Central Consortium of General Practitioners. All patients with CKD managed in secondary care were selected for the remote management program except i) those on immunosuppressive drugs and ii) those who were likely to need renal replacement therapy within the next 12 months. Patients had an individualized care plan generated by a consultant nephrologist specifying frequency of laboratory (lab) and blood pressure (BP) monitoring, thresholds for escalation of care with appropriate management plan. Laboratory and BP monitoring were performed at the local GP practice. Laboratory data was automatically uploaded to renal IT system whilst BP and clinical data were sent manually to secondary care. The nephrology outpatient consultation was replaced with a telephone consultation with a nurse specialist based at the tertiary centre. Clinical data was collated over 2 years before and 12 months after implementation of the DMP along with a patient satisfaction survey and travel data.

**Results:** There are currently 77 patients under remote management. There was no significant difference between the patients’ eGFR over 2 years before and 12 months after implementation of DMP, with their mean 28.7% (95% CI, 28.27-29.14) & 28.5% (95% CI, 28.14-28.86), respectively. The difference between BF before and after implementation of DMP was not significant. 90% of our survey respondents said they preferred receiving their kidney care in the community and felt more empowered about managing their CKD. The median distance travelled by patients to hospital was 5.4 miles whilst only 0.6 miles to their GP surgery, generating an annual carbon saving of 507 kg CO2 equivalent.

**Conclusions:** CKD is the 17th highest cause of disability worldwide. CKD progresses to ESRD in only about 0.15-0.2% of CKD III patients/year over 10-25 years. The financial cost of CKD care is huge, where Medicare reported expenditures on CKD and one of the ideal predictor of functional nephron number.

**SP216**

**A MILD DECREASE IN RENAL FUNCTION WITHOUT EVIDENCE OF THROMBOTIC MICROANGIOPATHY IS COMMON IN CANCER PATIENTS RECEIVING SHORT-TERM GEMCITABINE TREATMENT**

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**Introduction and Aims:** Gemcitabine (Gem) is a widely used nucleoside analog approved for treatment of several types of cancers. The development of thrombotic microangiopathy (TMA) in patients with advanced CKD on disease progression, patient satisfaction and environmental outcomes.

**Methods:**

**Introduction and Aims:** Chronic kidney disease (CKD) is common affecting 5-7% of worldwide & 5-10% of UK & 11.6% of US population with its frequency increasing with age. With an ageing population, the burden of CKD on the healthcare budgets, is increasing and therefore new sustainable service models are required to enable delivery of good quality care to CKD.

**Aim:** Evaluate the impact of a remote, community-based disease management program (DMP) for patients with advanced CKD on disease progression, patient satisfaction and environmental outcomes.

**Methods:** A pilot program was initiated between our hospital (tertiary referral centre) & our local Central Consortium of General Practitioners. All patients with CKD managed in secondary care were selected for the remote management program except i) those on immunosuppressive drugs and ii) those who were likely to need renal replacement therapy within the next 12 months. Patients had an individualized care plan generated by a consultant nephrologist specifying frequency of laboratory (lab) and blood pressure (BP) monitoring, thresholds for escalation of care with appropriate management plan. Laboratory and BP monitoring were performed at the local GP practice. Laboratory data was automatically uploaded to renal IT system whilst BP and clinical data were sent manually to secondary care. The nephrology outpatient consultation was replaced with a telephone consultation with a nurse specialist based at the tertiary centre. Clinical data was collated over 2 years before and 12 months after implementation of the DMP along with a patient satisfaction survey and travel data.

**Results:** There are currently 77 patients under remote management. There was no significant difference between the patients’ eGFR over 2 years before and 12 months after implementation of DMP, with their mean 28.7% (95% CI, 28.27-29.14) & 28.5% (95% CI, 28.14-28.86), respectively. The difference between BF before and after implementation of DMP was not significant. 90% of our survey respondents said they preferred receiving their kidney care in the community and felt more empowered about managing their CKD. The median distance travelled by patients to hospital was 5.4 miles whilst only 0.6 miles to their GP surgery, generating an annual carbon saving of 507 kg CO2 equivalent.

**Conclusions:** CKD is the 17th highest cause of disability worldwide. CKD progresses to ESRD in only about 0.15-0.2% of CKD III patients/year over 10-25 years. The financial cost of CKD care is huge, where Medicare reported expenditures on CKD and one of the ideal predictor of functional nephron number.

**SP217**

**GFR ESTIMATION BY URINARY SOLUBLE MEGALIN**

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**Introduction and Aims:** Gemcitabine is a widely used nucleoside analog approved for treatment of several types of cancers. The development of thrombotic microangiopathy (TMA) is common amongst cancer patients, particularly in male diabetic recipients who were given higher dose of Gem.

**Methods:**

**Introduction and Aims:** Chronic kidney disease (CKD) is common affecting 5-7% of worldwide & 5-10% of UK & 11.6% of US population with its frequency increasing with age. With an ageing population, the burden of CKD on the healthcare budgets, is increasing and therefore new sustainable service models are required to enable delivery of good quality care to CKD.

**Aim:** Evaluate the impact of a remote, community-based disease management program (DMP) for patients with advanced CKD on disease progression, patient satisfaction and environmental outcomes.

**Methods:** A pilot program was initiated between our hospital (tertiary referral centre) & our local Central Consortium of General Practitioners. All patients with CKD managed in secondary care were selected for the remote management program except i) those on immunosuppressive drugs and ii) those who were likely to need renal replacement therapy within the next 12 months. Patients had an individualized care plan generated by a consultant nephrologist specifying frequency of laboratory (lab) and blood pressure (BP) monitoring, thresholds for escalation of care with appropriate management plan. Laboratory and BP monitoring were performed at the local GP practice. Laboratory data was automatically uploaded to renal IT system whilst BP and clinical data were sent manually to secondary care. The nephrology outpatient consultation was replaced with a telephone consultation with a nurse specialist based at the tertiary centre. Clinical data was collated over 2 years before and 12 months after implementation of the DMP along with a patient satisfaction survey and travel data.

**Results:** There are currently 77 patients under remote management. There was no significant difference between the patients’ eGFR over 2 years before and 12 months after implementation of DMP, with their mean 28.7% (95% CI, 28.27-29.14) & 28.5% (95% CI, 28.14-28.86), respectively. The difference between BF before and after implementation of DMP was not significant. 90% of our survey respondents said they preferred receiving their kidney care in the community and felt more empowered about managing their CKD. The median distance travelled by patients to hospital was 5.4 miles whilst only 0.6 miles to their GP surgery, generating an annual carbon saving of 507 kg CO2 equivalent.

**Conclusions:** CKD is the 17th highest cause of disability worldwide. CKD progresses to ESRD in only about 0.15-0.2% of CKD III patients/year over 10-25 years. The financial cost of CKD care is huge, where Medicare reported expenditures on CKD and one of the ideal predictor of functional nephron number.

**SP218**

**PROGRESSION OF CHRONIC KIDNEY DISEASE IN THE IRISH POPULATION: INITIAL FINDINGS FROM A NATIONAL SURVEILLANCE PROGRAMME**

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**Introduction and Aims:** Chronic kidney disease (CKD) and subgroups who are most likely to progress to an essential part of preventive healthcare,
Abstracts

SP219

HEALTH RELATED QUALITY OF LIFE AMONG PREDIALYSIS CHRONIC KIDNEY DISEASE PATIENTS

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Introduction and Aims: Evaluating health related quality of life (HRQOL) among chronic kidney disease (CKD) patients is important for assessment of their care. It offers unique information for comparing different treatment modalities. The pattern of HRQOL among predialysis patients has received little attention. We aimed to assess HRQOL among predialysis patients using KDQOL-SF™ 1.3 questionnaire after Arabic translation, cultural adaptation, and validation.

Methods: The study included 600 predialysis patients (100 shared in the questionnaire validation) referred to the Main Alexandria University Hospital (serves four EgyptianGovernorate). Those with end stage renal disease, history of blood loss or transfusion were excluded. Clinical and laboratory data were collected. KDQOL-SF™ was administered by interviewing eligible patients. Test re-test reliability and internal consistency were estimated. Discriminant, concept, and construct validity were assessed. HRQOL data was summarized into physical, mental, and kidney disease composite summaries (PCS, MCS, and KDCS), respectively. The influence of the demographic and clinical variables on HRQOL was explored by univariate and multivariate analyses.

Results: All items of KDQOL-SF™ were reliable and reproducible except for three items in the kidney disease targeted scale with Cronbach’s α 0.7. The study questionnaire could significantly discriminate between patients’ subgroups. There was a significant correlation between all items with overall health rate except for work status, sexual function, emotional wellbeing, and role emotional. The correlation between the disease specific items with PCS and MCS was significant for all except the sexual function with MCS. In addition, the majority of the kidney disease targeted items were significantly inter-correlated. Principal component analysis of the disease targeted scale indicated that this part of the questionnaire could be summarized into 10 factors that together explained 70.9% of the variance. Patients enrolled for assessment of HRQOL (52% males, age mean±SD 51±14 years), 28.8% and 71.2% were in stage 3 and stage 4 CKD, respectively. Anemic patients comprised 67.8%. The mean±SD of PCS, MCS, and KDCS were 33.8±6.9, 43.6±7.1, and 60.2±9.0, respectively. In univariate analysis; older, non worker, smoker, and anemic scored significantly lower for PCS, MCS, and KDCS. Female, widow, and advanced stage of CKD had significant lower PCS and KDCS scores. Diabetics and hypertensive had significant lower PCS score. In multiple linear regression, anemia was the only significant variable with the three composite summaries.

Conclusions: The Arabic KDQOL-SF™ 1.3 questionnaire was a reliable and valid tool for assessment of HRQOL. Predialysis patients reported reduced HRQOL specially with anemia.

SP220

BASELINE SERUM URIC ACID LEVELS AND CARDIOVASCULAR OUTCOMES IN PATIENTS WITH CKD

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Introduction and Aims: Hyperuricemia, is highly prevalent in Chronic Kidney Disease (CKD) patients and is associated with cardiovascular (CV) outcomes and mortality.

Methods: Data are drawn from the PIRF registry and from regional mortality and hospital discharges registries. Study outcomes were: occurrence of non-fatal CV events, death due to CV acute events, combination of non-fatal CV events and death for CV events, all-cause death. UA levels were grouped in tertiles, CV death was defined following ICD-10 or ICD-9 codes. CV events included: acute myocardial infarction, ischemic heart diseases and cerebrovascular diseases. Univariate and multiple logistic regression models were carried out to examine the relationship between tertiles of baseline UA levels and each of the outcomes. Multivariate analyses were adjusted for age, gender, baseline CKD stage, all-cause death, diabetes, cholesterol level, urine proteins, blood pressure, previous CV events. Results: 1943 study sample includes 100 patients. Mean age was 70.7±12.8 years, 65.6% males and baseline tertiles of UA levels were: T1=1.5-5.6, T2=5.7-7.6, T3>7.13.8 mg/dl for males; T1=1.2-5.4, T2=5.5-6.8, T3=6.9-12 mg/dl for females. About one third of patients (36.5%) experienced non-fatal CV events, 37.1% combined and 33.1% all-cause death. Patients in the third tertile of UA had a significantly higher risk of non-fatal CV events and of combined outcome compared with patients in the first tertile. This relationship held both in univariate and multivariate analyses. No relationship was found between baseline UA levels and all-cause mortality or mortality for CV acute events.

Conclusions: This study indicates that in CKD patients UA levels exceeding 7 in males and 6.9 mg/dl in females are associated with a significantly higher risk of CV events but not with all-cause death.

SP221

RENAL BIOPSY IN CHRONIC KIDNEY DISEASE: LESSONS FROM A LARGE ITALIAN REGISTRY

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Introduction and Aims: Renal biopsy procedure in patients with chronic renal failure (CRF) may represent a valid tool to help clinicians in clinical practice. However, the use of this invasive method in CRF is variable and it reflects the hospital biopsy policy.

Methods: To better define the CRF-related histological patterns and to assess the clinical utility of this procedure in this extensive group, we analysed biopsy records of 1185 CRF patients living in a large North-Eastern Italian area from 1998 to 2010. Results: Data analysis showed that, although the biopsy incidence rate and the histological features resulted unchanged, the mean age of our CRF patients increased during the study period (R2=0.42, p<0.01). Primary and secondary glomerulonephritides (PGNs and SGNs) were the main histological presentations (53.9% and 23%, respectively). SGNs were over-diagnosed in female. Leading histological types were immunoglobulin A nephropathy (22%), focal segmental glomerulosclerosis (12.4%), membranous glomerulonephritis (MGN, 7.5%) and nephroangiosclerosis (7.3%). These forms were also highly frequent in CRF patients with elevated proteinuria and moderate/severe renal damage. Elderly were primarily affected by MGN. After biopsy, 49.5% of CRF patients with and 34.1% without nephrotic syndrome received immunosuppression therapy.

Conclusions: This study demonstrated that renal biopsy in CRF patients, regardless age and GFR levels, is safe and essential to perform a correct diagnosis and to start a correct therapy. Additionally, it revealed that, even in patients with severe renal damage, it is possible to perform an accurate histological diagnosis and, interestingly, end stage kidney disease seems not to be the primary form.
SP222 TNF-RECEPTOR 2 PREDICTS RENAL OUTCOME IN MILD TO MODERATE CKD IN UNIVARIATE ANALYSIS

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Introduction and Aims: In two recent reports TNF receptor serum levels strongly predicted renal outcome in patients with type 1 and type 2. Of note, TNF receptor levels outperformed almost all established prediction markers and thus have been discussed as a new prognostic biomarker in diabetic nephropathy. However, diabetics are a selected high risk CKD population, thus the predictive utility of TNF receptors remains unknown in other CKD etiologies.

Methods: In the ongoing CARE FOR HOMe cohort study we recruited 444 CKD patients representing CKD stages 2-4 referred to a tertiary center. Unstable clinical status, active inflammatory processes or immunosuppression were exclusion criteria. TNFRII levels were available in 435 / 444 patients, out of whom 48 patients had diabetic nephropathy. TNFRII was measured by ELISA, routine laboratory parameters were analysed by standard methods. GFR was estimated by MDRD equation and clinical parameters were recorded.

Results: At baseline TNFRII was very strongly correlated with GFR (r=0.710; p<0.001) and with albuminuria (r=-0.337; p<0.001). Moreover, significant correlations with CRP (r=0.197; p<0.001) and age (r=0.197; p<0.001) were found. Patients with diabetic nephropathy had significantly higher TNFRII 2 compared to patients with other etiologies (p=0.031). 55 patients experienced the end point; mean follow-up of the remaining was 2.3±1.6 years. In univariate Kaplan-Meier analysis TNFRII 2 predicted renal outcome (p=0.001; cf Figure 1); in step-wise multivariate regression analysis TNFRII 2 (p=0.001; ExpB=61.563) remained a predictor for renal outcome after adjustment for age, CRP and presence of diabetic nephropathy; however after further adjustment for GFR and albuminuria significance was lost (p=0.361).

Conclusions: In the present cohort of patients with mild to moderate CKD, TNFRII 2 predicted adverse renal outcome. Because of its strong co-linearity with eGFR, TNFRII however did not confer additional prognostic information after adjustment for renal function.

SP223 ORAL ANTIDIABETIC THERAPY AND KIDNEY FUNCTION IN THE BERLIN INITIATIVE STUDY

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Introduction and Aims: Diabetes mellitus (DM) is a major cause of chronic kidney disease. Despite the high prevalence of DM in the elderly, data regarding the association of antidiabetic medication with kidney function (KF) in this specific population are scarce. The present study investigates the relationship between DM, oral antidiabetic drugs (OADs) and KF in people ≥ 70 years of age.

Methods: DM patients were participants of the Berlin Initiative Study (BIS). The BIS is a population-based cohort study which was initiated in 2009 in Berlin, Germany, in order to evaluate KF in 2070 participants ≥ 70 years. DM was defined as either HbA1c ≥ 6.5% or prescription of antidiabetic medication. Medication and comorbidities were assessed through personal interviews, clinical and laboratory examinations. For the estimation of glomerular filtration rate (eGFR) the CKD-EPI equation as well as the newly developed, creatinine-based, elderly-specific BIS1 equation were used.

Results: DM in the BIS cohort was prevalent in 539 participants (26%). Of these 145 were on insulin, 314 patients received one or more OADs, and 136 had an elevated HbA1c only. Table 1 displays the main characteristics of the OAD patients and Figure 1 shows the frequency of the different OADs, with metformin (67.2%), gliclazide (26.8%) and glibenclamide (13.7%) being the agents most commonly taken. Patients treated with metformin (n=211) had a slightly higher mean eGFR compared to the total population treated with OADs (69 vs. 66 ml/min/1.73 m²).

Conclusions: Metformin is the most commonly used OAD in the elderly. Interestingly, a few patients received glibenclamide, a medication recently classified as potentially inadequate for the elderly. OAD patients with more intensive glycaemic control (HbA1c ≤ 7%) had a higher prevalence of cardiovascular comorbidities. Finally, we found a clinically relevant difference of eGFR values with BIS1 (57 ml/min/1.73 m²) and CKD-EPI (66 ml/min/1.73 m²).

SP224 MORNING SURGE ON 24-HOUR BLOOD PRESSURE MONITORING MORE PRONOUNCED IN MILD CHRONIC KIDNEY DISEASE

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Introduction and Aims: Non-dipping effect is associated with chronic kidney disease, but little is known about the levels of the morning surge. The aim of our study was to determine the level of morning surge at 24 hour ambulatory blood pressure monitoring in chronic kidney disease and differences between groups with and without morning hypertension.

Methods: Study group consisted of 72 hospitalized patients (38 males and 34 females), with chronic kidney disease (CKD), defined according to K-DOQI criteria. All patient had hypertension and 24 hour blood pressure monitoring was performed. Morning surge was defined as a difference between the hourly systolic blood pressure in the first two hours after waking and the mean systolic blood pressure that included the lowest
blood pressure during sleep. Two groups were defined - a group with morning surge (MS+) where the difference was >55 mmHg and a group without morning surge (MS-), difference of 55 mmHg or lower. The group with morning surge consisted of 12 patients (5 females and 7 males).

Results: Patients from (MS+) group were significantly older than (MS-) group (58.3±9.5 vs 47.±13.8, p=0.04). Target blood pressure was achieved in only 16% pts in (MS+) group and in 36% in (MS-) group. Neither the mean daily systolic blood pressure (153.8±24 vs 131.1±18 mmHg, p=0.02), nor mean nighttime blood pressure (53±13 vs 153±57.2±68 mmHg) differed significantly in both groups. The MS+ group had preserved nightly dipping (13.4±6.9% vs 6.5%±2.4%, p=0.043) and non-dipping was present in 50% of patients in (MS+) group vs 75% in (MS-) group. Serum creatinine was significantly lower in (MS+) group (163±56 vs 247±95 mmol/l, p=0.001) than during HD filtration rate (eGFR) are factors of increased cardiovascular risk and general morbidity. Until now, data on prevalence of chronic kidney disease (CKD) in Poland were based on the PolNef study conducted in one specified region. The aim of the NAPROMOL 2011 study was to assess prevalence of CKD, albuminuria and decreased eGFR in a representative sample of adult Polish citizens.

Methods: The study was conducted on a representative sample of 2413 of adults in Poland (1245 females – F, 1168 males – M), aged 18 to 79. The response rate was 66.5%. In each subject a detailed medical history was taken, arterial pressure and anthropometric parameters were measured, blood and urine samples were taken. The concentration of serum and urine creatinine was measured with an enzymatic method, whereas urine albumin concentration was measured with an immunoturbidimetric method. Urine albumin concentration was measured once in a morning urine sample. CKD was diagnosed for eGFR (estimated with abbreviated MDRD formula) < 60 ml/min/1.73 m2 or eGFR<60 ml/min/1.73 m2 with coexisting albuminuria (albumin-to-creatinine ratio: M >17 mg/g, K >25 mg/g).

Results: Prevalence of CKD in adults in Poland aged 18 to 79 years was 9.0% (7.8-10.4, CI 95%) and is higher in males (8.5% vs M 9.6%, p=0.194). It increases with age and in the age group 18 to 39 equals 4.0% (F 3.7%; M 4.2%; p=0.416), 40 to 59 years - 8.9% (F 7.6%; M 10.2%; p=0.117). The highest prevalence was observed in the age group 60 to 79 years - 19.8% (F 18.2%; M 21.9%, p=0.136). The prevalence of decreased eGFR (F 3.5% M 7.1% p=0.002) and increases across the age groups (18-39: 3.8%, 40-59: 7.9%, 60-79: 12.6%). It is higher in males in the age groups 40 to 59 and 60 to 79 to 7.6% vs 6.3%, and 18% vs 7.8%, respectively. In the age group 18 to 39 years is almost as frequent as in females (F 3.7% M 3.8%, p=0.542). Albuminuria is found 2.5 times more frequent than decreased eGFR (<60 ml/min/1.73 m2) and its prevalence is comparable with results from other countries.

Conclusions: Prevalence of CKD in population of adults in Poland aged 18-79 years is high and comparable with other countries in Europe and worldwide. Data prove CKD to be an essential problem and burden to public health in Poland.
Methods: The subjects of this study were 2017 Japanese individuals (885 men, 1132 women, mean age 63 years) without a history of kidney disease participated in local health checkups. The urinary excretion of uric acid was assessed by the uric acid clearance-creatinine clearance ratio (UACr/CCr) in morning spot samples of urine and blood, and was classified into low (UACr/CCr <5.5%), normal (5.5-11.1%), and high group (>11.1%), according to the guideline from Japanese Society of Gout and Nucleic Acid Metabolism.

Results: The mean value of serum uric acid and UACr/CCr was 5.0 ± 1.3 mg/dL and 7.3 ± 5.0%, respectively. The proportions of low, normal, and high group of UACr/CCr were 40.4%, 39.0%, and 20.6%, respectively. In simple regression analysis the UACr/CCr showed a significant negative correlation with serum uric acid in total subjects (r = 0.33, P <0.001). In the subgroup analysis the correlation coefficient between serum uric acid and UACr/CCr was higher in men (r = 0.37), subjects with diabetes (r = 0.46), alcohol consumption (r = 0.40) and renal insufficiency (estimated GFR <60 mL/min/1.73m²) (r = 0.37). Multiple linear regression analysis showed that UACr/CCr was related positively with HbA1c (β = 0.002 and negatively with HBA1c (β = -0.040), body mass index (β = -0.066) and male gender (β = -0.073). Additionally, UACr/CCr showed a positive correlation with serum adiponectin (r = 0.06, P = 0.069) and urinary albumin excretion (r = 0.07, P = 0.001), and a negative correlation with urinary beta2-microglobulin excretion (r = 0.14, P < 0.001). However, there was no significant correlation between serum insulin and UACr/CCr.

Conclusions: This study showed that urinary uric acid excretion plays an important role in the regulation of serum uric acid levels in the Japanese general population and the urinary excretion of uric acid might be affected by various factors including gender, life-style, comorbidities, and renal disorders.

SP229 ASSESSMENT OF LEVEL OF SELF-ESTEEM HEMODIALYSIS PATIENTS IN THREE OUTPATIENTS DIALYSIS CENTERS IN CHILE
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Introduction and Aims: Self-esteem is a good indicator of Mental Health. The "Rosenberg Self Esteem Scale" (RSES), is one of the tools validated for this purpose and has been used since 1965 in more than 53 countries. But we have no studies have evaluated the level of esteem in patients in Hemodialysis (HD), or the possible factors associated with it. Objective: Evaluation of self-esteem and analysis of possible factors that may influence this, in HD patients in outpatient dialysis centers.

Methods: We performed a descriptive cross-sectional study conducted in May 2011. Clinical nurses with more than one year of experience in HD, assessed the level of self-esteem in patients 3 type HD centers in Chile. The patients gave informed consent to participate in the study. RSES was applied consisting of 30 statements of feelings a person has about herself, 5 positive and 5 negative addressed. Graduation has 4 points (1 = strongly disagree, 2 = disagree, 3 = agree and 4 = strongly agree) and assigns the reverse score negatively addressed claims, the theoretical values range from 10 (low self esteem) and 40 (high esteem). It is a self-administered scale where patients mark an 'X' over the alternatives identified. Design is also a specific record that identified the following variables: age, sex, years of HD, patient cohabitation (living alone, living with relatives, lives in Shelter), Vascular Access Type fistula (Native or Prosthetic) or Catheter (temporary or tunneled), dependency patient (Delta Test), hematocrit, albumin, and Kt / V. Statistical analysis of individual variables was performed through a 2x2 contingency table, using the chi-square test for analysis of statistical significance.

Results: We applied the RSES in 150 patients in HD. Estee Level Number (96): Normal 100 (67%), Media 30 (20%), Female 70 (47%) and Male 70 (53%). Gender: Male 79 (52%), Age: 60.9 ± 16.1 years, Time on HD (months) 50 (1-272), Vascular Access: Fistula: 115 (76.5%), Catheter: 35 (23.3%), Hematocrit: 31.5 ± 5.0%, Albumin: 3.8 ± 0.2 g/dl, Kt / V: 1.5 ± 0.4, Cohabitation Patient Lives with relatives: 138 (92%), Live alone: 7 (4.7%), Live House with a partner: 7 (4.7%). The results of self-esteem in patients were Z = -0.71, P = 0.48.

Conclusions: This study showed that urinary uric acid excretion plays an important role in the regulation of serum uric acid levels in the Japanese general population and the urinary excretion of uric acid might be affected by various factors including gender, life-style, comorbidities, and renal disorders.

SP230 THE USAGE OF DRUGS INCLUDING NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) IN PATIENTS WITH CHRONIC KIDNEY DISEASE
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Introduction and Aims: The avoidance of NSAIDs is recommended for most individuals with CKD. The aim of presented study was to characterize patterns of drugs use including NSAID among persons with CKD in Gdansk Nephrology Center in Poland.

Methods: A total of 888 adult participants of the cross-sectional study responded to a questionnaire regarding their use of drugs.

Results: General characteristic of the study group is in the table 1. The most common comorbidities were hypertension, heart failure/ischemic heart disease and diabetes respectively in 71%, 26.2% and 22.9% of the group. The most often drugs used by our patients were: hypotensive agents (67.5%), vitamins (32.8%), statins (27.8%). The average number of drugs received per day was 5. 53.5% of participants used NSAIDs available over-the-counter without a doctor’s consultation The main causes of using NSAIDs were: bone and joint pains for 25.6% and headache for 25.6% respectively, 24.2% were aware of side effects of NSAIDs. The rest of the study group (75.8%) did not know the side effects or did not answer to this question. Current use (nearly every day for 30 days or longer) of any NSAIDs was reported by 5.3%. 10.1% of the studying population used NSAIDs at least once a week. 7.5% used at least two different NSAIDs simultaneously. The time of CKD was connected with using higher number of drugs (p<0.05) and the frequency of NSAIDs usage was connected with the number of using all drugs (p<0.05).

Conclusions: Patients with CKD use a large amount of drugs. Most of them use NSAIDs often or very often without being aware of side effects of them. It is necessary to systematically repeat the patient’s education concerning potential side effects of drugs.
for each practice, and compared with reported QOF prevalence (QOFP) for the same period. Prevalence was then standardised by age and gender using LabP and compared with deprivation, list size and rurality. Results: The LabP for our population was 5.76% (female 7.24%, male 4.2%), range from 0.11% to 8.29% (IQR 5.19, 6.35). QOFP and LabP are strongly correlated (r=-0.74, p<0.01), but there is a higher variance in QOFP. In 2011, LabP was higher than QOFP by 0.29% (95% CI 0.01, 0.57). In 2012, QOFP rose and the difference was reversed to -0.14% (95% CI -0.41, -0.13). Relative difference ((QOFP-LabP)/QOFP) was correlated to QOFP (r=0.60, p<0.01) but not to list size or rurality, suggesting practices reporting high prevalence rates tend to overestimate and vice versa. Prevalence was strongly correlated with deprivation (r=0.68, p<0.01), but not rurality or practice list size. Conclusions: CKD 3-5 is predominantly a laboratory diagnosis. In 2011, there were 1000 CKD patients not on the register. In 2012, QOFP is similar to LabP, but with significant inter-practice variation. Additionally, some individuals are erroneously labelled with CKD, and may be subject to unnecessary monitoring. Our study reveals a weakness in the QOF registers which can be improved through centralised laboratory reporting. The prevalence of CKD is associated with deprivation which may be due to the 'inverse care law'.

**EFFECT ON UREMIC TOXINS ON OXIDATIVE STRESS CAUSED BY NADPH OXIDASE ACTIVITY**

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Introduction and Aims: A number of cardiovascular diseases in chronic renal failure patients are characterized by increased concentration of reactive oxygen species (ROS). However, the link between genesis of cardiovascular complications, uremic toxicity and increased oxidative stress in patients with chronic kidney disease is not well-understood until now. In this study, we investigated the effect of seventy eight known and commercial available uremic toxins on the enzymatic activity of the lymphocytic NADPH oxidase.

Methods: Lymphotoocytes were isolated, lysed and incubated with NADPH in the presence and absence of the uremic toxin of interest. The degradation of NADPH by the lymphocytic NADPH oxidase was quantified by determination of the absorbance at 340 nm. Additionally, we investigated the effects of plasma on the NADPH oxidase activity.

Results: Thirty nine of seventy eight known uremic toxins showed an effect on the NADPH oxidase activity. Thirty five of the uremic toxins decreased the NADPH oxidase activity. Orotic acid has been characterized as the strongest inhibitor of the NADPH oxidase. Four of the investigated uremic toxins increased the NADPH oxidase activity. SDMA showed the strongest stimulating effect. Plasma from CKD patients before dialysis and the resulting hemolipotite showed a significant inhibitory effect on the NADPH oxidase activity. Plasma after dialysis did not show any effect on the NADPH oxidase activity. Discussion: Uremic toxins with stimulating effect on the NADPH oxidase activity seem to contribute to cardiovascular disease directly. On the other hand the inhibitory uremic toxins may fulfill a direct protective function in the development of the cardiovascular damage in patients with renal failure.

Conclusions: The results of the study demonstrate that uremic toxins may play an important role in the pathogenesis of the cardiovascular complications in chronic kidney disease by modulation of the NADPH oxidase activity.

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**SP233 SERUM URIC ACID LEVEL AND LONG TERM SURVIVAL IN DIALYSIS PATIENTS**

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Introduction and Aims: Recent studies suggest that high levels of uric acid (UA) may play an important role in developing hypertension, renal disease and cardiovascular events [1-4]; also elevated serum UA level may lead to chronic and end stage renal disease [5-6]. Concerning the effect of UA on glomerular filtration rate (GFR), it has been found that serum UA levels are independently connected with reduction of GFR and also contribute to an increased risk for cardiovascular disease and morbidity [7-8]. Further, it has been shown that there is a 1-shaped relationship between UA levels and mortality in chronic kidney disease patients [9]. Aim of the study was to examine whether dialysis patients baseline serum UA level predicts long term survival.

Methods: The study was performed after approval of the protocol by the Regional Ethical Review Board, Linköping, Sweden. 33 dialysis patients (29 male and 4 female, mean age 71±12 years) were followed during mean follow-up period of 24 months (1 - 45 months), 5 of them were treated with allopurinol. To estimate the effect of baseline serum UA level on survival, Kaplan–Meier analysis was performed. Grouping was made according to patients' mean baseline UA level 5.75 mg/dl (342 mmol/l), the range was 3.36-8.64 mg/dl (200-514 mmol/l).

Results: During the follow-up 22 patients died, 3 were transplanted and 8 survived. Analysis showed significant difference between survival in the two groups during follow-up. Survival was significantly higher in the group where patients mean baseline serum UA level was below 5.75 mg/dl (342 mmol/l). Figure 1 Survival analysis of dialysis patients participated in the study (log-rank test = 5.14; p=0.03).


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**SP234 PATIENTS OVER 75 YEAR FOLLOWED IN PREDIALYSIS CLINIC. GERIATRIC ASSESSMENT**

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Introduction and Aims: In patients older than 75 years with chronic kidney disease (CKD) stages 4 and 5, followed in pre-dialysis clinic, it is important to consider which patients could be benefit by treatment with dialysis (Intention to Treat with Dialysis (ITT)), and which patients would be better treated with Conservative Care (CC). For evaluation of patients, we introduce geriatric concepts including frailty phenotype. The aims of the study were the assessment and follow up of patients over 75 years, introducing geriatric concepts, and identify factors that could help us make decisions about treatments.
Methods: Our study was performed in 56 patients older than 75 years, the median time of follow up was 25 months (range 12-48). At baseline we analyzed: The frailty, it is defined by Linda P. Friend, as a clinical syndrome in which three or more criteria were present: "unintentional weight loss, self reported exhaustion, weakness, slow walking speed, an low physical activity". Those with two characteristics were prefrail. Other parameters analyzed were: Age, comorbidity, dependence for activities of daily living, cognitive impairment, depression, cardiovascular disease, and the presence of diabetes. With this assessment and in accordance with the patients and families, we classified patients on (CC), and patients with (ITD). In a longitudinal study we evaluate clinical and laboratory parameters, and re-evaluate the frailty, number of hospitalization, and mortality.

Results: Of the 56 patients, 20 patients were included for (CC), and 36 patients with (ITD). On univariate analysis, the predictive factors to determine (CC) were: Age, pre-frailty, cognitive impairment, and dependence for activities of daily living. In multivariable regression: Age (OR=1.25, CI 95%, 1.04-1.52, p=0.018) and pre-frailty (OR 17.6 CI 95%, 3.16-97.96, p=0.001), remained as independent predictors factors of the choice of (CC). We compared both groups during the follow up. Surprisingly the patients with ITD were more inflamed. (CRP 10 (2-150) vs 4 (1-10) mg/L; p=0.004). There was no significant differences in nutritional biomarkers, except cholesterol levels, which were lower in the patients with ITD (184 ± 40 vs. 206 ± 50 mg/dl; p=0.005), “inverse epidemiology”. 220. The Hb was higher in patients on CC (12.9 ± 0.5 vs. 12 ± 1.2 gr/dl, p=0.018), with the same erythropoeitin per week. The number of hospitalization was higher in patients with ITD. In survival analysis there were no significant differences.

Conclusions: The state of frailty in elderly patients with chronic kidney disease stages 4 and 5, lead to nephrologists to make decisions about treatment. Conservate treatment may be a good option in the aging populations.

Introduction and Aims: Despite increasing awareness of chronic kidney disease (CKD) burden, epidemiological data from many regions are still lacking. There are no data on CKD prevalence in Croatia, and our aim was to analyse it in rural Croatian area including endemic nephropathy (EN) villages using 4 different formulas to estimate GFR.

Methods: In this cross sectional survey we have enrolled 1573 subjects (consecutive sample, participation rate 91%, mean age 51.80±17.09). Subjects were from EN villages (N=1226) and from non-EN area (N=347). GFR was estimated using 4 formulas (C-G, MDRD, MCQE, CKD-EPI), and albumin/creatinine ratio were determined from nephrotic syndrome and/or renal dysfunction. The aim of this study was to analyze those patients with two characteristics were prefrail. Other parameters analyzed were: Age, comorbidity, dependence for activities of daily living, cognitive impairment, depression, cardiovascular disease, and the presence of diabetes. With this assessment and in accordance with the patients and families, we classified patients on (CC), and patients with (ITD). In a longitudinal study we evaluate clinical and laboratory parameters, and re-evaluate the frailty, number of hospitalization, and mortality.

Results: Of the 56 patients, 20 patients were included for (CC), and 36 patients with (ITD). On univariate analysis, the predictive factors to determine (CC) were: Age, pre-frailty, cognitive impairment, and dependence for activities of daily living. In multivariable regression: Age (OR=1.25, CI 95%, 1.04-1.52, p=0.018) and pre-frailty (OR 17.6 CI 95%, 3.16-97.96, p=0.001), remained as independent predictors factors of the choice of (CC). We compared both groups during the follow up. Surprisingly the patients with ITD were more inflamed. (CRP 10 (2-150) vs 4 (1-10) mg/L; p=0.004). There was no significant differences in nutritional biomarkers, except cholesterol levels, which were lower in the patients with ITD (184 ± 40 vs. 206 ± 50 mg/dl; p=0.005), “inverse epidemiology”. 220. The Hb was higher in patients on CC (12.9 ± 0.5 vs. 12 ± 1.2 gr/dl, p=0.018), with the same erythropoeitin per week. The number of hospitalization was higher in patients with ITD. In survival analysis there were no significant differences.

Conclusions: The state of frailty in elderly patients with chronic kidney disease stages 4 and 5, lead to nephrologists to make decisions about treatment. Conservate treatment may be a good option in the aging populations.
Results: Data of patients are presented in table 1. On univariate analysis UACR was associated with 25(OH)D (P<0.001) and cystatin C (P<0.006). Also 24hUA was associated with 25(OH)D (P<0.01) and cystatin C (P<0.01). With multiple regression analysis included variables: 25(OH)D, age, cystatin C, hs-CRP, 24hAPP, smoking, diabetes) UACR was associated with 25(OH)D (P<0.009) and cystatin C (P<0.012).

Conclusions: Albuminuria (urinary albumin/creatinine ratio, 24-hour urinary albuminuria) is associated with 25-hydroxyvitamin D and cystatin C in patients with CKD.

**SP239 FREQUENCY AND SIGNIFICANCE OF QT PROLONGATION AND QT DISPERSION IN CHRONIC RENAL FAILURE PATIENTS**

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Introduction and Aims: Cardiovascular mortality is high in chronic renal failure patients. Most studies have been reported that increase in QTc interval and QTc dispersion are risk factors that predispose to severe ventricular arrhythmias and sudden death. The aim of this study was to evaluate the frequency and predictive value of QT, QTc, QT dispersion (QTD) and QT corrected dispersion (QTD-c) in chronic renal failure patients, included or not in chronic dialysis program.

Methods: On 46 patients (46 male 40.3±1.6 years) with CRF we analysed QT, QTc interval with 12 lead electrocardiogram, QT dispersion, assessed the difference between minimum and maximum QT. 6/46 patients (13%) had QT max interval (>450 ms). After correction of QT interval, using Frederic`s formula (QTc), 19 patients (42%) had QT prolongation (>450 ms).

Results: Linear regression analysis showed that QTc prolongation is statistically significant correlated with number of years of renal failure (r=0.52), serum concentration of potassium (r=0.51) and calcium (r=0.37). QTd and QTd-c were in normal range 45±13.91 ms and 49±15.77 ms resp.

Conclusions: Despite the high incidence of QTc prolongation in these patients (42%), QTd and QTd-c were normal and short-term consequences are not as severe as those in cardiac patients. This is possibly explained by the different pathogenic mechanisms of arrhythmias in CRF when electrolyte disorders are the main cause for the development of arrhythmia.

**SP240 STRATEGIES TO PREVENT KIDNEY DAMAGE IN HOSPITALIZED PATIENTS: A SYSTEM THAT PROTECT PATIENTS FROM NEPHROTOXIC DRUGS AND CONTRAST MEDIA STUDIES**

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Introduction and Aims: More than 50% of hospitalized patients present some degree of renal failure. During their hospital stay these groups of patients are more suitable to receive a greater amount of drugs (i.e. older age and have more comorbidities) and underwent interventional studies. Both conditions increase the risk of kidney function damage together with an increase in patient morbidity and hospital length of stay. In daily clinical practice the opportunity to take actions in order to prevent kidney damage by an adequate prescription of medicines (i.e. dose) or hydration for prevent contrast media injury are limited. Our aim was to design, develop and implement an alert system that at bedside and in real time will inform about those medicines prescribed that will require dose adjustment and a correction proposal together with information regarding prophylactic measures to prevent kidney damage by contrast media depending of the patient renal function (MDDR-4).

Methods: The program was developed in collaboration with the departments of informatics, pharmacy and nephrology. Our center in a 900 beds facility and attend a population of 450,000 inhabitants. Initially the system was applied in patients admitted to internal medicine department during one month period in order to stabilize the requirements and suitability of the system. Then the program was extended to all hospitalized patients.

Results: During this period there were 330 admissions and in relation to the degree of kidney damage we observed: 72.1% has stage-2 CKD, 34.3% had stage-3 and 10% had stage-4+5. The number of patients that were receiving medicines suitable of dose adjustment was 264 (80%). Of these patients the amounts of medicines per patient (mean) that require dose adjustment were: 2.1 for stage-2, 3.3 for stage-3 and 4.2 stage-4+5. In this period the number of patients that were programmed for a contrast study were 21 (6.4%) all of them had stage-3 CKD.

Conclusions: This system allowed to detect instantly those patients that will require dose adjustment of nephrotoxic drugs and prophylactic actions to prevent renal damage.
damage caused by contrast media. These actions will decrease the morbidity and adverse events associated with kidney damage. At least in hospital settings the technology permits the development of cost-effective actions against chronic kidney disease.

**SP241 FASTING THE MONTH OF RAMADAN FOR PATIENTS WITH CHRONIC KIDNEY DISEASE: IMPACT ON KIDNEY FUNCTION AND CARDIOVASCULAR OUTCOMES**

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**Introduction and Aims:** Nephrologists all around the world are frequently asked by their muslim CKD patients for opinion about the medical feasibility of fasting. Fasting Ramadan is a religious obligation for Muslims who represent 20% of the world population. Fasting entails abstinance from eating and drinking for periods that may exceed 18 hours with the possibility of dehydration and hyperviscosity posing risks of deterioration of kidney function and vascular thrombosis of already diseased vessels. Little is known about the safety of fasting for these patients and the risk factors reflecting on their renal and cardiovascular health during fasting. This study was designed to follow CKD patients during fasting and disclose the outcomes relating to kidney functions and major adverse cardiovascular events on the short and medium term as well as factors influencing these outcomes.

**Methods:** This cohort study followed CKD patients with stable kidney function who chose to fast the month of Ramadan after being warned about possible hazards. Patients who chose to fast were urged to discontinue fasting in the face of any significant change of kidney function. A group of non-fasting CKD patients served as controls. Serum creatinine was recorded at the beginning of the month, after one week fasting, at the end of the month and 3 months later. Clinical data and follow up for major cardiovascular events were recorded (defined as acute coronary syndrome, stroke or acute peripheral vascular disease).

**Results:** Patients completing follow up of 52 fasting months and 54 non-fasting controls were included (mean eGFR 27.7, S.D. 13 and 21.5, S.D. 11.8 ml/min/1.73m² respectively). A rise of serum creatinine was noted during fasting in 60.4% of instances by day 7 which was associated with intake of RAAS antagonists (RR 2.9, 95% CI 1.2-3.5, P=0.002) and diuretics (RR 1.6, 95%CI 0.9-2.9, P=0.048) but lower in those on calcium channel blockers (RR 0.6, 95CI 0.3-0.9, p=0.014). Significant rise of serum creatinine (>30%) was seen in 9 instances and was once again associated with RAAS blockade (RR 8.3, 95% CI 1-62, P=0.006). Creatinine returned to baseline in most fast patients by the end of 3 months of follow up and remained elevated in only 12 patients, not significantly different from controls, p=0.17. Adverse cardiovascular events were observed in 6 patients in the fasting cohort all of whom had experienced worsening of kidney function after the first week of fasting (p=0.009) and 5 of whom had also pre-existing cardiovascular disease (RR 15, 95%CI 2-115, p=0.001). On the other hand only 1 event was recorded in the control group, p=0.036.

**Conclusions:** Among CKD patients, fasting was associated with deterioration of kidney functions that was associated with RAAS inhibitors and diuretics and was largely reversible. Adverse cardiovascular events occurred more frequently in fasting CKD patients particularly those who exhibited an early rise of serum creatinine and those with pre-existing cardiovascular disease.

**SP242 PRE-DIALYSIS CARE AND RATE OF PROGRESSION OF RENAL DISEASE: EXPERIENCE OF AN OUTREACH RENAL PREDIALYSIS SERVICE**

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**Introduction and Aims:** The number of patients with Chronic Kidney Disease (CKD) is rising and is associated with significant morbidity and mortality. The annual acceptance rate for renal replacement therapy in the United Kingdom is also rising steadily (1). Patients with advanced CKD have an increased cardiovascular risk that is rising and is associated with significant morbidity and mortality. In the Kidney Disease Outcomes Quality Initiative (KDOQI) classification system of CKD, preparation for renal replacement therapy has been recommended in CKD stage 4 with the estimated glomerular filtration rate (eGFR) to <30 ml/min. The term ‘pre-dialysis’ has not been officially defined in guidelines. However, most renal physicians will initiate pre-dialysis care in patients with an eGFR <15–20 ml/min. At our renal unit, patients are referred for pre-dialysis care with an eGFR < 20ml/min for optimization of treatment and patient education.

**Methods:** All patients who were referred to the pre-dialysis team with an eGFR < 20ml/min from 2010-2012 at a satellite outreach renal clinic were included. Data was collected retrospectively. The rate of renal disease progression and other important biochemical parameters over a 24 month period were recorded. The prevalence of diabetes and hypertension in this cohort were also reported.

**Results:** A total of 81 patients were included in data analysis who remained in pre-dialysis care. eGFR at time of analysis was 13.9 (mean) and 14 (median). At 12 months previously eGFR was 16.2 (mean) and 16 (median) at 24 months eGFR was 22.6 (mean) and 20 (median). Therefore, rate of renal disease progression was 4.4ml/ year (mean) and 3ml/year (median). The monthly rate of renal disease progression being 0.36 ml/month (median) and 0.25ml/month (median). Table: Renal progression: eGFR and serum creatinine (Cr) valuesA total of 30 patients went to dialysis during this period (24 haemodialysis and 6 peritoneal dialysis) and 10 patients died while on pre-dialysis care without reaching end stage renal disease (not included in this analysis).

**Conclusions:** Management of severe CKD requires a well organised and patient-focused multidisciplinary approach. Optimal pre-dialysis care can maintain the residual renal function for longer and delay progression and the need for renal replacement therapy. Therefore, specialised pre-dialysis care leads to improved quality of life for these patients and also have economic benefits.

References:


**SP243 KEEP IN INDIA**

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**Introduction and Aims:** Kidney diseases are increasing all over the world and in India, because of increasing burden of Type 2 Diabetes & Hypertension. Once the patient goes into CKD stage 5, Dialysis &Transplantation are available only for a minority of these patients, which is an economic burden to the family, society &Nation. The rest 90% are dying of CKD. The only solution to this is prevention of kidney diseases.

Screening & early detection of kidney disease & awareness programmes are definitely helpful to prevent progression of kidney diseases. Aim of the study 1. To find out the prevalence of kidney diseases in Northern districts of South India 2. To find out newly detected kidney diseases by screening programmes 3. To evaluate the usefulness of awareness classes in local language.

**Methods:** A prospective study conducted over a period of 1 year from June 2011 to July 2012. Screening camps were conducted in different districts of North Kerala with the help of socially active clubs. Detailed history, BP, BMI, Urinalysis for protein, microalbumin, blood, WBC were done. Serum uric acid was checked for those with Diabetes, Hypertension or BMI>25. All those with abnormal urinalysis will be called to nephrology OPD for further evaluation and treatment. Along with screening camps awareness classes regarding various aspects of kidney diseases were given. Before the class awareness among the people regarding kidney diseases were tested using preformed questionnaires. The same population were interviewed after 3 months to assess the improvement in awareness.

**Results:** During the last 1 year, 4840 people were screened. Male to female ratio was 1:1.7. Age group - <20years - 5%, 20-40 years - 21%, 40-60 years - 49%, >60 years - 25%. Prevalence of kidney disease as detected by any urinary abnormality was 12.3%. Of this, only 4.8% were already known to have kidney disease. Commonest urinary abnormality was proteinuria (6%) followed by microalbuminuria (15%). Of the 12.3% of patients with urinary abnormalities, 76% were with type 2 DM, 34% were with hypertension and the rest with other causes. Kidney disease awareness status was 24.8% before and 90% are dying of CKD. The only solution to this is prevention of kidney diseases.

**Introduction and Aims:** The incidence of end stage renal disease (ESRD) is increasing in Egypt. Furthermore, the etiology of ESRD in North Africa including Egypt is mainly interstitial nephritis, glomerulonephritis and diabetes mellitus. All are mostly preventable. The early detection and prevention of progressive CKD is the principle way to reduce the burden of these chronic NCDs in our developing countries through...
management of risk factors and interventions aimed at slowing the development and or the progression of CKD. To achieve such a goal a successful screening program for CKD is a need.

Objectives: Educational: To educate house-officers the principles of research in the field of prevention of NCD’s. Scientific: - To estimate the prevalence of chronic kidney disease, hypertension, diabetes and obesity in Alexandria Region which includes four governorates, as a representative for the whole Egyptian population. - To identify some possible risk factors that might play a role in the occurrence of CKD with the final aim of recommending a program for its prevention and control.

Methods: The cross section study was carried in Alexandria Region. Population based screening program for proteinuria, hypertension, diabetes and obesity was conducted. A representative sample (around 2000 persons) was considered to cover the four governorates of Alexandria Region. Trained house officer physicians were responsible for screening their adult family members and neighbors collecting the general information on the subject’s demographic data, diet, smoking, herbal use, alcohol and recreational drug consumption, caffeine exposure, analgesics and physical activity.

Screening campaigns were also performed to complete the allocated sample. Data about family and medical history for kidney disease, high blood pressure, diabetes and cardiovascular disease and, if any, current treatment, were also recorded. Physical examination was also performed for the whole screened population including the following: weight, height, waist and body mass index (BMI), blood pressure. Investigations included the followings: Urine protein concentration, serum creatinine concentration, fasting plasma glucose (FPG), fasting plasma cholesterol (FPC) and triglycerides.

Results: The prevalence of chronic kidney disease varied from 2-21%, diabetes reached up to 12%, hypertension exceeded 40% and obesity reached up to 83% in some regions in Alexandria Region- Egypt. The risk factors including smoking, drinking water, herbal use, dietary habits and others were found to be correlated with the occurrence of CKD and other NCD’s.

Conclusions: Similar projects could be applied in different universities to raise the awareness among junior staff about NCD’s prevention and control as well as to screen the whole country.
Introduction and Aims: In patients with chronic renal failure, secondary hyperparathyroidism (sHPT) sometimes requires parathyroidectomy. Prospectively, we compared total parathyroidectomy without autotransplantation and without thymectomy (tPTX) with subtotal parathyroidectomy with thymectomy (sPTX) for renal hyperparathyroidism.

Methods: From 11/2004 to 11/2008, 43 consecutive patients with sHPT were prospectively randomized to receive either tPTX (22 patients) or sPTX (21 patients). Patients were followed for a median of 36 months (11-62 months). Outcome parameters were parathyroid hormone (PTH), calcium, phosphate, alkaline phosphate (AP), vitamin D use, bone mineral density (DXA) and coronary calcification (Agatston score).

Results: PTH reduced PTH significantly lower than sPTX (17 vs 71 pmol/L; p=0.03). After a median of 36 (11-62) months after tPTX, serum calcium was measured with 2.15±0.23 mmol/L vs. 2.31±0.24 mmol/L (p=0.04) after sPTX. During the immediate postoperative period, the need for active vitamin D supplementation was higher after tPTX (12.20±9.24 μg/week) compared to sPTX (6.67±6.95 μg/week). There was no difference in reduction of AP (tPTX: preOP 159 ± 155 U/L, postOP 59 ± 16 U/L; sPTX preOP 174±101 U/L, postOP 71±27 U/L), reduction of serum phosphate (tPTX: from 1.52±0.55 to 1.59±0.5 mmol/L; sPTX: from 1.51±0.47 to 1.23±0.39 mmol/L), postoperative mortality (tPTX: 4/22 patients died after a median of 13.5 (6-42) months postOP; sPTX: 4/21 patients died after a median of 23 (7-52) months postOP), postoperative longterm dosage of vitamin D (cholecalciferal after tPTX: 7222±3610 μg/week; sPTX: 3373±228 μg/week), bone mineral density nor in the Agatston score of the coronary arteries. Bone mineral density improved similarly in both groups. The preoperative Agatston-Score was high in both groups and stayed high throughout the whole observation period: tPTX preOP 1869±2458, postOP 2865±5865; sPTX preOP 6999±11758, postOP 6854±15414.

Conclusions: tPTX is as safe as sPTX. tPTX is more effective than sPTX in reducing PTH. Immediately after tPTX, serum calcium is lower than after sPTX requiring a higher dose of active vitamin D. After both operations, tPTX as well as sPTX, bone mineral density increased and the otherwise expected progression of coronary calcification did not occur. Parathyroidectomy may stop vascular calcification.
Table: Mean change in fasting soluble vitamin levels from baseline to Weeks 12 and 24 (N=110,050)

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Baseline</th>
<th>Change (Week 12)</th>
<th>Change (Week 24)</th>
<th>Baseline</th>
<th>Change (Week 12)</th>
<th>Change (Week 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (µg/ml)</td>
<td>4.09</td>
<td>0.08</td>
<td>4.20</td>
<td>0.20</td>
<td>0.08</td>
<td>0.20</td>
</tr>
<tr>
<td>25(OH)D (nmol/L)</td>
<td>75.60</td>
<td>-0.50</td>
<td>75.10</td>
<td>-0.50</td>
<td>75.10</td>
<td>-0.50</td>
</tr>
<tr>
<td>T(µg/ml)</td>
<td>36.08</td>
<td>0.78</td>
<td>35.30</td>
<td>-0.18</td>
<td>35.18</td>
<td>-0.18</td>
</tr>
<tr>
<td>E (µg/ml)</td>
<td>32.04</td>
<td>2.29</td>
<td>55.24</td>
<td>62.15</td>
<td>55.24</td>
<td>62.15</td>
</tr>
<tr>
<td>K (µg/ml)</td>
<td>0.82</td>
<td>0.01</td>
<td>0.83</td>
<td>0.00</td>
<td>0.83</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Conclusions: PA21 did not affect systemic exposure to selected concomitant medications, based on AUC0-24 and AUC0-t. The small differences in Cmax with losartan, furosemide, omeprazole and digoxin may be partially explained by a known food effect on these drugs.

**Introduction and Aims:** Evidence suggests that serum phosphate (P) is associated with a host of adverse clinical consequences. Despite dietary restriction and phosphate binders, a sizable proportion of patients with kidney disease have serum P > 4.0 mg/dL. A previous report in Italian subjects suggested that serum P is 15-20X serum P and that a chitosan loaded chewing gum may reduce salivary and serum P. We conducted a series of clinical trials to characterize salivary P and establish the effect of this chewing gum on serum P in CKD.

**Methods:** Pilot investigations were conducted in patients with various levels of kidney function from normal to ESRD to characterize salivary P concentration and its diurnal variation. Subsequently, two clinical trials were conducted: 1) a randomized double-blind placebo-controlled 4-week trial in 91 subjects with ESRD with an open label extension and 2) an open label 2 week trial in 147 subjects with eGFR 20-45 ml/min with a randomized standard of care extension.

**Results:** In 99 subjects with kidney function ranging from >90 to >20 ml/min, there was NO correlation between eGFR and salivary P. Mean salivary P was 19.8 mg/dL in those with eGFR<90 ml/min and 18.3 mg/dL in those with eGFR > 20 ml/min. Eleven subjects with CKD were given diets of known P content and were observed as inpatients over the final 24 hours of each diet. There was no effect of diet on salivary P however a diurnal variation was seen in salivary and serum P. Salivary P was highest in the late night/early morning while serum P was highest in the early morning and in mid-afternoon. The randomized placebo controlled trial in subjects with ESRD given 20 mg chitosan gum BID (n=31) or 40 mg chitosan gum BID (n=31) over 4 weeks showed no significant difference in salivary or serum P between active and placebo (n=30) subjects. However during the post wash-out open label randomized phase in which all subjects were given 20 mg chitosan gum TID, a significant decrease in mean serum P -0.24 mg/dL was observed (p=0.03). In the multi-site open label clinical trial, 147 subjects were given 20 mg chitosan TID for 2 weeks, there was a statistically significant reduction in serum P (-0.13 mg/dl, p=0.009). After a 2 week washout, subjects who had a fall in their serum P during the open-label phase were then randomized to chitosan chewing gum or standard of care. During this 2 week randomized extension, a significant difference was observed between serum P among those chewing versus not chewing (p=0.03).

**Conclusions:** We have conducted a series of trials in North American subjects demonstrating that salivary P is approximately 5X serum P and that there is no correlation between eGFR and salivary P. Chitosan containing chewing gum did not reduce salivary P at any level of kidney function but was effective in reducing serum P in subjects with ESRD during an open-label extension and reduced serum P significantly in subjects with CKD, having an effect size similar to that seen with stringent dietary P restriction.

**Introduction and Aims:** Phosphate retention/hyperphosphatemia is a common finding with advanced kidney function impairment and also plays an important role in mineral bone diseases and vascular calcifications. Little is known if hyperphosphatemia can be an indicator for renal replacement therapy (RRT) initiation. The aim of this study was to assess the association of phosphate concentration before and at initiating hemodialysis in patients either with critically-ill acute kidney injury or with chronic renal failure in uremic stage.

**Methods:** This was a retrospective observational study at an inpatient hemodialysis unit of a tertiary medical center enrolling 385 adult advanced renal failure patients during Apr. 2010 to Oct. 2010. Among them, 148 patients were recognized to be the first-time dialyzed by nephrologists’ clinical judgments upon currently well-accepted indications for RRT initiation (azotemia, acidosis, fluid overload, hyperkalemia and uremic encephalopathy).

**Results:** The mean age of the 148 patients was 65.6 ± 16.2 years old (range from 18 to 95). The clinical data obtained “at the date indicated for RRT” showed significant
difference compared with data from their paired previous examinations (not yet indicated) by pair’s t-test in hemoglobin (Hb; -0.55 ± 1.80 g/dL, p < 0.001), blood urea nitrogen (BUN: 30.3 ± 3.40 mg/dL, p < 0.001), creatinine (Cr: 1.8 ± 2.17 mg/dL, p < 0.001), estimated glomerular filtration rate (eGFR; -12.59 ± 29.32 mL/min/1.73 m², p < 0.001), sodium (Na: -1.5 ± 7.4 meq/L, p = 0.025), potassium (K; -0.49 ± 1.01 meq/L < 0.001), and phosphate (P; 1.52 ± 2.11 meq/L < 0.001). There was no significant difference in calcium (Ca; -0.12 ± 0.79 mg/L, p=0.76) when used a cut off value of P > 6.00 meq/L (normal limit less than 4.7 mg/L). Hyperparathyroidism was a specificity of 54.7% and a sensitivity of 74.3% to predict the patients of RRT initiation. In contrast, the traditional indicator (anemia with creatinine > 6.5 mg/dL in this study), had only a sensitivity of 54.7% and a specificity of 60.1% to predict. Patients’ underlying diseases including diabetes mellitus, hypertension, coronary artery disease, cirrhosis and malignancy did not show statistical difference in their associated phosphate level when initiating RRT by t-test in SPSS Statistics.

Conclusions: Not only as a result of advanced kidney function impairment, hyperparathyroidism behaves like a marker of illness severity and as an independent predictor of RRT initiation in patients either with critically-ill acute kidney injury or with chronic renal failure in urinary stage.

Vidula Dixit1, Lin Cheng1, John Zhang1, Elizabeth Torkin1, Rajasekhar Jaladi1, Palakshi Obalapur1, Shashidhar Dodda1, Wishu Shrivastava1, Suresh Dama1, Seema Kantak1, Stephen Harrison1 and Steve Doberstein1

Introduction and Aims: Secondary hyperparathyroidism (SHPT) is one of the key contributors to increased risk of mortality in end stage renal disease (ESRD) patients receiving dialysis. Cinacalcet, the only approved calcimimetic for the treatment of SHPT, lowers parathyroid hormone (PTH), calcium (Ca) and calcium phosphate product (Ca × P); however, it suffers from poor patient compliance due to severe gastrointestinal side-effects. With the aim of improving compliance and safety, Nektar’s polymer conjugation technology has been applied to a clinically validated calcimimetic pharmacophore to generate a novel compound, NKTR-228, which can be administered intravenously (IV) and which has a pharmacokinetic (PK) profile consistent with three-times a week administration at the time of dialysis, and with providing coverage over the three day interdialytic period. The core pharmacophore of NKTR-228 is not different between Tx and non-Tx treated subjects (27.6 ±0.3 vs 31.0±6.0, pmol; p n.s.). The table shows the mean values of the parameters evaluated. Nektar showed a negative correlation with Alkaline Phosphatase (r = -0.375; p<0.05) and a positive correlation with FGF23 (r = 0.286; p<0.05) and 25D (r = 0.396; p<0.05). No correlation existed with others parameters.

Conclusions: Renal function does not seem to affect serum levels of Sclerostin in Tx. The negative correlation with AP indicates that Sclerostin maintains its modulatory role of osteoblastic activity in this population. The correlation with FGF23, which is in agreement with low FGF23 in Sclerostin null mice, suggests modulatory effects of both proteins on osteoblasts directly, through Wnt inhibition, for Sclerostin; indirect, through effects on 1,25D levels, for FGF23. Serum Sclerostin may be an additional marker of bone metabolism, useful to understand metabolic pathways in normal subjects and in CRF.

Lida Tartaglione1, Marzia Pascaolo1, Cristina Leonangeli1, Giusy Mandarico1, Maria Luisa Muci1, Silviero Rotondo1, Silvia Silas1 and Sandro Mazzaferrato1

Introduction and Aims: Sclerostin, by inhibiting the canonical Wnt pathway suppresses osteoblast activity and stimulates their apoptosis. Recent evidence has shown a possible role of Sclerostin in alterations of bone metabolism in CKD. In CKD stage 5D serum levels of Sclerostin are higher than in the general population and correlate positively with BMI and bone volume. Little is known about serum levels of sclerostin in non-dialysis CKD patients, and in renal transplant patients (Tx). Aim of our study was to evaluate serum sclerostin levels in Tx in whom no data are available. Methods: We performed a cross sectional observational study in 80 Tx (55±10 y.o.; 49M/31W) with CKD stage 2 4 (eGFR 47±16 ml/min). Thirty healthy subjects (34 ± 12 y.o.; eGFR 95 ± 19 ml / min) were used as control group. We evaluated in all patients Sclerostin, Calcium, Phosphate, PTH, FGF23 and Alkaline Phosphatase (A.P.). Results: Serum levels of Sclerostin were not different between Tx and non-Tx treated subjects (27.6 ±0.3 vs 31.0±6.0, pmol; p n.s.). The table shows the mean values of the parameters evaluated. With mild vitamin D insufficiency (25D: 26±11 ng/mL), transplant patients had normal 1,25D values, mild increment of PTH and Ca, and normal values of P. Serum levels of FGF23 were increased compared to controls (47.3±18.8 vs 30.0±19.0 pg/mL; p<0.05) Sclerostin showed a negative correlation with Alkaline Phosphatase (r = -0.375; p<0.05) and a positive correlation with FGF23 (r = 0.286; p<0.05) and 25D (r = 0.396; p<0.05). No correlation existed with others parameters.

Conclusions: Sclerostin is involved in the metabolic pathways of bone metabolism in renal transplant patients, but further studies are needed to confirm this association. The aim of our study was to evaluate if the use of S. is associated with reduced serum levels of fat-soluble Vitamins (D and K) in patients with end stage renal disease (ESRD).

Methods: In a cross-sectional study of 387 hemodialysis patients (42.1% on S. treatment) from 18 dialysis centers, we determined serum concentrations of: 25 (OH)-vitamin D and several vitamers of the vitamin K complex (vitK1, and vitamin K2 vitamers or menaquinones: MK4, MK5, MK6 and MK7) by high-performance liquid chromatography (HPLC). In addition, routine biochemistry and vitamin K related proteins (osteocalcin, or bone Gla Protein – BGP and matrix Gla protein - MGP), were also determined.

Results: Patients treated with S, compared with non-treated patients, we observed significant differences in serum levels of 25(OH)-vitamin D and of most vitamin K vitamers or menaquinones: MK4, MK5, MK6 and MK7 by high-performance liquid chromatography (HPLC). No correlation existed with others parameters.

Introduction and Aims: Sevelamer (S), a calcium free phosphate binder, is also known for its ability to reduce serum cholesterol due to its binding affinity for bile acids. The aim of this study was to evaluate if the use of S. is associated with reduced serum levels of fat-soluble Vitamins (D and K) in patients with end stage renal disease (ESRD).

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1CNR – Institute of Neuroscience, Aging Section Padua Italy, 2CNR – Istituto di Biomeccanica Reggio Calabria Italy, 3Nephrology Unit University of Padua Padua Italy, 4Nephrology and Dialysis Unit Hospital of Padua Padua Italy, 5Clinica Medica1 University of Pavia, Pavia Italy, 6Nephrology and Dialysis Unit Hospital of Trento Trento Italy, 7Nephrology and Dialysis Unit Hospital San Carlo Borromeo Milan Italy

Introduction and Aims: We determined serum concentrations of 25(OH)-vitamin D and several vitamers of the vitamin K complex (vitK1, and vitamin K2 vitamers or menaquinones: MK4, MK5, MK6 and MK7) by HPLC in 387 hemodialysis patients (42.1% on S. treatment). From 18 dialysis centers, we determined serum concentrations of: 25(OH)-vitamin D and several vitamers of the vitamin K complex (vitK1, and vitamin K2 vitamers or menaquinones: MK4, MK5, MK6 and MK7) by high-performance liquid chromatography (HPLC). In addition, routine biochemistry and vitamin K related proteins (osteocalcin, or bone Gla Protein – BGP and matrix Gla protein - MGP), were also determined.

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Jeff-gao Shin1, Su Hyun Kim1 and Suk-Hee Yu1

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Introduction and Aims: Osteoporosis and its related fractures are a significant cause of morbidity and mortality. Osteoporosis is often accompanied by metabolic syndrome (MetS) and chronic kidney disease (CKD). In this study, we demonstrated the relationship between MetS, CKD and osteoporosis, and investigated the roles of MetS and CKD in the occurrence of osteoporosis in a healthy Korean population.

Methods: Data were analyzed from subjects who visited the Health Promotion Center at Chung-Ang University Hospital, Seoul, Korea from January 2007 to December 2010. The eGFR was calculated using the abbreviated Modification of Diet in Renal Disease (MDRD) study equation. The diagnosis of MetS was made according to the updated guidelines from the American Heart Association/National Heart, Lung, and Blood Institute.
Nephrology Dialysis Transplantation

Both MetS and CKD in males. However, lower bone mineral density was negatively related to an increased prevalence of both MetS and CKD. In females, lower bone mineral density was positively related to decreased BMD. In males, BMI and eGFR were lower in those with decreased BMD (p=0.001 and p=0.012, respectively). In males, both the presence of MetS components and lower eGFR had protective effects on BMD values in both simple and multiple logistic analyses (p=0.021 and 0.161, respectively).

Methods: There is a correlation among MetS, CKD and osteoporosis in both sexes. In females, lower bone mineral density was positively related to an increased prevalence of both MetS and CKD. However, lower bone mineral density was negatively related to both MetS and CKD in males.

Introduction and Aims: For many years obesity has been considered protective against bone loss and osteoporosis especially in women. Serum leptin able to influence bone balance however the physiological mechanism involved remain poorly understood. Hemodialysis patients (HD) display a very high serum leptin, mainly in women and obese people. Despite leptin fulfill the definition of a uremic toxin, its role in physiopathology of bone metabolism has is unclear. The aim of this study was to evaluate in HD patients associations between leptin with anthropometric data and bone histomorphometry.

Methods: Anthropometric, biochemical and hormonal analyses including FGF23, FSH, estradiol, osteocalcin and esclerostin, beyond the transiliac bone biopsy. Exclusion criteria were of liver disease, cancer or steroid used in past 6 months. Men and women were analyzed together and separately, respecting the physiological differences. This study was approved by ethics committee on human research. Data were expressed as median and range and analyzed Spearman’s rank correlation, Mann-Withey test and multiple logistic regression for all patients, respectively. In multiple logistic regression for all patients, PTH was the only variable able to significantly differentiate between females with normal BMD and those with decreased BMD (p<0.001).

Results: 60 dialysis patients - mean age 65 +/- 16 years. 28 men 32 women. 31 black, 20 white. 51 on vitamin D, 5 on calcimimetics, 31 on phosphate binders. Inter and intra-assay CVs were < 2% for both PTH assays at mean concentrations of 41, 105, 131 pg/mL. The results from the two assays were closely correlated (r = 0.98, p < 0.0001). In the dialysis cohort, the intact (second generation) PTH concentration was significantly higher 426 +/- 442 pg/mL compared to biointact (third generation) PTH 266 +/- 251 pg/mL (p < 0.001). Blabd-Altman plot revealed a significant average bias of -60%.

Conclusions: PTH and calcium concentrations are normally very tightly coupled. The inability of intact PTH assays to show a correlation with simultaneous plasma calcium concentrations (r = 0.26, p < 0.05).

Methods: The possibilities of different PTH assays and their results were compared with traditional biochemical parameters in dialysed patients.

Results: The leptin (LEP/BMI) was higher in women (p= 0.019) and only women while esclerostin showed negative influence on bone mineralization. There was no influence of estradiol on these bone parameters.

Conclusions: Our study was the first to show a correlation between leptin and bone microarchitecture in hemodialysis patients. Maybe leptin could be a differential factor in women towards a more robust and reliable PTH assay methodology.

Methods: We studied 55 patients, M:F 38:17, age 72 years (18-87). 17 diabetics, 9 on ACEi/ARB, CKDstage 3/4/5, 15 with SHPT, who received oral paricalcitol in individualized doses, based on serum intact parathyroid hormone (iPTH), Ca and P, for 12 months. Patients having received vitamin D or bisphosphonates within 3 months were then excluded. The possibility of metabolic acidosis was eliminated by means of pH and bicarbonate levels.

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Results: The leptin (LEP/BMI) was higher in women (p= 0.019) and only women while esclerostin showed negative influence on bone mineralization. There was no influence of estradiol on these bone parameters.
months prior to treatment, and those with malignancy were excluded. Three months before and 12 after treatment start we measured, monthly, serum iPTH, Ca, P, and cTnI. Mean weekly paricalcitol dose was higher in CKD3 vs CKD4: 6.2 μg (2.7) vs 3.8 μg (2.7), P = 0.04. Levels were higher in females than males (4.6 ± 0.9 vs 3.9 ± 0.8 mg/dl, P = 0.005). P, cTnI, ALP, and iPTH were higher in CKD4 than CKD3 throughout the study. Males under paricalcitol did not change their serum Ca and P levels significantly but dropped their LDL (102.1 ± 28.2 to 95.8 ± 25.9 mg/dl, P = 0.03). Diabetics had significantly higher serum P than non-diabetics. There was a positive effect on ALB in the ACEi/ARB group (3.7 ± 0.04 to 3.8 ± 0.03, P = 0.02) and their serum Ca remained stable. P in CKD3 and Ca in CKD4 also remained stable. Significant positive correlation between mean weekly paricalcitol dose and end of study iPTH and negative to CKD stage, as well as a significant negative correlation between terminal CCR and P, cTnI, iPTH, anemia and UPROT were observed.

Conclusions: Long-term oral paricalcitol is efficient and safe treatment of SHPT in CKD3–5 patients in daily clinical practice. Renal function remained stable during follow-up. Calcium and/or Phosphate elevations, especially in females CKD4 patients and diabetics, although within normal range, emphasize need for close follow-up, additional dietary counseling and early phosphate-binders administration.

**SP258**

**CASE SERIES OF DENOSUMAB AND ITS EFFECTS ON SERUM CALCIUM LEVELS IN DIALYSIS PATIENTS**

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**Introduction and Aims:** Denosumab is a human monoclonal antibody that inhibits osteoclast formation, function and survival thereby decreasing bone resorption. It is an effective therapy for osteoporosis in post-menopausal women. Its use has not been examined extensively in end-stage renal disease (ESRD) especially in dialysis patients. We report 5 dialysis patients who received Denosumab for osteoporosis. All of them had severe osteoporosis based on DXA scan and high C-Terminal telopeptide (CTX). All patients had secondary Hyperparathyroidism.

**Methods:** We are reporting case series of five dialysis patients who received Denosumab for osteoporosis. Data on serum calcium, PTH, CTX, and DEXA scan has been collected from computerised system. Other clinical data was collected from case notes.

**Results:** Case 1: Seventy seven year old male on peritoneal dialysis was administered a single dose of Denosumab 60 mg subcutaneously (S/C). Serum corrected calcium (Ca) level plummeted from 2.77 mmol/l to 1.58 mmol/l and required hospital admission for intravenous calcium. Patient developed long QT but there were no cardiac arrhythmias. Patient was treated with oral calcium and Alfacalcidol. Case 2: Fifty year old female on maintenance haemodialysis, received two doses of Denosumab 60 mg S/C six months apart. She was hospitalised on both occasions to receive intravenous calcium treatment for symptomatic hypocalcemia. Hypocalcemia took approximately 6 weeks to resolve completely despite optimal treatment. Case 3: Seventy two year old female on haemodialysis had two doses of Denosumab 60 mg S/C six months apart. She developed hypocalcemia on both occasions which was managed with oral calcium and high doses of Alfacalcidol as an outpatient. She had no hypocalcaemic related symptoms on both occasions. Case 4: Fifty five year old male on haemodialysis received single dose of Denosumab 60mg S/C. Serum calcium level dropped but remained within normal limits. Case 5: Sixty four years old female on haemodialysis was given single Denosumab 60 mg S/C dose. Serum calcium level dropped significantly but patient remained asymptomatic. She was managed with oral calcium and Alfacalcidol as an outpatient.

**Conclusions:** Denosumab can cause symptomatic hypocalcemia in dialysis patients. Hypocalcemia is observed in the first few days post Denosumab and takes several weeks to settle completely. Close monitoring of the calcium levels is essential and will help to avoid serious consequences.

**SP259**

**VITAMIN D (25(OH)D AND 1,25(OH)2D3) LEVELS AND ABDOMINAL AORTIC CALCIFICATION IN PATIENTS WITH CHRONIC KIDNEY DISEASE**

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**Introduction and Aims:** Vascular calcification is an independent risk factor for cardiovascular disease, which is the leading cause of death in patients with chronic kidney disease (CKD). Low vitamin D levels might have affected vascular calcification. CKD patients revealed a high prevalence of vitamin D deficiency. The aim of this study was to investigate the abdominal aortic calcification according to vitamin D levels in patients with advanced kidney disease.

**Methods:** We reviewed medical records of the 149 patients with CKD stage III–V at the Daegu Catholic University Medical Center between January 2011 and August 2012. Vascular calcification was evaluated by abdominal aortic calcification 8 scales with lateral spine imaging using plain x-ray. Statistical significance between abdominal aortic calcification score (AACS) > 3 or ≤ 3 and biochemical, clinical, and vitamin D levels was assessed by univariate and multivariate analysis. **Results:** We found a high prevalence of 25(OH)D and 1,25(OH)2D3 deficiency in our patients with advanced kidney disease. Low vitamin D levels might have affected vascular calcification. CKD patients revealed a high prevalence of vitamin D deficiency. The aim of this study was to investigate the abdominal aortic calcification according to vitamin D levels in patients with advanced kidney disease.

**Conclusions:** Denosumab can cause symptomatic hypocalcemia in dialysis patients. Hypocalcemia is observed in the first few days post Denosumab and takes several weeks to settle completely. Close monitoring of the calcium levels is essential and will help to avoid serious consequences.

**SP258**

<table>
<thead>
<tr>
<th><strong>Case</strong></th>
<th><strong>T score</strong></th>
<th><strong>T score</strong></th>
<th><strong>PTH (1.1–6.5 ng/ml/L)</strong></th>
<th><strong>CTX (0.1–0.5 μg/L)</strong></th>
<th><strong>Pre dose (Ca 2.20 – 2.60 mmol/L)</strong></th>
<th><strong>Post dose (Ca)</strong></th>
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<tbody>
<tr>
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<td>-1.3</td>
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<td>Case 2</td>
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<td>-4</td>
<td>105</td>
<td>3.77</td>
<td>2.65</td>
<td>1.88</td>
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**Case 1**

1<sup>st</sup> dose, ** 2<sup>nd</sup> dose
NUTRITION / INFLAMMATION

SP260 PREDICTORS OF NUTRITIONAL RESILIENCE AND EFFECTS OF HOSPITALIZATION ON NUTRITIONAL PARAMETERS IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Malnutrition and protein-energy wasting, as assessed by a combination of several nutritional parameters, are associated with increased morbidity and mortality in hemodialysis (HD) patients. “Nutritional resilience” refers to the maintenance of an adequate nutritional status in the face of stressors such as intercurrent illness and hospitalization. We conducted a retrospective cohort study in incident HD patients with the aims of identifying changes in nutritional parameters around the time of hospitalization, and assessing predictors of nutritional resilience.

Methods: The patient cohort was derived from the Fresenius Medical Care North America database, and included incident patients who 1) started HD between 2007 and 2012, 2) were hospitalized for 7-14 days during this period and 3) started HD >60 days prior to hospitalization and survived >60 days after hospitalization. Only data from the first hospitalization per patient during 2007-2012 were used. To assess temporal patterns of nutritional parameters, serum albumin (Alb), creatinine (Crea), phosphate (P), equilibrated normalized protein catabolic rate (enPCR) and interdialytic weight gain (IDWG) were plotted over 3 months prior to and after hospitalization. Change in albumin (the percent difference between serum albumin within 30 days before admission and within 30 days of discharge) was analyzed by hospitalization diagnosis groupings. Logistic regression was performed to assess factors associated with a decline in albumin >5% after hospitalization.

Results: 31,632 patients were included in the analysis. Prior to hospitalization, most nutritional parameters declined, although there was an increase in enPCR, likely reflecting increased tissue catabolism (Figure). The greatest declines in albumin were observed in hospitalizations for injuries resulting in amputation or fracture (-9.3%) or other musculoskeletal injuries (-8.6%). Statistically significant factors that were “protective” against a >5% decline in albumin were higher creatinine, younger age, non-white race, shorter hospitalization, and cardiovascular disease as a comorbidity.

Conclusions: Worsening of nutritional parameters is observed with hospitalization in the HD population, and the degree of albumin decline varies with type of intercurrent illness and hospitalization. We conducted a retrospective cohort study in incident HD patients with the aims of identifying changes in nutritional parameters around the time of hospitalization, and assessing predictors of nutritional resilience.

SP261 ABNORMAL HIGH-DENSITY LIPOPROTEIN INDUCES ENDOTHELIAL DYSFUNCTION AND HYPERTENSION VIA ACTIVATION OF TOLL-LIKE RECEPTOR-2

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Introduction and Aims: In healthy subjects, high-density lipoprotein (HDL) represents a potent atheroprotective agent mainly by preserving endothelial integrity. However, recent evidence suggests that the vascular effects of HDL can be heterogeneous in different clinical conditions. The aim of the present study was to determine the vascular effects of HDL from patients with chronic kidney disease (CKD) as a population with a dramatically increased risk for cardiovascular events.

Methods: HDL was isolated from CKD patients and respective healthy control subjects using ultracentrifugation. Endothelial nitric oxide (NO) and superoxide production were measured using electron-spin resonance (ESR) spectroscopy. Blood pressure in mice after HDL injection was determined with a tail-cuff approach. Methylarginine levels in serum as well as HDL were measured by ESI-MS/MS. Moreover, we conducted bone-marrow transplant experiments in a cross-cross-design between wildtype (WT) and TLR2-/- mice. eNOS phosphorylation was determined by Western Blot analyses.

Results: We found that HDL from patients with even incipient CKD (HDL-CKD) substantially inhibited endothelial NO production and increased endothelial superoxide production, while HDL from healthy subjects (HDL-Healthy) stimulated endothelial NO production. Notably, after injection into WT mice, HDL-CKD increased arterial blood pressure in vivo. Surprisingly, using ESI-MS/MS we identified symmetric dimethylarginine (SDMA) and not asymmetric dimethylarginine (ADMA) to accumulate in HDL-CKD. By supplementing HDL-Healthy with SDMA, we confirmed SDMA as the culprit mediating the adverse vascular effects of HDL-CKD. Moreover, we newly identified Tolle-like receptor-2 (TLR-2) on endothelial cells as the receptor mediating the adverse vascular effects of HDL-CKD. In addition, we identified a novel intracellular pathway, by which endothelial TLR-2 activation directly reduces endothelial NO bioavailability by inhibiting eNOS activating phosphorylation and stimulating NADPH-oxidase dependent superoxide formation in a TLR-1- or TLR-6 co-receptor independent manner.

Conclusions: These findings indicate that accumulation of SDMA in the HDL fraction of CKD patients substantially deteriorates the vasoprotective effects of HDL. We could document that these effects of HDL-CKD are mediated by TLR-2 via a novel pathway linking innate immunity, endothelial dysfunction and arterial hypertension.

SP262 FACTORS AFFECTING THE RESPONSE TO FERRIC CARBOXYMALTOSE IN NONDIALYSIS CHRONIC KIDNEY DISEASE PATIENTS. THE ROLE OF OXIDATIVE STRESS

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Introduction and Aims: Nearly half of nondialysis chronic kidney disease (CKD) patients respond to iron therapy. Factors affecting anaemia response to iron are not well characterized. Oxidative stress (OS) is a recognized factor for anaemia in CKD and promotes ESA resistance, but their influence to predict the response to i.v. iron in this population has not been evaluated.

Methods: Forty-seven patients with nondialysis CKD stages 3 to 5 (mean eGFR 26 ±10.4 ml/min/1.73 m²) and iron-deficiency anaemia (hemoglobin < 11 g/dL, transferrin saturation < 20% and/or ferritin < 100 ng/mL), received a single injection of 1000 mg of ferric carboxymaltose (FCM) and were followed for 12 weeks. According to the erythropoietic response, defined as a ≥ 2 g/dL increase in hemoglobin level, patients were classified as responders and nonresponders. Baseline conventional markers of iron status (transferrin saturation and ferritin), inflammatory markers (C-reactive protein and IL-6), endothelial adhesion molecules (ICAM, VCAM) and OS markers...
CIRCULATING CELL-FREE DNA LEVELS IN HEMODIALYSIS PATIENTS AND ITS ASSOCIATION WITH IRON METABOLISM, INFLAMMATION AND rhEPO THERAPY

Elísio Costa1,2, Sandra Ribeiro1,2, Maria do Sameiro-Faria3,4, Vasco Miranda1, Alexandre Quintanilha1,5, Elisa Bronza-de-Rocha2,3, Luis Belo2,4 and Alice Santos-Silva1,5

Introduction and Aims: Inflammation is a common feature in hemodialysis (HD) patients, and is usually enhanced in patients who develops resistance to rhEPO therapy. The mechanisms/factors triggering the inflammatory process are still poorly clarified. Recently, it was reported that these patients present high circulating cell-free DNA levels, probably due to the release of DNA from cellular necrosis and apoptosis. The mechanisms of factors triggering the inflammatory process are still poorly clarified. However, the release of DNA from cellular necrosis and apoptosis is a common feature in hemodialysis (HD) patients, and is usually enhanced in patients who develop resistance to rhEPO therapy. The mechanisms/factors triggering the inflammatory process are still poorly clarified.

Methods: We studied 153 HD patients and 20 healthy individuals. The analytical panel included socio-demographic factors, hematological and dialysis adequacy data, iron metabolism and inflammatory markers. The circulating cell-free DNA levels were assessed directly in serum samples, as recently described by Goldstein et al (Ann Clin Biochem 2009; 46:488-94).

Results: We found that HD patients presented a significant decrease in hemoglobin concentration, hematocrit, erythrocyte and lymphocytes counts, and in mean cell hemoglobin concentration, and an increase in mean cell volume, when compared with the control group; significant changes in iron metabolism (a decrease in iron transferin, and an increase in transferrin saturation, soluble transferrin receptor (sTfR), ferritin and hepcidin levels) and in inflammatory markers (a decrease in paraoxonase 1 and an increase in adipopectin, CRP and IL-6). Moreover, patients showed an increase in the circulating cell-free DNA levels when compared with controls. Significant correlations were found between circulating cell-free DNA levels and IL-6 (r=0.333; p<0.001), CRP (r=0.418; p<0.001), iron (r=-0.237; p=0.002), transferrin (r=0.545; p<0.001), sTfR (r=0.357; p<0.001) and rhEPO doses (r=0.284; p=0.001).

Conclusions: Our data suggest that higher bilirubin levels are associated with beneficial effects in HD patients, by improving lipid profile and reducing the inflammatory grade, which might contribute to increase iron availability and protect for CVD. Moreover, we describe for the first time, an association between high bilirubin levels, within the normal range, with higher adiponectin and PON1 activities.

A PRO-INFLAMMATORY CHANGE IN NUMBERS OF MONOCYTE AND DENDRITIC CELL SUBTYPES OCCURS EARLY IN THE COURSE OF CKD

Evie Schepens1, Griet Glaheux1, Tim Van den Abbeel1, Nathalie Nietsyck2 and Raymond Vanholder3

Introduction and Aims: Antigen-presenting cells like monocytes and circulating dendritic cells (DCs) play an important role in the chronic inflammation known to be associated with accelerated cardiovascular disease and immune dysfunction. Both cell types consist of three subpopulations: the monocyte subtypes: CD14+CD16- (classical), CD14+CD16+ (intermediate), and CD14-CD16+ (non-classical) and the subtypes of circulating DCs: myeloid DC1 (mDC1), mDC2 and plasmacytoid DC (pDC). The CD14+CD16+ monocytes are described as the pro-inflammatory subtype and for DCs the mDCs are the ones with antimicrobial activity while pDCs are mainly mediators of antiviral immunity. No study up till now evaluated changes at earlier stages of these cell types in different stages of CKD.

Methods: This study for the first time describes the proportional distribution of the monocytes and circulating DC populations in 198 patients throughout the consecutive stages of CKD and/or on renal replacement therapy (stage 1: n=58; stage 2: n=30; stage 3: n=94; stage 4: n=22; stage 5: n=10; and ESRD 5 on HD: n=7; ESRD 5 on PD: n=11) in comparison to a healthy control group (n=27). Flow cytometric analysis on whole blood was performed. Monocytes were identified based on the pan-monocytic marker CD14 and the 3 subpopulations were distinguished based on CD14 and CD16 expression. For pDC, a specific monoclonal antibody directed against the IL-6 receptor (Milenyi) was applied. Both the absolute numbers and the percentage fraction of the total leukocyte population were evaluated.

Results: Although no difference in the total monocyte number was observed versus control, a significant increase of the CD14+CD16+ monocytes was found from CKD stage 3 (99±17) in 66±36 cells/μl/p to 0.05, which rises further in the following stages up to a threefold rise in patients on HD (149±110 cells/μl/p <0.002). Only in HD patients a significant decrease in number and percentage of CD14+CD16- cells (359±170 vs 379±114 cells/μl/p <0.05 and 3.75±1.92 vs 5.58±2.12%, p <0.01) in combination with an increase in CD14+CD16+ monocytes (11.5±72 vs 50±26 cells/μl/p <0.001 and 1.68±0.97 vs 0.74±0.35%, p <0.01) was found. In patients on PD no changes were observed. The DCs on the other hand were already significantly decreased, by more than 25% from stage 3 onwards. This was mainly attributed to a decrease in pDC. The PD group was the only population in which, next to the pDCs also the number and percentage of mDC1 was decreased (654±3136 vs 1008±3443 cells/μl/p <0.01 and 0.97±0.054 vs 1.10±0.066% p <0.05). An inverse correlation could be found between CD14+CD16+ and the pDCs throughout the consecutive stages (r=-0.17; p<0.02).

Conclusions: An increase in the CD14+CD16+ monocyte subtype and a decrease in the pDC population suggest a pro-inflammatory role for these cells during the progression of CKD. This points to the importance of studying these leukocyte subtypes more in depth in different stages of CKD.
SP266 | DOES BETA-2-MICROGLOBULIN EXERT A VASCULAR DAMAGING EFFECT BY ACTIVATING LEUKOCYTES?

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**Abstracts**

**Introduction and Aims:** Chronic kidney disease (CKD) is characterized by low-grade inflammation and an increased risk for cardiovascular disease. Interest in beta-2-microglobulin (B2M) as a novel marker for peripheral artery disease and cardiovascular outcome both with and without CKD has constantly grown. Several clinical studies suggested that B2M could be actively involved in the pathogenesis of this vascular disease, for which chronic leukocyte activation is a pathogenic factor. In this study, we investigated whether B2M, at concentrations as registered in CKD, is pro-inflammatory by inducing oxidative burst in leukocytes.

**Methods:** Leukocyte oxidative burst was measured at baseline and after stimulation with FMLP, E. coli or PMA (Phagoburst™). Leukocytes were separated from whole blood by density gradient centrifugation and leukocytes were stimulated with 100 nM FMLP or 5 x 10^6 E. coli or PMA or 100 ng/mL LPS. B2M concentrations of dialysates were assessed by ELISA.

**Results:** Free radical production after leukocyte activation and should be seen as a marker rather than as a consequence of leukocyte activation.

**Conclusions:** B2M, a traditional marker for middle molecule retention and a novel marker for peripheral artery disease and cardiovascular outcome, does not by itself influence the inflammatory response by induction of free radical production after leukocyte activation and should be seen as a marker rather than as a culprit.

SP267 | RESISTIN LEVELS AND PROTEIN ENERGY WASTING OF PATIENTS WITH CHRONIC KIDNEY DISEASE; IS THERE ANY INTERACTION?

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**Abstracts**

**Introduction and Aims:** The aim of this study was to evaluate the levels of adiponectin in chronic kidney disease patients and the change in serum levels of these peptides in patients with Protein Energy Wasting (PEW).

**Methods:** 150 patients (89 male, 61 female) with mean age of 45.4 ± 15.9 years, without active infections or chronic inflammatory conditions were recruited into the study. Study group consisted of 30 patients with normal kidney function (serum creatinine level of 0.75 ± 0.14 mg/dL), 30 patients with chronic kidney disease (CKD) stages 1 and 2 (n=30) and dialysis group (n=60).

**Results:** Serum levels of resistin were significantly higher in patients with PEW compared to control patients (p<0.01). Serum levels of adiponectin were significantly different between patients and controls (p<0.001), as well as in all four groups (p<0.001). The levels of resistin and adiponectin were significantly higher in patients in stage 1 and 2 of CKD than in patients with normal kidney function and in patients with stage 3 of CKD (p<0.05). The levels of resistin and adiponectin were significantly different between patients and controls (p<0.01). Serum levels of resistin were significantly higher in patients with stage 1 and 2 of CKD than in patients with stage 3 of CKD (p<0.05).

**Conclusions:** Serum levels of resistin were found to be independent risk factors of oxidative stress in early stages of type II diabetic nephropathy.

SP268 | MATRIX METALLOPROTEINASE-2 IS ASSOCIATED WITH OXIDATIVE STRESS IN PATIENTS WITH EARLY STAGES OF TYPE II DIABETIC NEPHROPATHY

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**Introduction and Aims:** Matrix metalloproteinase-2 (MMP-2) is considered to be the main enzyme that degrades col IV and has been implicated in chronic kidney disease (CKD) and cardiovascular disease (CVD). The evolution of oxidative stress from early stages of renal function decline is not fully clear. The concentration of 15-F2t-IsoP (15-F2t-IsoP) in serum has been considered to be a reliable biochemical index of oxidative stress in patients with cardiovascular disease.

**Methods:** CKD patients of stages 1 and 2 with type II DN (n=30) were included. Patients with active inflammatory disease or malignancy were excluded. As controls, there were two groups, patients with diabetic type II without CKD (n=15) and healthy individuals (n=15). Clearance (Cl-) and albumin excretion (AER) were examined in the 24h urine, MMP-2 and 15-F2t-IsoP levels were measured by an ELISA method. Intima media thickness (IMT) of carotid and femoral arteries and atherosclerotic plaque were determined by a high resolution ultrasonography.

**Results:** There were significant differences in the studied parameters between patients and controls (p<0.01) as well as in all four groups (p<0.01). The levels of MMP-2 and 15-F2t-IsoP were significantly higher in patients than in controls (p<0.01). Further, MMP-2 levels were independent correlates of oxidative stress, IMT as well as of atherosclerotic plaque (p<0.01).

**Conclusions:** This study suggests that serum levels of MMP-2 were found to be independent risk factors of oxidative stress in early stages of type II diabetic nephropathy.
Methods: Male Wistar rats (386±40 g) underwent one-side kidney nephrectomy to induce experimental model of CKD. Animals were further assigned to 3 different diets protocol: RD – regular with fructose concentration <3%, F10 – 10% fructose in drinking water and F60 – 60% fructose as pellets (Harlan). After 8 weeks of experiment serum concentration of creatinine (Cr), fructose (F), uric acid (UA), soluble intercellular adhesion molecule (sICAM) and homocysteine (Hcy) were measured. Additionally protein to creatinine ratio (PCR), N-Acetyl (D)-Glucosaminidase (NAG) to urinary creatinine ratio (NAG/Cr) and MCP-1 to urinary creatinine ratio (MCP-1/Cr), as well as urinary uric acid excretion (UAe) and sodium excretion (NaE) in a 24-hour urine collection were assessed. Creatinine clearance (CrCl) was calculated upon Cockcroft-Gault formula.

Results: Animals didn't differ in total calories intake per day between groups at the end of diet protocol. Results are presented as mean ± SD in Table 1.

Conclusions: Increasing dietary fructose consumption in unipennected rats was associated with prominent increase of systematic inflammatory mediators as HCY, proteinuria and increased uric acid and sodium excretion in urine. These factors may contribute in further progression of CKD.

Introduction and Aims: Oxidative stress is prevalent in many diseases and is considered to be an important pathogenic mechanism. Uric acid plays a special role in processes of oxidative stress, and the available evidence regarding the antioxidant role of uric acid. Gout is a disease caused primarily by chronic hyperuricemia and inflammation. 30-50% patients with gout have renal involvement. It is known as increase of products of oxidative stress among patients with chronic kidney disease (CKD). Taking it into account, exploration of oxidative stress is very important for patients with gout with or without CKD.

Methods: We had compared products of oxidative stress in 19 healthy persons and 2 patients with gout with or without CKD.

Results: Kruskall-Wallis ANOVA test has showed significant difference of LPO, TAS, SOD between controls and patients The MDA level in both groups of patients reliably didn’t differ from group of control. Products of oxidative stress and antioxidant activity in patients and control group

In comparison to controls all patient groups had significant elevated LPO, p<0,01, compared to T0 in both the HS and CKD. The same trend was also seen in the group CKD compared to T0 in both the HS and CKD.

Conclusions: In patients with gout, there is an increase of oxidative stress and antioxidant activity change. And it does not depend on the presence of CKD in patients.
**SP273** ADMINISTRATION OF N-ACETYLCysteINE CAUSES BENEFICIAL POSTTRANSLATIONAL MODIFICATIONS OF TRANSTHYRETIN IN HEMODIALYSIS PATIENTS

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**Introduction and Aims:** The thiol antioxidant N-acetylcysteine (NAC) may mediate interactions with protein-associated cysteine residues, however, information on protein level in vivo is missing. Therefore, in the present study we aimed to analyze N-acetylcysteine-induced modifications of the protein transthyretin (TTR) in plasma from hemodialysis patients in a randomized, placebo-controlled study in vivo and analyze administration to plasma in vitro. TTR was selected due to its low molecular weight and the free cysteine residue in the polypeptide chain, which is known to be extensively modified by formation of mixed disulfides.

**Methods:** Plasma levels of TTR were determined by a non-commercial enzyme-linked immunosorbent assay (ELISA) using polyclonal rabbit anti-human TTR antibodies. Spectra of immunoprecipitated TTR were obtained using an AutolysExpsed matrix assisted laser desorption ionization-time of flight (MALDI-TOF) mass spectrometer (Bruker Daltonik, Bremen, Germany). The samples were analyzed in triplicates. For ionization, a desorption matrix containing 30% of a-Cyano-4-hydroxycinnamic acid (CHCA) was used and 1500 ng spot per well spotted. For spectra calibration an external standard was used. Spectra were evaluated using the software flexAnalysis. TTR variants were expressed as relative amounts of the summed intensity of all observed TTR variants.

**Results:** The administration of NAC during a hemodialysis session resulted in a substantial increase of native TTR from median 15% (range 8.8-30%) to median 40% (37-50) and a reduction of S-cysteinylated TTR [51% (44-60) vs. 6.6% (2.4-10)]. Additionally the pronounced formation of a TTR-NAC adduct was detected. However, all these modifications seemed to be reversible. Additionally, in vitro incubation of plasma with NAC confirmed the in vivo results and indicated that changes in PTM pattern of TTR were a function of NAC concentration.

**Conclusions:** We conclude that the interaction of N-acetylcysteine with proteins may alter protein functions due to beneficial modification of cysteine residues in hemodialysis patients.

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**SP274** ACTION OF NICOTINIC ACID ON ADIPONECTIN, LEPTIN AND PLASMINOGEN ACTIVATOR INHIBITOR 1 PRODUCTION AND EXPRESSION IN 3T3-L1 ADIPOCYTES UNDER OXYGEN DEPRIVATION

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**Introduction and Aims:** Obesity has been considered one of the major contributors to the current global mortality and morbidity. Recent studies suggest the dysregulation production of adipokines is partly responsible for obesity linked cardiovascular diseases. The aim of this study was to investigate the effect of nicotinic acid (NA) on adipokines production and expression in 3T3-L1 adipocytes before and after hypoxia.

**Methods:** The mature adipocytes were pretreated with NA for 24h and induced by hypoxia for different periods. Levels of adipokin in medium and total hypoxia inducible factor-1 alpha (HIF-1α) were quantified using ELISA. Adipokines expression was assessed by real time PCR.

**Results:** Adipocytes treated with NA had lower leptin production in comparison to spontaneous production (6.6±2.6 vs 170.24 ± 31.41pg/mL, p<0,05) and NA treatment (146.5 ± 48.0 pg/mL vs 653.8 ± 142.3 pg/mL) comparing to spontaneous expression (9915±7467 vs. 10,650 ± 2,447 pg/mL, p<0,05). Real time PCR showed a raise of adiponectin mRNA in adipocytes treated with NA in comparison to spontaneous expression (9915±7467 vs 890±94). We also observed NA treatment reduced PAI-1 expression in comparison to spontaneous expression (1,440 ± 1,670 vs 1,16 ± 0.27 pg/mL, p<0,05). NA increased adiponectin production during hypoxia (18,8±4,07 vs 1,16±0,27 pg/mL, p<0,05). NA increased the production of adiponectin comparing to spontaneous production (1,42±0,62 pg/mL, p<0,05) and NA treatment 4h:8h:12h:17.1±11.5pg/mL). It was observed a decrease of leptin levels in cells pretreated with NA compared to cells submitted to periods of hypoxia (4h:6,4±1.3 pg/mL vs 9,85±6.9pg/ mg/mL; 8h:7,9±4,8 pg/mL vs 15,3±5,7pg/mL; 12h:7,7±3,7 pg/mL vs 17,1±1,6 pg/mL, p<0,05). Our results showed an increase on Plasminogen Activator Inhibitor 1 (PAI-1) production in adipocytes under hypoxia (4h:3,3±1.67 pg/mL vs 8h:3,0±1,71 pg/mL; 12h:4,6±1,77 pg/mL) compared to spontaneous production (4,1±2,62 pg/mL, p<0,05) and NA treatment (1,16±0,27 pg/mL, p<0,05). NA increased the production of adiponectin comparing to spontaneous production (18,8±4,07 vs 11,0±1,0 pg/mL, p<0,05). Pretreatment with NA increased adiponectin production during hypoxia (4h:5,5±5,77 pg/mL vs 7,92 ±0,6312h:3,4±1,77pg/mL). HIF-1α increased in adipocytes submitted to oxygen deprivation (4h:3,68±4,35 pg/mL; 8h:4,80±3,80 pg/mL; 12h:653,8±142,3 pg/mL) comparing to spontaneous production (170,24 ± 31,41pg/mL, p<0,05) and NA treatment (146,5 ± 48,0 pg/mL, p<0,05). We also observed a reduction of HIF-1 in cells pretreated with NA and submitted to hypoxia in comparison to cells under oxygen deprivation (4h:1,59±3,97 pg/mL vs 3,68±4,35 pg/mL; 8h:20,9±74 pg/mL vs 480±3,80 pg/mL; 12h:317,11±49,0 pg/mL vs 653,8 ±142,3 pg/mL, p<0,05). Real time PCR showed a raise of adiponectin mRNA in adipocytes treated with NA in comparison to spontaneous expression (9915±7467 vs 890±94). We also observed NA treatment reduced PAI-1 expression in comparison to spontaneous expression (1,10±1,13 vs 1,46±0,80, but didn’t exert effect on spontaneous leptin. Hypoxia, in all periods, increased the leptin and PAI-1 expression and decreased adiponectin expression.

**Conclusions:** In adipocytes pre-treatment with NA blunted the production of leptin and PAI-1 production and expression, in spontaneous conditions and under hypoxia. Adiponectin production and expression increased under nicotinic acid treatment. The translation of such “in vitro” nicotinic acid benefits to the clinical setting should be object of future studies.
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SP277 PREDICTORS ASSOCIATED TO LOWER LIMB ULCER IN PATIENTS WITH CHRONIC RENAL FAILURE

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Introduction and Aims: Lower limb ischemia in dialysis patients is frequent and clinically relevant: this event influences quality of life, physical activity and life expectancy. The aim of this study was to investigate risk factors associated to the occurrence of ischemic foot ulcers, considering variables from three main domains: clinical, laboratory and therapy.

Methods: This retrospective cohort observational study was based on data recruited from the clinical monocentric database of Nephrology and Dialysis department of Alessandro Manzoni Hospital in Lecco. All incident patients who started dialysis between 1.1.1999 and 29.2.2012 were enrolled and followed until 15.5.2012; temporary guests, patients with acute renal failure or with previous limb ischemia or amputation were excluded. Multivariate Cox regression analysis was performed in two steps: firstly identifying relevant covariates from each domain, and then matching them in a final model. We used time-dependent approach to take into account the evolution of some prognostic factors during the follow-up.

Results: 526 uremic patients were recruited; 120 of them developed a lower limb ischemic lesion after a median survival time of 13 months. In the final model the main predictors significantly related to an increased risk of lower limb ulcer occurrence were age (Hazard Ratio, HR=1.07 for each year increase), gender (HR=1.96 male vs female), diabetes (HR=4.67), ischemic cardiopathy (HR=2.21), iron therapy (HR=4.55), anticoagulant drugs (HR=3.91), calcium based binders (HR=2.54), blood phosphorus (HR=2.70) and triglycerides (HR=1.20) levels.

Conclusions: Incidence rate of lower limb ulcers was higher in the early follow-up. Some modifiable predictors like calcium-based binders, phosphorus and triglycerides levels were independently associated to this phenomenon, in addition to the well-known role of diabetes. Iron therapy could have a pathogenic role but further studies are needed to explore better this aspect.

SP278 RELATIONSHIP OF NUTRITIONAL STATUS AND BIOIMPEDANCE PHASE ANGLE USING WHOLE BODY AND CALF MEASUREMENT IN HEALTHY SUBJECTS

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Introduction and Aims: Whole body (wBIS) and calf (cBIS) bioimpedance spectroscopy are non-invasive and relatively simple techniques to measure body composition and fluid volume in healthy subjects (HS) and patients. Phase angle (PA) measured by wBIS is a good parameter to assess nutritional status (Francis D. et al J. Physiol. 2010). The aim of this study was to evaluate correlation of wBIS and cBIS methods and their ability to reflect amount of muscle mass in healthy subjects.

Methods: Multifrequency bioimpedance spectroscopy Hydra 4200 (Xitron Technologies, Inc, San Diego, CA) with frequencies from 5 to 1000 kHz was used to examine body composition and fluid volumes in healthy subjects (HS) age (40 – 80 years). Each subject was measured by wBIS (wrist to ankle) and cBIS (Zhu et al Physiol Meas, 2008), PA at 50 kHz was obtained from the raw data by wBIS (w_PA) and by cBIS (c_PA) measurements respectively. Extra (Re) and intracellular (Ri) resistances were obtained from wBIS and cBIS to calculate extra- (ECV) and intracellular (ICV) fluid volumes, respectively. Total body muscle mass (TBMM) was calculated using a published model (Kaysen et al Am J Clin Nurt 2005). Linear regression was used to assess the relationship between w_PA to c_PA, TBMM to w_PA and c_PA and w_PA to age. Serum albumin (S_Alb) was used as a nutritional marker. Demographic and anthropometric data were obtained and recorded.

Results: Sixty four HS (age: 54±10 years, 37 females, weight: 78±15 kg) were studied. w_PA and c_PA (r2=0.6) were correlated. TBMM correlated with both w_PA and c_PA. Age was negatively correlated with w_PA (figure 1). Albumin level was 4.5±0.3 g/dL; albumin levels correlated with both w_PA and c_PA (r2=0.2, p<0.01) and (r2=0.3, p<0.01), respectively.

Conclusions: The good correlation between w_PA and c_PA suggests that calf phase angle can assess the total body nutrition status. Since the calf is more uniform in body composition than the whole body, calf measurement might provide nutrition information with less error. In addition, measurement of the calf segment can be useful for the subjects who have a pacemaker or metal implants in their bodies.

SP279 THE CLINICAL IMPACT OF PLASMA LEPTIN LEVELS IN A COHORT OF CHRONIC KIDNEY DISEASE PATIENTS

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Introduction and Aims: Recent research has clarified the relationship between adipokines, metabolic syndrome (MS) and cardiovascular disease (CVD). The results of animal and clinical studies have revealed a positive relationship between leptin and vascular smooth muscle cell counts and calcification, arterial rigidity, carotid thickness and the incidence of CVD. However, despite leptin fulfilling the definition of a uremic toxin, its exact role in chronic kidney disease (CKD) has yet to be determined. The objective of the present study was to investigate putative links between leptin, MS and clinical outcomes by evaluating biochemical and clinical parameters (including vascular calcification scores, inflammatory and bone markers and overall and cardiovascular mortality) in a cohort of stage 2–5D CKD patients.

Methods: On hundred and forty-two CKD patients (stages 2–5D) participated in this study, followed at least 20 months, at our University Medical Center.

Results: Leptin was negatively correlated with the glomerular filtration rate (GFR), total adiponectin (TAdip) and high-molecular weight adiponectin and positively correlated with age, waist circumference, body mass index (BMI), aortic calcification score (ACS), C-reactive protein (CRP), triglycerides, insulin and parathormone (PTH). Leptin and insulin were significantly correlated with the MS score. The BMI, insulin, MS score and PTH were independent predictors of leptin levels (P = 0.002, 0.016, 0.028 and 0.017, respectively). Leptin, insulin and TAdip were independent predictors of the presence of MS (P = 0.05, 0.04 and 0.04). However, leptin levels were not significantly predictive of the clinical outcomes.

Conclusions: Our study was the first to demonstrate a significant, independent link between leptin and MS (but not clinical outcomes) and PTH in patients at different CKD stages. Future studies will have to assess the involvement of leptin in MS and clinical outcomes in CKD, and the potential modulation of leptin by PTH.
Introduction and Aims: Cardiovascular disease is common in CKD patients and is the most frequent cause of death. Diabetic CKD patients are at especially high risk for cardiovascular mortality. PWV assesses arterial stiffness and is a predictor of both mortality and cardiovascular outcomes. Some studies suggest that vascular injury is so advanced at the diastolic stage that the response to some interventions, like statin treatment, is quite poor. Finding predictors of vascular stiffness in earlier stages of CKD in diabetics may identify potentially modifiable risk factors for adverse cardiovascular outcomes. To identify predictors of PWV in a prospective cohort of diabetic non-dialysis CKD patients.

Methods: This is a cross-sectional analysis of a prospective cohort of seventy seven diabetic CKD patients (53 males, 24 females, mean age 63.9 ± 12.9 years). 40 laboratory parameters potentially related to cardiovascular risk, echo-cardiogram and carotid-femoral PWV (Sphygmocor) were prospectively assessed. CKD stage distribution among those patients was 8 (11%) stage 1, 23 (34%) stage 2, 21 (28%) stage 3A, 16 (16%) stage 3B, 4 (6%) stage 4 and 2 (3%) stage 5. Albuminuria 30-300 mg/g Cr was present in 36 patients (52.3%), 300-1000 in 17 (26.6%) and >1000 in 11 patients (17.2%).

Results: Mean carotid femoral PWV was 12.84 ± 5.1 m/sec. Higher than expected for age values were observed in 38 (49.4%) patients. A univariate analysis showed that PWV had a significant positive correlation with age (p<0.0001), systolic blood pressure (p=0.009), left ventricular ejection fraction (p=0.0495), urinary creatinine (p=0.0025), valvular calcification (p=0.0246) and a close to significant correlation with urinary protein/creatinine ratio (p=0.0575). A negative correlation was with serum vitamin E (p=0.0140) and serum phosphorus (p=0.0270). A multivariate analysis using those variables yielded a model with an r²=0.44. Age (p=0.0053), urinary protein/creatinine ratio (p=0.0118) and serum vitamin E (p=0.0473) significantly and independently contributed to predict PWV in this model. Every 1% increase in serum vitamin E is associated with a 1.7% reduction of the mean PWV.

Conclusions: To our knowledge, this is the first study showing that proteinuria and low serum vitamin E values are associated with high PWV; indicating higher vascular stiffness, in early CKD diabetic patients. Prospective studies should explore whether nutritional vitamin E supplementation improves arterial stiffness in this context.

Introduction and Aims: Dipeptidyl peptidase-4 (DPP-4) is an enzyme which mainly degrades incretins such as glucagon like peptide-1 (GLP-1) and is altered in a variety of inflammatory disorders. DPP-4 and GLP-1 receptor are abundantly expressed in the kidney cells. We have recently found that DPP-4 inhibitors ameliorate vascular injury in diabetic rats by blocking the harmful effects of advanced glycation end products (AGEs). However, how circulating DPP-4 level is regulated remain unknown.

Methods: We examined anthropometric and metabolic variables, including AGES are independently correlated with circulating DPP-4 levels in 432 consecutive outpatients. We further investigated the effects of AGES on DPP-4 in cultured human renal proximal tubular epithelial cells (RPTECs).

Results: Mean serum AGES and DPP-4 levels in our patients were 8.96±2.5 U/mL and 520±33.9 ng/mL, respectively. Multiple regression analysis revealed that female (p<0.001), HDL-cholesterol (p<0.001), HbA1c (p<0.001), and serum AGES (p<0.03) were independent determinants of DPP-4. In vitro, AGES significantly increased DPP-4 expression in RPTECs and stimulated the secretion of soluble DPP-4, both of which were completely blocked by an anti-oxidant N-acetylcyesteine.

Conclusions: These present results suggest that AGES may stimulate renal DPP-4 expression via oxidative stress, which could partly explain for the positive association between serum DPP-4 and AGES.
compare the diagnostic performance of the different index tests of UAC and ACR for random urine samples, for detecting microalbuminuria in diabetic patients.  

Methods: We systematically searched PubMed, MEDLINE, and Scopus for English publications from the earliest available date of indexing through 31 Jul 2012, for clinical studies assessing either UAC or ACR of random urine sample as a diagnostic test to evaluate diabetic patients for the presence of microalbuminuria. We used a hierarchical summary receiver operating characteristic curve analysis. 

Conclusions: The area under the curve was 0.91 (0.88 to 0.93) and 0.94 (0.91 to 0.95) for UAC and ACR, respectively. No difference in sensitivity (P = 0.70), specificity (P = 0.63), or DOR (P = 0.59) between UAC and ACR was found. Figure 1 shows hyperglycaemia, renal tubular cells undergo selective ubiquitination of specific target proteins. Here, we describe a urinary pattern of DN-specific ubiquitinated proteins (Ub-prot) that may open new perspectives into understanding of the DN pathophysiology and could serve to monitor the progression of renal damage. 

Introduction and Aims: T2D, the most common metabolic disorder worldwide, represents a leading cause of chronic kidney disease in developed countries with 20–40% of T2DM patients (pts) expected to ultimately develop ESRD. We previously reported an increased release of free ubiquitin in urine of T2D pts with biopsy-proven diabetic nephropathy (DN) and further demonstrated that, when exposed to high glucose, renal tubular cells undergo selective ubiquitination of specific target proteins. Here, we describe a urinary pattern of DN-specific ubiquitinated proteins (Ub-prot) that may open new perspectives into understanding of the DN pathophysiology and could serve to monitor the progression of renal damage. 

Methods: Urine samples from 20 normoalbuminuric (NORMO), 20 microalbuminuric (MICRO) and 20 macroalbuminuric T2D pts (DN), were collected. Each sample was concentrated and protein content was assessed spectrophotometrically. Five-hundred micrograms urine proteins from each group were pulled then Ub-prot were purified with a specific anti-ubiquitin antibody. An aliquot of the samples was analysed by 1D-SDS page and Coomassie-stained to highlight all Ub-prot (lys-63 and lys-48), another aliquot was immunoblotted using Ub-lys63 specific antibody. Coomassie gel and blotted filters were compared to recognize lys63 and lys48 Ub-prot. The most relevant DN-specific bands were then excised, trypsin digested and identified by MALDI TOF/MS. Finally the Ub-prot dataset was employed for a bioinformatics pathway analysis. 

Results: Ubiquitome analysis revealed a remarkable increase of Ub-prot in urine of DN pts. Ub-prot were almost absent in urine of NORMO pts and slightly visible in MICRO pts. Most of the proteins were detectable only in urine of DN pts. Some lys63 Ub-prot matched those found in tubular cells cultured under high glucose. Bioinformatic analysis revealed their involvement in cytoskeleton rearrangement (i.e. β-actin), extracellular matrix expansion (i.e. alpha-collagen) and metabolic pathways (i.e. Histone Methyltransferase). 

Conclusions: We demonstrated that the progression of the renal damage in T2D correlates with an increased excretion of Ub-prot. Comparative analysis suggests that part of the Ub-prot may have tubular origin and their urine excretion could reflect the impaired intracellular signaling activated by the hyperglycaemic stimuli. The identification of all the Ub-prot and the analysis of this protein network will serve to better understand the pathophysiology of the renal damage in T2D and, potentially, to set up non invasive tests for diagnosis and prognosis.
mg/24h) or high-normal albuminuric (UAE≥11.0 mg/24h) based on median UAE of at least two 24-h urine collections. Correlations and multiple linear regressions analysis were performed to identify relationships between serum lipids and UAE.

**Results:** Total HDL (1.74±0.4 vs 1.65±0.3 mmol/L, p=0.02) and HDL3 cholesterol (1.21±0.3 vs 1.13±0.3 mmol/L, p=0.01) levels were higher in low-normalalbuminuric subjects as compared to high-normalalbuminuric subjects. In logistic regression analysis, after adjustment for age, sex, BMI duration of diabetes and HbA1c, lower total HDL (odds ratio=0.43, 95% CI=0.22-0.82, p=0.01) and HDL3 cholesterol (odds ratio=0.34, 95% CI=0.15-0.76, p=0.009) were significantly associated with risk of higher UAE in our normalalbuminuric subjects.

**Conclusions:** Dyslipidemia play a significant independent role in the development of diabetic nephropathy, decline in renal function and progression of albuminuria. In this study of normalalbuminuric type 1 diabetic patients we have shown that elevated total HDL and HDL3 cholesterol may indicate a protection from the development of microalbuminuria.

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**Cutaneous Advanced Glycation End Products (AGEs) - a Predictor of Diabetic Nephropathy?**

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**Introduction and Aims:** AGEs accumulate in the skin and vascular wall and are implicated in diabetic complications. Cutaneous AGEs in skin biopsies correlate with skin autofluorescence (skinAF). In previous studies, skinAF correlated with compound micro- and macrovascular complications in cross-sectional studies (Noordzij et al, Diabet Med 2012). However, the association of skinAF with renal phenotypes has not previously been studied and is the aim of this study.

**Methods:** We measured skinAF in a random subgroup of patients of the DIACORE (DIAbetes COOhReTi) study, using the AGE-reader (DiagOptics, Groningen, NL). For each patient, the mean of 3 measurements were used for the current analysis. DIACORE is a prospective cohort study recruiting Caucasian diabetes mellitus type 2 (DM2) patients for at least 10 years of follow-up, with a phenotyping protocol including an online questionnaire, physical examination, and biobanking of biomaterials. In the baseline data of patients with skinAF measurements (n=503) previously been studied and is the aim of this study.

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**Conclusions:** We found associations between skinAF and multiple renal phenotypes, which are ongoing work in the DIACORE study.

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**Evaluation of Role of Doxycycline (a Matrix Metalloproteinaseinhibitor) on Renal Functions in Patients of Diabetic Nephropathy**

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**Introduction and Aims:** This study was conducted to see the effect of doxycycline on renal functions, especially proteinuria, inpatients of diabetic nephropathy (DN).

**Methods:** The study included 40 clinically proven adult patients of DN. All patients were on stable doses of angiotensin-converting enzyme inhibitors (ACEIs) and or angiotensin receptor blockers (ARBs) for 2 months before the study. The patients were divided into two groups of 20 patients each. Group A patients were maintained on stable dose of ACEIs and/or ARBs, whereas Group B patients received doxycycline (100 mg/day) for a period of 3 months in addition to ACEIs and or ARBs. Adequate glycemic control was achieved with insulin or oral hypoglycemic agents in all the patients. Renal parameters were assessed at the beginning of the study, at 1, 3, and 6 months (after a washout period of 3 months).

**Results:** All renal parameters remained unaltered during the study in both groups. However, proteinuria showed improvement in Group B (doxycycline group). The mean basal value of proteinuria was 1.74 ± 1.70 g/day for Group A and 2.17 ± 2.95 g/day for Group B. At the end of 3 months, proteinuria was 1.22 ± 2.11 g/day in Group B whereas it was 1.50 ± 1.50 g/day in Group A (p<0.05). However, the decrease in proteinuria at 6 months in the two groups did not show any statistically significant difference. No significant side effects of doxycycline were observed.

**Conclusions:** The study showed that doxycycline was effective in reducing proteinuria in patients of DN when used for the short duration of 3 months.
**Abstracts**

**SP290 ABO BLOOD GROUPS RELATE WITH DIABETIC NEPHROPATHY**

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**Introduction and Aims:** ABO antigens are expressed on the surface of many cells other than erythrocytes such as epithelial cells including uroepithelium, gastrointestinal, mucosal and lung. Alterations on the cell surface structures as blood group antigens, can lead to changes in the interactions in between cells or cells and extracellular matrix. In this study, we aimed to investigate any possible relationship between DN and ABO-Rh blood groups.

**Methods:** The study included 743 patients with diabetic nephropathy and 2525 healthy donors that admitted to Erciyes University Blood Bank in year 2012. Diabetic nephropathy was defined as overt proteinuria (i.e. protein excretion above 300 mg/day) or otherwise unexplained renal dysfunction (i.e. serum creatinine above 1.4 mg/dL) in diabetic patients. The correlation between DN and blood groups was investigated using the chi-square test. Post hoc power analysis was used to evaluate the power of statistic analysis.

**Results:** shows comparison of ABO blood groups and Rh factor between patients with DN and control group. There was significant difference between patients with DN and control group in terms of distribution of ABO blood groups and Rh factor (p = 0.002; 0.959 of the power of statistical analysis). A Rh positive blood group was frequent in patients with DN. Table 2 shows comparison of ABO blood groups between patients with DN and control group. There was significant difference between patients with DN and control group in terms of distribution of ABO blood groups (p = 0.001; 0.942 of the power of statistical analysis). A blood group was frequent in patients with DN.

**Conclusions:** DN is closely related to ABO-Rh blood groups, especially A Rh positive blood group. Possible genetic or other mechanisms of this relationship may be revealed in future studies. Physicians may consider this observation in treatment and prevention in patients with diabetes mellitus.

**SP291 EVALUATION OF RENAL BIOPSIES IN THE TYPE 2 DIABETIC PATIENTS**

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**Introduction and Aims:** Diabetic nephropathy is usually diagnosed according to clinical and laboratory findings. Thus, the necessity of renal biopsy in diabetic patients is always controversial. In this retrospective study, we aimed to reveal renal biopsy findings in diabetic patients.

**Methods:** In our clinic, 536 native renal biopsies were performed between August 2007- August 2012. 51 biopsies obtained from patients with type II diabetes mellitus were included to our study. Based on the biopsy findings patients were divided into three groups: Group I, diabetic nephropathy (DN); Group II, Non-Diabetic Renal Disease (NDRD); Group III, NDRD superimposed on DN. The relationship between clinical and histological findings was evaluated using appropriate statistical methods.

**Results:** 52 patients were female and 29 male with a mean age 53.8± 10.8 years. Mean duration of diabetes were 82.7±94.9 months [2-480 months]. Almost all of the patients were hypertensive (n =49). Diabetic retinopathy was diagnosed in 45 patients (85%). Indications for renal biopsy included: nephrotic syndrome in 22 (43.1%), acute renal failure in 10 (19.6%), non-nephrotic range proteinuria in the patients were hypertensive (n =49). Diabetic retinopathy was diagnosed in 45 patients (85%). Indications for renal biopsy included: nephrotic syndrome in 22 (43.1%), acute renal failure in 10 (19.6%), non-nephrotic range proteinuria in 12 (22.7%), chronic renal failure in one (2%) patient. There were 18 patients in Group I, 28 patients in Group II and five patients in Group III. The most common NDRDs were FSGS (n=17), minimal change disease (n=3), amyloidosis (n=2), mesangioproliferative GN (n=2), IgA nephritis (n=1), membranoproliferative GN (n=1), membranous GN (n=1) and interstitial nephritis (n=1).

In group III, acute interstitial nephritis was the most common feature and all cases were not associated with acute renal failure. Clinical characteristics were summarized in Table 1.

**Conclusions:** In diabetic patients with nephrotic level of proteinuria and rapid deteriorating renal function, interstitial cell infiltration was accompanying findings of DN. It is still controversial that this significant interstitial cell infiltration is whether cause or result by worsening of DN.
Nephrology Dialysis Transplantation

SP296

EMPHYSEMATOUS PYELONEPHRITIS IN TYPE 2 DIABETES MELLITUS PATIENTS: A PROSPECTIVE STUDY

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Introduction and Aims: Emphysematous pyelonephritis (EPN) is life threatening warranting early and aggressive management. It is antibiotic therapy alone sufficient or early nephrectomy needs to be contemplated? The present study was aimed to know the spectrum of emphysematous pyelonephritis and its management.

Methods: This prospective study was undertaken from July 2009 to December 2011. Hospitalised adult type 2 diabetes mellitus with pyelonephritis were included. The diagnosis of pyelonephritis was made on basis of classical clinical features supported by ultrasonography or CT finding and culture positivity, EPN was characterised by presence of gas and was classified as per Huang classification. Patients were treated with appropriate antibiotics and percutaneous drainage (PCD) as and when indicated. Nephrectomy was carried out in EPN patients refractory to conservative measures for 2 weeks. Outcome was termed as poor it there was a need of nephrectomy or the patient died.

Results: One hundred and five patients were admitted with pyelonephritis, the mean age was 57.1+9.2 (30-75 yrs). Of 105, 26 (20.3%) had EPN and 79 (79.7%) had non EPN. Stone disease/prostatic enlargement were predisposing factors in 7.6% and 14% in EPN and non EPN respectively. Poorly controlled blood sugar (HbA1c >7.6) was more in EPN than non EPN [26 (100%)] vs. 55 (69.6%); p<0.05. E. coli was the commonest causative organism 84% vs 75% followed by pseudomonas 8% vs 7.5% and fungi 16% vs 6.7% in EPN and non EPN respectively. None of EPN had associated papillary necrosis and abscess as compared to 4% and 13% in non EPN respectively, Blood culture was positive in 20 (77%) in EPN as compared to 35 (44%) in non EPN patients. Renal dysfunction was seen in 20 (73%) and 74 (93%) EPN and non EPN patients respectively. Diabetic support was required in 5 (23%) EPN and 13 (16.4%) non EPN patients. Class 1 EPN was seen in 2 (7.7), IIa in 8 (30.7), IIIa in 7 (27). IIIB in 5 (19.3) and IV in 4 (15.3) patients. Ten (38.5%) EPN patients were treated with antibiotics alone, 11 (42.3%) underwent additional PCD. Nephrectomy was required in 5 (19.2%) 4 were class IIIB and 1 class IV EPN. Of 5 patients subjected to nephrectomy 3 survived. In non EPN forty-nine (62%) patients were treated with antibiotics alone, 17 (21.4%) with additional PCD. None required nephrectomy. Survival was comparable [22(84.6%)] vs.70 (88.6%); pns. However poor outcome (mortality or nephrectomy) though not significantly different was more in EPN 8 (30.82%) as compared to non EPN 9 (11.3%). Of different prognostic variables in EPN and non EPN viz glycemic control, leukocytosis, thrombocytopenia, shock, altered sensorium, renal dysfunction only shock (62.5% vs 5.5% p<0.0045) and altered sensorium (50% vs 12.5% p<0.002) were associated with poor outcome in EPN.

Conclusions: Poor glycemic control is associated with EPN. Class I to IIIB can be managed with antibiotics and PCD, but class IIIB and IV may need nephrectomy. Presence of shock and altered sensorium are poor prognostic factors in EPN and warrant early and aggressive intervention.
IMPAIRED RESPONSE OF FIBROBLAST GROWTH FACTOR (FGF)-23 INCREMENT TO ORAL PHOSPHATE LOADING IN CKD PATIENTS WITH TYPE 2 DIABETES MELITUS (DM): POSSIBLE MECHANISM OF ATHEROSCLEROSIS

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Introduction and Aims: Vascular calcification, a predictor of cardiovascular mortality, is highly prevalent in the patients with CKD complications of DM. Evidence has been accumulated to indicate that phosphate (Pi) loading into circulation might be responsible for vascular calcification, in which FGF-23, and the resultant rise in intact parathyroid hormone (iPTH) acts as its protective factor to cause phosphaturia. Serum FGF-23 and iPTH increase during CKD stage 2 and 3, respectively. Since DM osteopenia is characterized by impaired functions of osteoblast (OB)/osteocyte (OC) and parathyroid gland, the possible impairment of FGF-23 and iPTH secretion in response to Pi loading might easily induce hyperphosphatemia, resulting in vascular calcification. To estimate the significance of impaired FGF-23 and iPTH secretion in the advanced vascular calcification in DM CKD patients, we examined whether incremental response of serum FGF-23 and iPTH after oral Pi stimulation is impaired in type 2 DM patients.

Methods: Serum FGF-23, iPTH and Pi were measured before, and 2 and 4 h after oral Pi administration at the single dose of 1.0 g as a mixture of 0.82 g Na2HPO4 and 0.18 g NaH2PO4 dissolved in 25 ml water, in type 2 DM (n=10) and non-DM patients (n=10), and its measurement was performed 2 days after administration of oral Pi at the daily dose of 2.9 g.

Results: Neither age, BMI, body weight nor eGFR differed significantly between DM and non-DM patients. DM patients revealed a significantly higher values than the non-DM in A1c (0.04±1.50% vs 0.53±0.24%, p<0.001). No significant differences existed in FGF-23, and the mean values of serum Pi, FGF-23, iPTH 1.25(OH)2D3, and Ca. After the start of Pi stimulation test, serum FGF-23 significantly increased by 2h (P=0.046) and iPTH significantly by 4h (P=0.007) in non-DM patients, but not in DM. Serum FGF-23 (P=0.009) and iPTH (P=0.048) again increased in non-DM patients after 2 days of oral Pi stimulation, but not in DM. In all patients, initial changes of serum FGF-23 (0-2h) and iPTH (0-4h), which correlated positively with each other (r=0.528, p<0.05), showed a significant and negative correlation with later change of serum Pi (2-4h) (r= -0.457, P = 0.042, r= -0.673, P= 0.001). Consistent with the lack of change in serum FGF-23 and iPTH in DM patients, serum Pi (2-4h) significantly increased (P=0.020), in contrast with insignificant rise in non-DM. Conclusions: It was demonstrated that incremental response of serum FGF-23 and iPTH by Pi stimulation was impaired in DM patients, and thus suggested that it was one of the mechanism for the advanced atherosclerosis in DM CKD patients.

METABOLIC SYNDROME AND CALCIUM NEPHROLITHIASIS

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Introduction and Aims: Nephrolithiasis remains a formidable worldwide health problem. Metabolic syndrome (MS), characterized by truncal obesity, hypertriglyceridemia, hyperinsulinemia and insulin resistance, has been found to be associated with an increased prevalence of uric acid nephrolithiasis. In this retrospective study, the incidence and risk factors for calcium kidney stones formation have been evaluated in selected groups of patients with MS.

Methods: A total of 126 patients were selected for the study. They were divided in three groups: 42 adults with nephrolithiasis (N), 44 patients with metabolic syndrome and nephrolithiasis (MS + N), 40 subjects with metabolic syndrome without a stone (MS), but without a self or family history of kidney stones. Demographic and biochemical characteristics were evaluated for each group. All participants collected a 24-h urine for evaluation of urinary composition.

Results: Urinary Calcium excretion was significantly higher in N and N+MS than in MS patients (FeCa 1.4% and 1.7%, p=0.016), showed a significant and negative correlation with later change of urinary Calcium excretion (145 ± 56 mg/24 h; FeCa 1.3%) when compared with patients in the same group but with high blood pressure (238±114 mg/24 h; FeCa 1.7%). In MS group there were no urinary abnormalities that allow the formation of calcium stones (urinary Calcium 108 ± 81 mg/24 h, Urinary Phosphorus 0.9 ± 0.3 g/24 h, Urinary Oxalate 30 ± 5 mg/24 h) with significant differences compared to the other groups (p<0.05 MS vs SM+N vs N).

Conclusions: In patients with MS and family or self history of nephrolithiasis, risk factors associated with calcium nephrolithiasis increased with the number of features of MS. Hypercalciuria had a major prevalence in patient with hyperinsulinemia and MS.

FACTORS PREDICTING INCREASED URINE EXCRETION IN PATIENTS WITH TYPE 2 DIABETES

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Introduction and Aims: Evaluation of the urine for proteinuria is routinely used as a screening tool for detecting the presence of nephropathy in patients with diabetes. Several studies have however shown that patients with type 2 diabetes can have normal urine protein excretion despite significantly impaired renal function. These findings suggest that factors other than reduced glomerular filtration rate (GFR) may affect urine protein excretion in patients with type 2 diabetes. The aim of this study was to identify factors predicting the presence of increased urine protein excretion in patients with type 2 diabetes.

Methods: This was a cross-sectional study of patients with type 2 diabetes attending the diabetes clinic of our teaching hospital. Data was retrieved using a structured interviewer-administered questionnaire. Information retrieved included the patients’ demographic characteristics, lifestyle, personal and disease history, and current drug therapy. Each patient’s weight, height, waist circumference and blood pressure were measured. The patients had examination of the retinal fundus after pupillary dilatation with a midratic. 5ml of blood was drawn from each patient for determination of serum creatinine. 10ml of early morning urine was also obtained for determination of the urine protein to creatinine ratio (PCr). GFR was estimated from the serum creatinine, using the 4-variable version of the the Modification of Diet in Renal Disease study equation. Patients were stratified into two groups based on their urine PCR. Patients with urine PCR < 0.2 were defined as having normal urine protein excretion while patients with urine PCR >0.2 or greater were defined as having increased urine protein excretion.

Results: A total of 358 patients were recruited for the study. Of these, 221 (61.7%) were females. The mean age of the study population was 57.84 ± 11.12years and the patients had been diabetic for a mean duration of 8.63 ± 7.53years. Urine protein excretion was increased in 191 (53.4%) of the patients studied. Compared to patients with normal urine protein excretion, patients with increased urine protein excretion were more likely to be hypertensive (75.4% vs 58.1%; p<0.01), and more likely to be on an angiotensin converting enzyme inhibitor (ACE) or angiotensin II receptor blocker (ARB) (72.8% vs 53.9%; p<0.01). They also had a higher mean systolic blood pressure (138.49 ± 21.53 vs 0.819 ± 0.001), age (AUC=0.740 p=0.001), and eGFR (AUC=0.238 p=0.001) are predictors of carotid artery intima-media thickness.

Conclusions: We found that insulin resistance (IRR) and inflammation were associated with clinical atherosclerosis in type 2 diabetics with mild to moderate kidney disease. Further studies are needed to evaluate if this new insulin resistance index can be a marker of cardiovascular morbidity and mortality in diabetic patients with chronic kidney disease.
Conclusions: In our patients with type 2 diabetes, the only factor that predicted increased urine protein excretion was a GFR less than 60ml/min/1.73m². Also, patients on an ACEI or ARB had a 50% reduced odds of having increased urine protein excretion [OR=0.51 (0.27–0.96); p=0.04].

Introduction and Aims: Glucose is being reabsorbed together with sodium (Na⁺) in the proximal convoluted tubule using the SGLT2 co-transporter. The energy needed for glucose reabsorption is provided byNa⁺/K⁺ ATPase pump which creates a sodium gradient resulting in glucose movement into the tubular cells. The over activity of sodium-glucose co-transporter results in phosphorus losses due to suppression of Na/Pi co-transporter. The enhanced phosphorus losses may lead to lower plasma levels which might ameliorate the presence of severe diabetic complications. The purpose of this study was to investigate the correlation of metabolic control with phosphorus and magnesium urine losses in diabetic patients.

Methods: In this study we included 22 diabetic (NIDDM) patients (12 males, 10 females) with good metabolic control. Their mean age was 71.2±9.8 years old, their mean weight 84.8±11.4 Kg and their mean eGFR was 60.8±24.8 ml/min. Patients receiving medications influencing Pi or Mg⁺⁺ excretion (e.g. diuretics) were excluded from the study. The scope of the study was to investigate the possible correlation between HbA1C plasma glucose levels with phosphorus and magnesium levels in the urine.

Results: The patients' mean HbA1C values 6.9±0.9 %, the mean plasma glucose was 139±44.03 mg/dl, the mean plasma magnesium was 1.4±0.88 mg/dl, and the mean urine protein to creatinine ratio was 0.62±0.37. The patients' urine concentration of phosphorus and magnesium was 18.8±8.6 mg/dl and 3.07±1.2 mg/dl respectively. Statistical analysis (Pearson Correlation) revealed a statistically significant correlation between HbA1C and phosphorus urine levels (r=0.546, p=0.013) as well as magnesium levels (r=0.461, p=0.02).

Conclusions: The good metabolic control in diabetic patients minimizes phosphorus and magnesium losses through the urine thus preventing the possible correlation between HbA1C and phosphorus urine levels (r=0.546, p=0.013) as well as magnesium levels (r=0.461, p=0.02).
The relationship between neutrophil/lymphocyte ratio, anemia and albuminuria in diabetic patients

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Introduction and Aims: In this study, we aimed to investigate whether N/L ratio and anemia are associated with albuminuria in patients with diabetes mellitus.

Methods: This study was performed on 170 (98 female, 72 male) patients with diabetes mellitus of overall mean age of 58 ± 13 years. An estimated glomerular filtration rate (eGFR) was calculated using the MDRD formula. Albuminuria was assessed using urinary albumin creatinine ratio (UACR). Normoalbuminuria, microalbuminuria, and macroalbuminuria were defined as UACR <0.030, UACR 0.030-0.300, and UACR >0.300, respectively. Anemia was defined by WHO criteria (hemoglobin <13 g/dL for men and <12 g/dL for women).

Results: shows comparison of demographic and biochemical parameters among three groups. UACR values, N/L ratios, and presence of anemia increased step-wise from normoalbuminuric group to macroalbuminuric group. On the other hand, step-wise decreases were detected in eGFR values. Age was significantly lower in patients with normoalbuminuria than in other two groups whereas there was no significant difference between microalbuminuric group and macroalbuminuric group. Hemoglobin concentration was significantly lower in macroalbuminuric group compared to other two groups, but there was no significant difference between normoalbuminuric group and microalbuminuric group. HbA1c value was significantly lower in normoalbuminuric group compared to microalbuminuric group, however, there was no significant difference between microalbuminuric group and other two groups with regard to HbA1c value. UACR value positively correlated with N/L ratio and age and negatively correlated with eGFR and hemoglobin concentration (Figure).

Conclusions: N/L ratio significantly associates with albuminuria in diabetic patients, especially at macroalbuminuric stage. Anemia is a common complication in diabetic patients even at microalbuminuric stage.
**Results:** 97 patients from the initial cohort of 120 (80.8%) survived the 12-month observation period. During the 3rd, 6th, 9th month mortality rate was at 13.3%, 2.5%, 2.5% respectively. Annual mortality rate was 19.2%. The only independent mortality risk factors in the Cox proportional hazard regression model was the type of initial vascular access (p= 0.005); the significant superior survival demonstrated the patients who initiated HD with a functional arteriovenous fistula.

**Conclusions:** Diabetes did not exert the significant impact on the early survival in HD patients. A native arteriovenous fistula provides a significant survival advantage within the first year of HD. The greatest mortality occurred in early 90 day initiation HD period.
**CLINICAL NEPHROLOGY - IGA NEPHROPATHY, LUPUS NERPHRISIS, VASCULITIS**

**SP307**

**EFFICACY AND SAFETY OF TELMISARTAN, CLOPIDOGREL, AND LEFLUNOMIDE IN PATIENTS WITH IGA NEPHROPATHY – A MULTICENTRE, PROSPECTIVE, RANDOMIZED, DOUBLE-BLIND AND -DUMMY CONTROLLED CLINICAL TRIAL**

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Introduction and Aims: To evaluate the efficacy and safety of telmisartan combined with clopidogrel and/or leflunomide for patients with Iga nephropathy and whether the combination therapy surpass telmisartan in decreasing proteinuria and protecting renal function.

Methods: We enrolled 400 patients aged 18-55 years from 13 centers in Beijing who had proteinuria 0.5-3.5g per day, baseline serum creatinine (Scr) <265µmol/L (3mg/dl). All patients were eluted by taking telmisartan 80mg per day for 4 weeks and then randomly assigned to receive at least 24 weeks of treatment with telmisartan 80mg per day + clopidogrel placebo + leflunomide placebo (group A), telmisartan 80mg per day + clopidogrel 50mg per day + leflunomide placebo (group B), telmisartan 80mg per day + clopidogrel placebo + leflunomide 20mg per day (group C), telmisartan 80mg per day + clopidogrel 50mg per day + leflunomide 20mg per day (group D).

Comparison of 24-hr urinary protein excretion, the serum creatinine, eGFR, albumin, cholesterol and uric acid, before and after the therapy were assessed.

Results: No statistically significant differences were observed for any baseline clinical data including age, gender, BMI, blood pressure, proteinuria, serum creatinine, eGFR, serum uric acid in the four groups (P>0.05). After treatment for 24 weeks, a significant decline of proteinuria was observed in the four groups (P<0.05), while those in group C (1.02±0.75 vs 0.77±0.42g/24h) and group D (1.16±0.63 vs 0.87±0.49 g/24h) were decreased more significantly than in group A (1.15±0.87 vs 0.92±0.58 g/24h) and group B (1.11±0.83 vs 0.89±0.42g/24h) (P<0.05). Mixed effects were showed that telmisartan, clopidogrel, and telmisartan combined with leflunomide were effective in lowering proteinuria (P<0.01) by model analysis. The extent of serum creatinine decline in group C and group D displayed more significantly than that in group A and group B (P<0.05). The levels of eGFR in group C and group D were increased more than those in group A and group B. The decline of serum uric acid in group C and group D displayed more significantly than group A and group B (P<0.05). There were no significant differences in the results of albumin and cholesterol among the four groups (P>0.05). No obvious adverse reactions were found in the four groups.

Conclusions: In the selected patients with Iga nephropathy, telmisartan combined with leflunomide was safe and effective in decreasing proteinuria and protecting short-term renal function. Larger randomized studies would be needed to confirm these results in the long run.

**SP308**

**A PROSPECTIVE RANDOMIZED STUDY ON THE EFFICACY OF CORTICOSTEROID COMBINED WITH CYCLOPHOSPHAMIDE OR FK506 IN PRIMARY IGA NEPHROPATHY WITH MILD OR MODERATE RENAL INJURY**

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Introduction and Aims: The aim of this study was to evaluate the efficacy and drug safety of cyclophosphamide or FK506 with corticosteroid in primary Iga nephropathy (IgAN) with mild or moderate renal injury.

Methods: From 2010 to 2011, 36 primary IgAN patients with 30ml/min<Scr<1.02/24h, and urinary protein excretion >1.0g/24h (with or without hypertension) were enrolled to this study prospectively. There were three groups(Corticosteroid, Corticosteroid combined with cyclophosphamide (CTX) or FK506), each group included 12 patients for 24-weeks treatment. In each group, corticosteroid initial dosage was 0.5-0.8mg/kg/d, decreasing the dosage gradually after 8 weeks.

Corticosteroid combined with CTX group: CTX 0.5-0.75g/m²/month; Corticosteroid combined with FK506 group: FK506 0.1mg/kg/d (effective serum drug concentration 6-10ng/ml). Maintenance period were 24 weeks: corticosteroid 10-15mg/d, CTX 0.5-0.75g/m²/week; FK506 0.05mg/d. Evaluation of the effect: (1) Remarkable effect:24-hour urinary protein excretion <0.3g/24h, serum creatinine decreased >10% than baseline; (2) Effect: 24-hour urinary protein excretion decreased over 50% in pre-treatment and serum creatinine was stable; (3) Non-effect:24-hour urinary protein excretion did not meet the above criteria, or serum creatinine increased >8% per year.

Results: 36 patients were enrolled, M 26/F 10, average age 37.3±5.1yrs (20-70). There is no difference among the three groups in their laboratory features at the base line. After 3 months, 6 months and 12 months, 24-hour urinary protein excretion was decreasing 0.90±0.75g, 0.76±0.73g and 0.35±0.35g in corticosteroid group; 1.40±1.24g, 0.87±0.83g, 1.43±2.59g in corticosteroid with CTX group and 1.10±1.31g, 0.78±0.69g, 0.69±0.82g in corticosteroid combined with FK506 group prospectively (P<0.05). After 6 months, the serum creatinine decreased both in corticosteroid group (Scr 111.72±31.23μmol/L) and corticosteroid combined with CTX group (Scr 111.33±22.76 umol/L) (P<0.05); while no change in corticosteroid combined with FK506 group. Remarkable effect: corticosteroid group 9 patients(75%), corticosteroid combined with CTX group and corticosteroid combined with FK506 group were both 7 patients(58%); Effect: corticosteroid group combined with FK506 group both 3pts(25%), corticosteroid combined with CTX group 5 pts(42%); corticosteroid combined with FK506 group had 2pts(17%)non-effect. Adverse events included I hyperglycemia and 1 liver dysfunction in corticosteroid group, including 2 hyperglycemia, 1 IGT and 1 liver dysfunction in corticosteroid combined with FK506 group.

Conclusions: It suggested that CTX and FK506 were beneficial for controlling proteinuria without significant serum creatinine increasing.

**SP309**

**RELATIONSHIP BETWEEN THE BODY MASS INDEX AND THE PROGRESSION OF IGA NEPHROPATHY EVEN IN LEAN INDIVIDUALS**

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Introduction and Aims: In chronic kidney disease, obesity is an important risk factor for disease progression. Likewise, in IgA nephropathy (IgAN), several studies reported that excessive body weight (body mass index (BMI): 25 kg/m² or greater) had an impact on the prognosis. The impact of BMI, however, remains unclear in smaller individuals like Japanese. The objective of the present study is to determine the impact of BMI and metabolic factors on the prognosis of IgAN patients in Japanese.

Methods: All IgAN patients were diagnosed in the Juntendo University Hospital between 1999 and 2009. Patients with diabetes mellitus or autoimmune disease, purpura nephritis were excluded. There were 95 male (49.2%) and 98 female (50.8%) patients, and median age was 32.8±11.3 years old (range 12-65). Patients were divided into three groups equally according to BMI: Group L (lean group) (n=65, BMI: 15.57-20.18kg/m²), Group M (middle group) (n=64, BMI: 20.20-23.04 kg/m²) and Group O (overweight group) (n=64, BMI: 23.11-31.89 kg/m²). Clinical and pathological data at the time of renal biopsy were analyzed. Levels of serum creatinine (sCr), urinary protein (UP), urinary red blood cell (uRBC) of L, 2, 3, 4 and 5 years after the renal biopsy were also compared.

Results: In multivariate logistic regression analysis, the excessive BMI (OR 1.19, 95%CI 1.02-1.40) and hypoaalbuminemia (OR 0.16, 95%CI 0.05-0.46) at the time of renal biopsy were significant predictors of remission of proteinuria. At the time of renal biopsy, there were no significant difference in UP, the degree of hematuria, serum urea nitrogen, total protein, albumin, IgG, IgM, and IgA. The ratio of female to male was significantly higher in group L, it was much lower in Group O. Systolic blood pressure (BP) and diastolic BP in Group O were significantly higher than those in Group L and Group O. Estimated GFR (eGFR) in Group L was higher than that in Group O. Triglyceride (TG), LDL cholesterol, Uric acid (UA), Hemoglobin (Hb), C-reactive protein, C4 and C3 in Group O were significantly higher than those in Group L and Group M. Estimated GFR (eGFR) in Group L was higher than that in Group O. Triglyceride (TG), LDL cholesterol, Uric acid (UA), Hemoglobin (Hb), C-reactive protein, C4 and C3 in Group O were significantly higher than those in Group L and Group M. UA, TG, C4, Hct, Hb, C3, HDL-c, cSCR, systolic BP and diastolic BP were significantly correlated with BMI. In five years, although the progression of eGFR and the degree of RBC were similar among the three groups, the remission of urinary protein was significantly delayed in Group O.

Conclusions: This is the first study that shows BMI and metabolic factors have impacts on the prognosis of IgAN even in Japanese whose body is smaller than Caucasian. It appears that the overweight is a risk factor for disease progression. Therefore, BMI should be paid more attention, and we should aggressively recommend patients with IgAN to reduce weight and treat their metabolic factors.
SP310

ALTERED MONOCYTE GENE EXPRESSION AND EXPANSION OF CD14+CD16+ CELL SUBSET IN IgA NEPHROPATHY PATIENTS

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Introduction and Aims: Immunoglobulin A nephropathy (IgAN) is the most common form of primary glomerulonephritis worldwide. The basic defect lies within the IgA immune system and in peripheral blood leukocytes rather than local kidney abnormalities. Our previous work evidenced a more profound altered gene expression pattern in monocytes compared to B and T cells isolated from IgAN patients and thus our aim here was to study the monocyte subset more closely at a genome wide level. Human monocytes can be classified into two main subsets with distinctive characteristics: classical (CD14+/CD16-) and non classical (CD14+/CD16+) monocytes, the latter cells characterized by a more marked apoptotic propensity.

Methods: A total of 33 IgAN patients and 33 healthy subjects (HBD) were included in this study. Illumina microarray technology was used to evaluate global differences in gene expression between monocytes isolated from IgAN patients and HBD. Bioinformatic analysis was performed with GenomeStudio and Genespring software. The connectivity between genes was evaluated using Ingenuity Pathway Analysis. Aberrantly expressed genes and pathways were then validated in independent set of patients with RT-PCR western blot and flow cytometry analysis.

Results: Bioinformatic analysis revealed 710 differently regulated probes with FDR-corrected p value<0.05 in IgAN patients. These probes were primarily involved in Apoptosis Signaling, mitochondrial dysfunction, tnfrsf1a and death receptor signaling canonical pathways. Four representative genes belonging to these pathways (TNF, CD83, TNFRSF1A, NDUFS3) were chosen for validation purposes and the normalized gene expressions obtained were in line with the gene expression array. All mitochondrial respiratory chain subunits were found modulated. In particular, the protein levels of NDUFS3 were statistically up-regulated in IgAN patients confirming an aberrant mitochondrial homeostasis. The enhanced apoptotic phenotype seen with the gene expression in monocytes was confirmed at the protein level, in fact CD14+ cells exhibited a significantly higher percentage of annexin-V and 7-AAD double positive staining. Next we demonstrated this phenotype was due to a different distribution of monocyte subsets in IgAN patients compared to HBD. Surprisingly we found that CD14+ CD16+ subset was significantly expanded in all IgAN patients tested even though the total monocyte count was unchanged.

Conclusions: Taken together, our findings demonstrate an aberrant modulation of the mitochondrial respiratory system in monocytes isolated from IgAN patients and a specific up-regulation of NDUFS3. Furthermore, the aberrant expansion of the CD14+CD16+ subset in IgAN patients could explain the enhanced apoptotic function seen in these cells thus, revealing a potential pathogenic role of these cells in IgAN.

SP311

RELIABILITY OF STATISTICAL MODELS TO PREDICT AN IgA NEPHROPATHY

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Introduction and Aims: Models are increasingly used in clinical practice to improve the accuracy of diagnosis. The aim of our work was to compare Bayesian network to logistic regression to forecast an IgA nephropathy (IgAN) from simple clinical and biological criteria.

Methods: Retrospectively, we pooled the results of all biopsies (n=155) performed by nephrologists in a specialist clinical facility between 2002 and 2009. Two groups were constituted at random. The first sub-group was used to determine the parameters of the models adjusted to data by logistic regression or Bayesian network, and the second was used to compare the performances of the models using Receiver Operating Characteristics (ROC) curves.

Results: An IgAN was found in 45 patients. Areas under the ROC curves provided by both methods were highly significant but not different from each other. Based on the highest Youden indices, sensitivity reached (100% vs 67%) and specificity (73%/vs 95%) using the bayesian network or the logistic regression respectively.

Conclusions: A Bayesian network is at least as efficient as a logistic regression to estimate the probability of a patient suffering IgAN, using simple clinical and biological data obtained at consultation.

SP312

CORTICOSTEROID THERAPY IS THE MOST IMPORTANT FACTOR INFLUENCING TA PROTEINURIA AND RENAL SURVIVAL IN IgA NEPHROPATHY (IgAN)

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Introduction and Aims: Time Average Proteinuria (TAP) is an important prognostic factor in patients (pts) with IgAN: when proteinuria remains <1 g/d, progression towards ESRD is rare. The aim of this study is to search for association between proteinuria <1 g/d (favourable prognostic factor) and some clinical variables, especially the treatment.

Methods: From 1989 to 2005, we enrolled 325 pts affected by IgAN, presenting any plasma creatinine values and proteinuria above 1 g/d. Mean follow-up was 65.3±31 months and pts were evaluated six months after the enrollment and then every year. The considered variables were: age, sex, histological score, blood pressure (BP), immunological therapy, RAS blockers and statins. Pts were divided in 3 groups according to mean proteinuria values at follow-up: group 1, pts with proteinuria steady >1 g/d; group 2, pts with proteinuria in turn > or <1 g/d; group 3, pts with proteinuria steadily <1 g/d. Considered endpoints were ESRD, 100% and 50% increase of plasma creatinine.

Results: Pts were distributed as follows: 51 (15.7%) in group 1, 156 (48.0%) in group 2, 118 (36.3%) in group 3. At last observation, the percentage of pts who reached the endpoints of ESRD, 100% and 50% increase of plasma creatinine in group 1 was 46.15%, 48.7% and 64.1%, respectively, in group 2 10.6%, 17.5% and 30.0%, respectively, and in group 3 3.1%, 5.5% and 11.1%, respectively. In group 3 a stable reduction of proteinuria occurred in 66.9% by 6 months and in further 18.7% by 12 months. Therefore, proteinuria reduction occurred especially when pts received immunosuppression (first six months). Considering the immunological therapy, 43 pts had no treatment, 171 received steroids (ST) and 111 steroids+azathioprine (ST+A); in group 1, 41.0% of patients had no treatment, whereas 17.9% received ST and 41.1% ST+A; in group 2, 9.4% had no treatment, 58.1% received ST and 32.5% ST+A; in group 3, 9.5% had no treatment, 56.5% received ST and 34.5% ST+A. At logistic univariate analysis pts treated with ST or ST+A, compared to not treated pts, had more possibilities of reducing proteinuria <1 g/d (RRR 7.0 and 3.2 respectively; p <0.01). Age, sex, histological score, BP at baseline and use of statins were not associated with proteinuria steadily below 1 g/d; the use of RAS blockers resulted significant only in group 2 (p <0.03).

Conclusions: Our data show that the only factor associated with proteinuria steadily below 1 g/d was the immunosuppression treatment. Particularly, ST resulted effective in reducing TAP, whereas the add of A didn’t produce further advantages. Histological grade and hypertension at baseline didn’t seem to be associated with a low TAP. Use of RAS blockers had a significant role in pts with more variability of proteinuria values.
gelatinase-associated lipocalin (NGAL) is one of the most sensitive tubule markers. The aim of our study is to investigate if the serum or urine NGAL might predict the prognosis in patients with IgA nephropathy.

**Methods:** From January 2005 to December 2010, patients with biopsy proven IgA nephropathy whose serum and urine samples at the time of kidney biopsy were conserved in a frozen state, were enrolled in this study. We retrospectively reviewed their clinical data and followed them up till October 2012. Serum and urine NGAL levels were measured using ELISA kit. Renal progression was defined as GFR decline more than 50% or progression to end-stage renal disease (ESRD).

**Results:** A total of 121 patients were enrolled in this study. During the median follow up period of 41.49 months, renal progression was found in 9 patients(7.4%). In our study, serum or urine NGAL alone could not predict renal progression, however, when the serum and urine NGAL levels were combined, the high NGAL group independently predicted the renal progression (HR=4.58,95% CI=1.13−18.59, p=0.03) along with the tubular damage graded by the Oxford classification T2 (HR=6.61, 95% CI=1.31−28.91, p=0.004). The Kaplan−Meier curve for renal survival showed a significantly higher renal progression in the high NGAL group (Log rank, p=0.004).

**Conclusions:** In patients with IgA nephropathy, high serum and urine NGAL levels at the time of kidney biopsy, predicted renal progression.

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**SP315**

**EFFECT OF LEUKEMIA INHIBITORY FACTOR (LIF) ON IgA1-PRODUCING CELLS FROM TONSILS OF PATIENTS WITH IgA NEPHROPATHY (IgAN)**

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**Introduction and Aims:** IgA1-producing cells from tonsils of patients with IgAN secrete galactose-deficient IgA1 (Gd-IgA1), a key factor in the IgAN pathogenesis. Upper-respiratory tract infections frequently associate with episodes of macroscopic hematuria in IgAN patients, but little is known about the role of tonsils and production and glycosylation of IgA1 by tonsillar cells. Moreover, genetic studies revealed an association of a locus encompassing the gene encoding LIF with serum IgA levels in patients with IgAN. LIF, a member of the IL-6 family of cytokines, is involved in mucosal immunity. Here, we assessed the effect of LIF on IgA1 production and glycosylation using IgA1-secreting cells derived from tonsils of IgAN patients.

**Methods:** We assessed the effect of LIF, as compared to IL-6 as a control, on production and O-glycosylation of IgA1 in EBV-immortalized IgA1-secreting cells derived from tonsils of IgAN patients (IgAN-T) and controls (patients with sleep apnea syndrome; HC-T). IgA1-secreting cells were isolated from the circulation of IgAN patients (IgAN-P) and healthy controls (HC-P) as controls. Gd-IgA1 was determined by lectin ELISA with Helix aspersa agglutinin (HAA).

**Results:** LIF decreased production of IgA1 in IgAN-T and HC-T (−2.2%±1.4% and −3.7%±1.2%, as well as in IgAN-P and HC-P (9.1%±6.1% and −6.7%±6.1%). Conversely, IL-6 increased production of IgA1 in IgAN-P and HC-P by 55.8% and 16.9%, respectively, whereas the increases in IgA1 production in IgAN-T and HC-T were less robust (14.5% and 3.5%). Cells from IgAN patients (IgAN-P and IgAN-T) secreted more Gd-IgA1 compared to the cells from controls (HC-T and HC-P) (28.0% and 24.2%, 13.5% and 15.5% expressed as HAA reactivity; 100% is binding to standard Gd-IgA1). LIF increased Gd-IgA1 production by IgAN-T but not by HC-T (relative change, 24.2%±3.7% vs. −0.1%±0.1%). LIF increased production of Gd-IgA1 in IgAN-P but not in HC-P (relative change, 15.3%±3.6% vs. −1.5%±2.8%; p<0.01). IL-6 increased production of Gd-IgA1 in IgAN-T but not in HC-T (relative change, 32.5%±3.7% vs. −0.1%±0.1%) and increased Gd-IgA1 production in IgAN-P but not in HC-P (relative change, 24.0%±15.9% vs. −4.0%±4.2%; p<0.01). Thus, LIF or IL-6 stimulation of IgA1-secreting cells from IgAN patients increased production of Gd-IgA1.

**Conclusions:** IgA1-secreting cells from IgAN patients responded abnormally to a cytokine encoded in a locus identified by genetic association studies. Understanding the abnormalities will aid development of new diagnostic approaches and future IgAN-specific therapy.
**Introduction and Aims:** Previous studies found crescent may be associated with clinical outcomes in patients with IgA nephropathy (IgAN). However, due to the small sample size and the controversial results of these studies, the clinical significant of crescents in IgAN remain fully elucidated. The aim of this study is to evaluate clinical-pathological characteristics of IgAN patients with crescents formation and compare renal outcomes between patients with or without crescent in an extended Chinese IgAN cohort.

**Methods:** We recruited 539 biopsy-proven IgAN patients in this study. IgAN patients secondary to systemic diseases were excluded. All participants in this study were divided to two group (Cre+ group and Cre- group) based on whether crescents were found in the renal tissue. Clinical data was recorded at baseline and during follow-up. Histological parameters were scoring semi-quantitatively by one experienced pathologists. Crescent was defined as cellular crescent or fibrocellular crescent that involved >10% of the circumference of Bowman’s capsule.

**Results:** There are 226 patients in Cre+ group and 313 patients in Cre- group. The mean follow-up time is 3 years. Mean age was 37.1±12.2 in Cre+ group and 35.0±12.1 years in Cre- group. Of all patients in Cre+ group, 91(40.3%), 94 (41.6%), 30 (13.3%), 11 (4.6%) had the percentage of crescents was <10%, 10-25%, 25-50%, >50% respectively. At baseline, renal biopsy patients in Cre+ group had lower Hemoglobin (12.4±2.1 vs 13.1±2.1 g/dl, p<0.001), higher proteinuria [1.76(0.04-11.26) vs 1.26(0.03-13.91)g, P<0.001] than in Cre- group. On histology, Cre+ group had a higher percentage of mesangial hypercellularity (44.1% vs 37.1%, P=0.015) and endocapillary hypercellularity (60.6% vs 17.0%, P<0.001), higher intensity of C3 deposition (83.0% vs 73.4%, P=0.016). In total, ESRD occurred in 56 individuals. Patients in Cre+ and Cre- group had a similar renal survival time. By multivariate Cox proportional hazards model, four bivarsables were independently related to ESRD which including serum albumin [HR = 0.53(0.32-0.88), p = 0.02], systolic blood pressure[HR = 1.02(1.00-1.04), p = 0.04], eGFR [HR = 0.96(0.94-0.97), p = 0.00], hemoglobin [HR = 0.83(0.72-0.94), p=0.01]. In Cre+ group, there are three baseline variables associated with ESRD: sex[HR = 0.17(0.04-0.85), p = 0.03], systemic blood pressure[HR = 1.05, 95% CI 1.02-1.09, p=0.001], eGFR [HR = 0.94(0.91-0.97), p=0.001].

**Conclusions:** Our study suggested crescent is associated with clinical and pathological characteristics in patients with IgAN. While crescent is not associated with ESRD, IgAN patients with crescent have different risk factors for ESRD compare with that without crescent.

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**SP317**

**RISK OF PROGRESSION OF IgA NEPHROPATHY (IgAN) IN CHILDREN BASED ON OXFORD CLASSIFICATION (OC) AND IgA/C3 SERUM RATIO**

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**Introduction and Aims:** The aim of the study was to assess the risk of progression of IgAN in children at the onset of the disease, based on OC and IgA/C3 serum ratio. Methods: A total 58 children, in mean age 9.56 ± 4.99 yrs, with IgAN from 5 nephrology centers in Poland were enrolled. Renal biopsy was performed in all children with histological number of risk factors.

**Results:** Results of proteinuria and IgA/C3 ratio in MEST groups are presented tabl. 1. Most commonly histological lesions were: M1-77.6% pts, S1-37.9% Proteinuria was higher (p<0.05) in pts with E1, S1 vs. E0, S0. IgA/C3 serum ratio was significantly higher (p<0.05) in children with M1, S1 and T1 vs. M0,S0,T0, in E1 vs E0, NS. Significantly higher values of IgA/C3 (p<0.05) were revealed in pts with 4 risk factors of poor histological prognosis in OC (M=E+S+T+V=4). pts without risk factors (M+E+S+T=0).

**Conclusions:**
1. The serum IgA/C3 ratio may be a marker severe histological lesions in children with IgAN.
2. The renal biopsy Oxford Classification performed in children at the onset of the disease is useful in evaluation of IgAN severity.
associated with CD like abdominal pain, abdominal distention or diarrhea. In addition, none of the patients had IgA deficiency, anaemia or hypobuminemia. Celiac serology was positive in 5 (12%) children. Endoscopic evaluation was performed in 3 patients and one of them was diagnosed as CD. Prevalence of CD in children with HSP was significantly higher compared to healthy Turkish children (p<0.001).

Conclusions: Celiac seropositivity was 12% in children with HSP and this rate is significantly higher compared to healthy Turkish children (p<0.001).

Prevalence of CD in children with HSP was significantly higher than the rate in healthy children. Although the number of children with HSP is small in this preliminary study, this result suggests that celiac screening may be considered in children with HSP.

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**SP322**

RE-EVALUATION OF CHINESE ANCA-ASSOCIATED RENAL VASCULITIS PATIENTS WITH HISTOPATHOLOGICAL CLASSIFICATION

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Introduction and Aims: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) includes microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), Churg-Strauss syndrome and their localized forms. Renal involvement is present in more than half of the patients at disease onset and affects the prognosis. Recently, a histopathological classification of AAV was proposed and validated in Caucasians. Little is known of its application in Asian population.

Methods: Patients with biopsy proven AAV diagnosed in Ruijin hospital from 1997 to 2011 were retrospectively analyzed. According to definition proposed, patients were classified into “focal”, “mixed”, “crescentic” and “sclerosis” group. Patients with antiglomerular basement membrane disease or secondary causes of vasculitis were excluded.

Results: There were 116 patients enrolled in current study, with 90 MPA (90/116, 77.5%), 8 GPA (8/116, 6.9%), 15 renal limited vasculitis (RLV) (15/116, 12.9%) and 3 GSV (3/116, 2.6%). The mean age at presentation 56.1±15.8 with the male to female ratio of 1.03±0.48. During follow-up, 34 patients progressed to end stage renal disease (ESRD) and depended on dialysis. 41 patients died during follow-up. The probability of developing ESRD increased with the ascending category of focal, crescentic, mix and sclerosis (p<0.01). And the total survival decreased with the descending category of focal, crescentic, mix and sclerosis (p<0.05).

Conclusions: This cohort study clearly validated the Absolute Renal Risk of Dialysis/Death concept also in second stage AAV with utility to individual management and for the design of future clinical trials.

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**SP324**

SERUM SOLUBLE LECTIN-LIKE LOW-DENSITY LIPOPROTEIN-1 RECEPTOR IN ANCA-ASSOCIATED RENAL VASCULITIS

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Introduction and Aims: Circulating levels of soluble Lox-1 (sLox-1) are increased in inflammatory and atherosclerotic conditions. In our previous study we found an overexpression of Lox-1 gene in renal biopic tissue and in circulating leukocytes of ANCA-associated vasculitis patients (presented earlier at this forum, not yet published). It seemed worthwhile to investigate the sLox-1 level in ANCA-associated renal disease.

Methods: 22 patients with ANCA-associated vasculitides (age 63.5 ± 12.5 years; 8 males) and 7 control subjects without renal disease (age 44.6 ± 17.2; 4 males) were investigated. All patients had renal biopsy at clinical onset of their renal involvement. ANCA serology was performed by using indirect immunofluorescence technique and ELISA was performed for antibodies to PR3 and MPO. The serum soluble (sLox-1) receptor concentration was measured in serum by using the Human Lox-1 ELISA Kit (CELL BIoLABS, INC.). The ANCA-associated disease activity was evaluated with the Birmingham Vasculitis Activity Score (BVAS).

Results: Twelve patients had pANCA and 10 had cANCA positivity. Twelve patients showed signs of the disease activity (6 with cANCA and 6 with pANCA positivity), 10 patients were in complete remission. Circulating sLox-1 receptor concentrations of ANCA vasculitis patients (142.8 ± 19.6 pg/mL) were not significantly different from the controls (139.0 ± 3.8 pg/mL). However, when we separately analysed the serum receptor concentration of the diseased patients in the active phase compared to the values of patients in remission, we received significantly lower receptor concentration in the active phase patients (85.2 ± 18.2 pg/mL vs. 200.5 ± 24.8 pg/mL; p<0.001).

There was no significant difference in the sLox-1 levels between the pANCA positive
and the cANCA positive patients. We found a significant inverse correlation between
the sLox-1 and BVAS values (n = 22; r² = 0.43; p < 0.001).

Conclusions: Our present finding of a decreased concentration of circulating soluble
Lox-1 in ANCA vasculitis patients, with regard to previous observations of the
overexpression of Lox-1 gene in the organ tissue, raises the possibility that Lox-1 may
be highly expressed locally in response to proinflammatory stimuli, and via a feed-back
effect decreases the circulating soluble receptor level. It could be suggested that serum
soluble Lox-1 concentration might be a useful marker for the disease activity in
ANCA-associated renal vasculitis. Further investigations are needed to clarify the
pathomechanism of the decreasing receptor concentration in active ANCA vasculitis.

Introduction and Aims: ANCA-associated vasculitis (AAV) is a rare, life-threatening
disease with a one-year mortality of approximately 80% in untreated patients. Renal
involvement is a common manifestation, and may lead to end-stage kidney disease
(ESKD). Treatment requires systemic immunosuppression and carries inherent risks,
including sepsis. Our unit is the sole tertiary referral centre for renal AAV in Southwestern
Ireland. We identified all patients diagnosed with Renal AAV from 2007 - 2012. Our
objectives were to calculate the incidence of Renal AAV in Ireland and to describe the
clinical features and outcomes of Renal AAV in this patient population.

Methods: We identified a cohort of patients with a first diagnosis of AAV with clinical
evidence of renal involvement, over a six year period using our integrated laboratory
and patient database. A retrospective review of patient charts, correspondence and
laboratory results was performed.

Results: 59 patients met the inclusion criteria. Of these, 34 (58%) were male. The
median age at diagnosis was 62 years (IQR 55-72); 42% had clinical, radiological or
histological evidence of pulmonary involvement; 36% had upper airway involvement.
64% were MPO positive and 36% were PR-3 positive. The incidence of AAV with renal
involvement in Southwestern Ireland over the six year period was 15.4 cases per million
person years (95% CI 11.9-18.9). Median creatinine at presentation was 285μmol/L (IQR
152-420). Median creatinine at one year was 137μmol/L (IQR 112-174). 22 (37%) patients
were admitted with sepsis in the follow-up period. 32% (12 out of 38) of patients
treated with oral cyclophosphamide (CYC) were admitted with sepsis during the
follow-up period as compared to 15% (2 out of 13) of patients treated with IV CYC. 17
(35%) patients received Plasma Exchange (PEX). The median creatinine of PEX-treated
patients at presentation compared to non-PEX treated patients was 426μmol/L (IQR
147-992) vs 276μmol/L (165-344), with 71% of patients receiving PEX having significant
pulmonary involvement. At one year the PEX treated patients had a median creatinine of
170μmol/L (IQR 112-219) vs 134μmol/L (IQR 112-168) in the non-PEX treated group
reflecting the more severe initial presentation in the former group. The patient survival
rate at one year was 92% (n=48) comparing favourably to international published outcomes.
10 patients (17%) had died within 1 year. Independent predictors for the end-point (CVE/
death) were: maintenance prednisolone dose (hazard ratio (HR) 1.18-2420), cumulative
cyclophosphamide dose (HR 15.98 [0.005-0.83]), haemoglobin level at the end of follow-up (HR 0.6 [0.262-0.987]), serum PR3-ANCA levels at onset (HR 0.97 [0.995 – 0.99]) and history of prior CVE (HR 5.3 [1.015-27.69]). A cumulative RTX
dose <6g was associated with higher maintenance prednisolone dose (p=0.016).

Conclusions: CVE/death risk in AAV patients is especially high within the first 1 and 5
years of diagnosis. Prior CVE, low serum PR3-ANCA levels at onset and lower
haemoglobin levels at the end of follow-up are associated with increased risk. Intensive
immunosuppressive treatment of AAV at onset and avoidance of high long-term
prednisolone dosage may have a protective effect against atherosclerosis. Rituximab
therapy was associated with a steroid-sparing effect.

TABLE 1: Group A (Serum creatinine <500μmol/l), number=19

<table>
<thead>
<tr>
<th>Baseline creat</th>
<th>Creat at 3 months (IQR)</th>
<th>Creat at 6 months (IQR)</th>
<th>Creat at 12 months (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(μmol/l)</td>
<td>(μmol/l)</td>
<td>(μmol/l)</td>
<td>(μmol/l)</td>
</tr>
<tr>
<td>209(190)</td>
<td>154(66)</td>
<td>15(189)</td>
<td>146(145)</td>
</tr>
<tr>
<td>Group B (serum creatinine &gt;500 μmol/l), number 13</td>
<td>649(454)</td>
<td>352(66)</td>
<td>294(180)</td>
</tr>
</tbody>
</table>

Significance compared to baseline

<table>
<thead>
<tr>
<th>Group A</th>
<th>Group B</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.09</td>
<td>0.79</td>
<td>0.002</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Conclusions: We showed that the incidence and one year mortality rates of renal
AAV in Ireland fall within international norms. Furthermore, they support the
significance difference in infections, relapse, malignancy and mortality rate in the 2
groups at their first year of rituximab therapy.

Introduction and Aims: ANCA-associated vasculitis (AAV) (granulomatosis with
polyangiitis (GPA), and microscopic polyangiitis (MPA)) is associated with an increased
frequency of cardiovascular events (CVE). Objectives: To characterize cardiovascular
outcomes and predictors, including the role of vasculitis therapies, for CVE/death in AAV.

Methods: A single center retrospective review of 307 AAV patients (173 GPA, 134 MPA;
47% male, 12% diabetic; mean age 53 ±17 years) followed up for 61 (±33) years. The
primary end-point was CVE (defined as acute coronary syndrome, new onset angina;
symptomatic peripheral vascular disease, stroke or transient ischaemic attack), or death.
Results: Fifty-one CVE occurred in 42 patients (13.6%) with 28 (9%) deaths. 15.7% CVE
occurred at the onset of AAV, 57.4% CVE/death occurred within first year of AAV
diagnosis, and 27.8% between 1 - 5 years. Independent predictors for the end-point (CVE/
death) were: maintenance prednisolone dose (hazard ratio (HR) 169.6 [95% CI
1.18-2420]), cumulative cyclophosphamide dose (HR 15.98 [0.005-0.83]), haemoglobin
level at the end of follow-up (HR 0.6 [0.262-0.987]), serum PR3-ANCA levels at onset (HR
0.6 [0.995 – 0.99]) and history of prior CVE (HR 5.3 [1.015-27.69]). A cumulative RTX
dose <6g was associated with higher maintenance prednisolone dose (p=0.016).

Conclusions: CVE/death risk in AAV patients is especially high within the first 1 and 5
years of diagnosis. Prior CVE, low serum PR3-ANCA levels at onset and lower
haemoglobin levels at the end of follow-up are associated with increased risk. Intensive
immunosuppressive treatment of AAV at onset and avoidance of high long-term
prednisolone dosage may have a protective effect against atherosclerosis. Rituximab
therapy was associated with a steroid-sparing effect.
and respiratory failure. The introduction of glucocorticoids and immunosuppressive drugs contributes to toxicity and organ damage. 50% of patients relapse within five years and 10-20% have a refractory disease course. Novel therapeutic strategies are required for these patients.

Methods: RITAZAREM (EudraCT 2012-001102-14; ClinicalTrials.gov NCT01697267) is a 1:1, parallel, open randomized trial evaluating the efficacy of rituximab or azathioprine maintenance therapy in relapsing AAV. 190 patients with relapsing AAV will be enrolled across Europe, North America, and Australasia to receive rituximab (4 x 25mg/m²), and glucocorticoid, induction therapy. Those with stable disease at month 4 will be randomised to receive repeat rituximab (1g at 4, 8, 12, 16, 20 months) or azathioprine (2mg/kg/day, stopping at month 27) maintenance therapy. All patients will receive glucocorticoids (standardized taper) concomitant with their alloted maintenance regime. The primary objective is to demonstrate whether or not fixed interval, repeat rituximab is superior to azathioprine in the prevention of disease flare in AAV patients with relapsing disease. Secondary objectives are to demonstrate sustained disease remission beyond the 24 month treatment period, long term safety of rituximab administration, and the optimal remission maintenance therapy in AAV following induction of remission with rituximab. The primary endpoint is the time to disease relapse from randomisation. Patients will be followed, after the 24 month treatment period, for 12 months (minimum) and 24 months (maximum). There will be a preplanned close out of the trial when the last patient reaches 12 months follow up, 36 months after entry.

Results: RITAZAREM is a joint venture of two international collaborative networks, the European Vasculitis Study Group (EUVAS) and the Vasculitis Clinical Research Consortium (VCRC). Rituximab is supplied free of charge by Roche and Genentech. RITAZAREM will inform the future standard of care for patients with AAV, and provide data describing the long term safety of rituximab therapy in AAV patients.


**Introduction and Aims:** Updated Sapporo criteria have provided a tool which should allow clinicians to better classify patients (pts) with anti-phospholipid antibodies (aPL) and anti-phospholipid syndrome (APS).

**Methods:** In pts with biopsy-proven lupus nephritis (LN) and positivity for Lupus Anticoagulant (LA), anticardiolipin antibodies (aCL) and anti-β2-glycoprotein antibodies (anti-β2GPI) we analysed: APS, APS-associated nephropathy (APSN) and main clinical outcomes, employing as classifying criteria Myakis-Class I (any combination), Ia (LA only), Ib (IaC1 only) and Iic (anti-β2GPI only).

**Results:** Out of 101 pts, 70 were aPL negative and 31 aPL positive: 18 Class I, 10 Class Ia, 1 Class Ib, 2 Class Ic. Overall LA was present in 27/31 (87%), triple association in 4/18 (22.2%) and anti-β2GPI in 8/31 (25.8%). APS was present in 15/31 aPL-positive pts; 7 Class I, 7 Class Ib and 1 Class Ic. APS was present in 9 pts, 5 of Class I and 4 of Class Ia; all pts with APS were LA positive and anti-β2GPI negative. In 3 pts (2 pts of Class I and 1 of Class Ia) APSN was an isolated histological picture, whereas in 6 other pts (3 pts of Class I and 3 of Class Ia) typical lesions of LN coexisted (5 diffuse proliferative LN and 1 Membranous nephropathy). Multivariate analysis showed that aPL significantly worsen thrombosis-free survival but do not reduce renal survival, which is instead much worse in proliferative classes of LN (HR 5.37). These classes were significantly less represented in aPL positive pts than in negative ones (35% vs 60%, p = 0.01). Five pts who started dialysis had APSN (G2=7,52, p=0.006).

**Conclusions:** These findings confirm that LA is a strong risk factor for APSN and suggests that anti-β2GPI antibodies positivity may have a protective role, aPL positivity alone does not worsen renal survival, probably because of a lower frequency of proliferative classes in this subset of pts, whereas coexistence of APSN is a risk factor for ESRD.

**Introduction and Aims:** Few studies have analyzed the impact of anti-neutrophil cytoplasmatic antibody (ANCA) on the outcome of lupus nephritis (LN). The aim of this study was to evaluate the influence of ANCA seropositivity in the renal outcome of LN.

**Methods:** A retrospective analysis was carried out on all SLE patients (345) submitted to a kidney biopsy between 1999-12. Patients that fulfilled ACR lupus criteria and tested for ANCA were enrolled. Positive ANCA patients (POS) were randomly matched to ANCA seronegative patients (NEG) according to the type of LN and baseline clearance(MDRD simplified formula). Clinical and laboratory data were collected at baseline, after one year and at the end of follow up. Treatment was decided by the clinical staff based on conventional literature protocols.

**Results:** We included 128 patients (32 POS/96 NEG). Perinuclear ANCA was detected in 87.3% (n=28) of POS patients. At baseline, POS and NEG groups were similar regarding age, complement levels, ANA, anti-DNA antibody, eGFR (46.3±36v44±25m/ min/1.73), proteinuria (3.4±2.6 vs 4.6±4.4 g/day), WHO LN classes, histological activity index, chronicity index, vascular lesions and follow up time. Interestingly, after one year of follow up, Pos group was significantly associated with a lower serum Cr (86.7±22vs106±5±33mg/dl p=0.01) and positive Anti-dsDNA (66%vs31% p<0.01). At the end of follow up, the POS group showed a tendency to have a lower eGFR (56 eGFR±9 vs 71±36m/min/1.73 p=0.09) as well as more patients with eGFR<60m/min(56,3% vs33,3% p=0,03). Finally, logistic regression analysis showed that ANCA is an independent predictor of eGFR<60m/min during follow up, even after adjustments for initial eGFR and chronicity index.

**Logistic Regression Analysis**

**SP329**

**ANCA AND THE RENAL OUTCOME OF LUPUS NERVIUS**

**Serena Simeone**1, **Enrico E. Minetti**1 and **Giorgio Mello**1

**1Nephrology Unit, Careggi Hospital Florence Italy, 2Obstetric Unit, Careggi Florence Italy**

**Introduction and Aims:** Systemic Lupus Erythematosus (SLE) predominantly affects women, especially during fertile ages. Lupus Nephritis (LN) was considered one of the risk factors for maternal and fetal complications during pregnancy. The aim of our study is to compare pregnancies of women with SLE/LN and pregnancies in women with SLE, without LN, to evaluate the role of LN on the maternal and fetal outcome. We have also sought to identify renal risk factors for preeclampsia, preterm delivery before 34th week of gestation and IUUGR below the tenth percentile.

**Methods:** A retrospective study was conducted on 99 pregnancies in 88 women with SLE since 2003 to 2011. The data were analyzed by a multivariate logistic regression.

**Results:** The results showed that there aren’t significant differences in terms of pregnancy outcome between nephropathies women and not, except for the incidence of renal failure, greater in nephropathies women. There were no differences between the two groups for fetal outcome.

**SP330**

**LUPUS NEPHRITIS AND PREGNANCY: MATERNA AND FETAL OUTCOMES, RENAL RISK FACTORS, THERAPEUTIC PERSPECTIVES**

**Calogero L. Cirrini**1, **Pamela Gafo**1, **Elena Romoli**1, **Federico Mecacci**2, **Serena Simeone**2, **Enrico E. Minetti**1 and **Giorgio Mello**1

**1Nephrology Unit, Careggi Hospital Florence Italy, 2Obstetric Unit, Careggi Hospital Florence Italy**

**Introduction and Aims:** Increased Sapporo criteria have provided a tool which should allow clinicians to better classify patients (pts) with anti-phospholipid antibodies (aPL) and anti-phospholipid syndrome (APS). ANCA and the renal outcome of lupus nephritis (LN) was considered one of the risk factors for maternal and fetal complications during pregnancy. The aim of our study is to compare pregnancies of women with SLE/LN and pregnancies in women with SLE, without LN, to evaluate the role of LN on the maternal and fetal outcome. We have also sought to identify renal risk factors for preeclampsia, preterm delivery before 34th week of gestation and IUUGR below the tenth percentile.

**Methods:** A retrospective analysis was carried out on all SLE patients (345) submitted to a kidney biopsy between 1999-12. Patients that fulfilled ACR lupus criteria and tested for ANCA were enrolled. Positive ANCA patients (POS) were randomly matched to ANCA seronegative patients (NEG) according to the type of LN and baseline clearance(MDRD simplified formula). Clinical and laboratory data were collected at baseline, after one year and at the end of follow up. Treatment was decided by the clinical staff based on conventional literature protocols.

**Results:** We included 128 patients (32 POS/96 NEG). Perinuclear ANCA was detected in 87.3% (n=28) of POS patients. At baseline, POS and NEG groups were similar regarding age, complement levels, ANA, anti-DNA antibody, eGFR (46.3±36v44±25m/min/1.73), proteinuria (3.4±2.6 vs 4.6±4.4 g/day), WHO LN classes, histological activity index, chronicity index, vascular lesions and follow up time. Interestingly, after one year of follow up, Pos group was significantly associated with a lower serum Cr (86.7±22vs106±5±33mg/dl p=0.01) and positive Anti-dsDNA (66%vs31% p<0.01). At the end of follow up, the POS group showed a tendency to have a lower eGFR (56 eGFR±9 vs 71±36m/min/1.73 p=0.09) as well as more patients with eGFR<60m/min(56,3% vs33,3% p=0,03). Finally, logistic regression analysis showed that ANCA is an independent predictor of eGFR<60m/min during follow up, even after adjustments for initial eGFR and chronicity index.

**Logistic Regression Analysis**

<table>
<thead>
<tr>
<th>OR</th>
<th>95%CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANCA</td>
<td>3.62</td>
<td>1.3-9.46</td>
</tr>
<tr>
<td>Initial eGFR</td>
<td>0.98</td>
<td>0.97-1.00</td>
</tr>
<tr>
<td>CI</td>
<td>1.4</td>
<td>1.1-1.7</td>
</tr>
</tbody>
</table>

**Conclusion:** In our study, positive ANCA was significantly associated with a worse renal outcome of LN when compared to matched negative ANCA patients.
Risk factors for maternal and fetal complications are: decreased renal function at conception and pre-existing chronic hypertension. Thrombophilia and nephropathy were not risk factors for maternal and fetal adverse events.

SP330

<table>
<thead>
<tr>
<th>Outcome</th>
<th>OR</th>
<th>Std.Err.</th>
<th>Z</th>
<th>P&gt;Z</th>
<th>IC95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombophilia</td>
<td>0.34</td>
<td>0.18</td>
<td>-1.99</td>
<td>0.05</td>
<td>0.12 0.98</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>0.38</td>
<td>0.23</td>
<td>-1.66</td>
<td>0.11</td>
<td>0.12 1.23</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2.75</td>
<td>1.33</td>
<td>2.1</td>
<td>0.04</td>
<td>1.07 7.09</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>2.45</td>
<td>1.5</td>
<td>1.46</td>
<td>0.14</td>
<td>0.74 8.16</td>
</tr>
<tr>
<td>SCR&lt;1.2mg/dl</td>
<td>1.25</td>
<td>0.45</td>
<td>0.63</td>
<td>0.53</td>
<td>0.62 2.53</td>
</tr>
<tr>
<td>Quiescence</td>
<td>0.87</td>
<td>0.39</td>
<td>-0.32</td>
<td>0.75</td>
<td>0.36 2.11</td>
</tr>
<tr>
<td>eGFR&lt;90ml/min/1.73m²</td>
<td>18.73</td>
<td>13.96</td>
<td>3.93</td>
<td>0</td>
<td>4.35 80.70</td>
</tr>
</tbody>
</table>

Conclusions: Our study shows that pregnancy in patients with LN can be completed safely, thanks to a multi-disciplinary approach in specialized centers, with the preconception assessment of the relative risk and subsequent prophylaxis of adverse events.

SP331

**MYCOPHENOLATE AS MAINTENANCE THERAPY FOR LUPUS NEPHRITIS WITH IMPAIRED RENAL FUNCTION**

Francisco Rivera1, Alfonso Segarra2 and Manuel Praga on behalf of the Glomerular Spanish Glomerular Study Group (GLOSEN)3

1Nephrology Hospital General de Ciudad Real Ciudad Real Spain, 2Nephrology Hospital Vall d’Hebron Barcelona Spain, 3Nephrology Hospital Universitario 12 de Octubre Madrid Spain

Introduction and Aims: Mycophenolate (MF) is effective as maintenance treatment after induction therapy in patients with lupus nephritis (LN). However, little is known about its role in patients with impaired renal function. The purpose of this study was to evaluate the efficacy and safety of MF as maintenance therapy for LN and its association with renal function.

Methods: Data were obtained for 56 patients from 13 Spanish renal units who were receiving MF as maintenance therapy for LN. All of them had received intravenous cyclophosphamide as induction therapy. Patients were classified into 2 groups according to renal function at the onset of MF treatment: Group 1 (estimated glomerular filtration rate [eGFR] ≥60 mL/min/1.73m²) and Group 2 (eGFR <60 mL/min/1.73m²). Primary endpoints of the study were the rates of renal relapses and responses (partial or complete) and their relationship with baseline renal function. Secondary outcomes were the appearance of side effects during treatment.

Results: At initiation of MF treatment, there were no differences between groups except age, hemoglobin levels, anti-DNA antibody titer, proteinuria and renal function. In Group 1 (n=38) eGFR was 98±34 mL/min/1.73m² and in Group 2 (n=18) was 43±14 mL/min/1.73m². Exposure to prednisone and MF was similar. The number and percentage of cases that relapsed are indicated in Table 1.

<table>
<thead>
<tr>
<th>SP332 WHY HAVE OUTCOMES OF LUPUS NEPHRITIS BEEN IMPROVING OVER THE LAST 40 YEARS? A MONOCENTRIC EXPERIENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marco Quaglia1, Elisabetta Randi1, Cristina Izzo1, Andrea Airoldi1, Elisa Lazzarich1, Riccardo Bonfiglio1 and Piero Stratta1</td>
</tr>
<tr>
<td>1Translational Medicine Amedeo Avogadro University, <em>Maggiore della Carità</em> Hospital, Nephrology and Transplantation Novara Italy</td>
</tr>
</tbody>
</table>

Introduction and Aims: Outcomes of patients with lupus nephritis (LN) have been improving due to a variety of reasons and relative contributions are difficult to assess. Methods: We included all patients with biopsy-proven LN followed-up at our center and analysed evolution of epidemiological, clinical, histological features and therapeutic immunosuppressive protocols over the last 4 decades.

Results: We enrolled 130 patients stratified by diagnosis over the following periods: ≤1980, n = 43; >1980≤1990, n = 34; >1990≤2000, n = 33; >2000, n =20. Age at diagnosis decreased from 30 to 26 years old and the interval between diagnosis of Lupus and that of LN has extended from 1 to 3 years. The mortality rate fell from 41.8 % to 0%, paralleling decrease in complications. The proliferative classes remained the most represented (59.2 %); the need for dialysis has been dramatically reduced (from 23% to 0%). The most significant therapeutic changes in induction therapy between the first and fourth decade were the increasing use of pulse steroid (ST) (from 0% to 65 %) and the association of cyclophosphamide (CYCLO) (from 25% to 65 %).

Cumulative load of oral drugs was sharply reduced: ST decreased from 533 to 269 mg/Kg and CYCLO from 505 to 180 mg/Kg over the first 5 years. Multivariate analysis showed that survival improvement is mainly associated with the youngest age at diagnosis and on more recent historical periods. The renal prognosis was worse in male, age>30 years, renal failure, proliferative classes with indexes of chronicity, while it appeared to improve with induction therapy other than only oral STER and with high activity index.

Conclusions: The most important factors which determined improved outcomes of LN over the last 4 decades were a progressively earlier diagnosis (from 30-31 to 26-29 years old) and qualitative/quantitative modifications in therapeutic strategies. Adoption of sequential schedules of aggressive induction and fast tapering of immunosuppression have been crucial to achieve better control of the acute phase and reduced toxicity long-term.
CD68 POSITIVE CELLS IN RENAL BIOPSY PREDICT LONG TERM PROGNOSIS IN PROLIFERATIVE LUPUS NEPHRITIS

Cristiane Bitencourt Dias1, Jin Lee2, Letícia Jorge1, Denise Malheiro1, Rui Toledo Barros1 and Viktoria Woronik1
1Nefrologia Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo São Paulo Brazil, 2Pathologia Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo São Paulo Brazil

Introduction and Aims: Studies in proliferative lupus nephritis (LN) showed that in more severe clinical forms the renal histology showed increase macrophages detected by immunohistochemistry. However no long-term assessment of this data is known. The aim of this study was to describe any relations of renal outcomes with tecidual macrophages (CD68+) expressed in renal biopsy specimens obtained on the diagnosis.

Methods: Forty six newly diagnosed patients with proliferative LN were prospectively followed-up during 3.5 (3.2 - 4.0) years. Conventional laboratory tests were collected on diagnosis and on last follow-up. Renal biopsy was done on diagnosis and immunohistochernical study was performed with monoclonal antibody anti CD68 (DAKO) and macrophages MCP-1 (R&D), and results are expressed as cells/microscopic fields. Patients were stratified in two groups according to renal outcome: GFR ≤ 60 mL/min/1.73m2 at the end of follow-up (n=24) and GFR > 60 mL/min/1.73m2 (n=22).

Results: Considering all patients (n=46) tubule and interstitial CD68+ cells showed negative correlation with final MDRD (r = -0.3, p=0.01 and r = -0.45, p=0.001). Macrophages MCP-1 interstitial had positive correlation with chronicity index (r=0.4, p=0.0031).

Conclusions: Tubule and interstitial CD68+ cells expression on renal biopsies may predict long term GFR in proliferative lupus nephritis.

USAGE OF CYCLOSPORINE IN LUPUS NEPHRITIS CLASS III, IV AND V – ONE CENTRE EXPERIENCE

Elena V. Zakharova1 and Ekaterina S. Stolyarevich2
1Nephrology City Clinical Hospital n.a. S.P. Botkin Moscow Russian Federation, 2Pathology City Nephrology Center Moscow Russian Federation

Introduction and Aims: Current KDIGO Guidelines for Glomerulonephritis and EULAR/ERA-EDTA Recommendations for Management of Lupus Nephritis suggest cyclosporine (CYC) as alternative option for initial treatment of lupus nephritis (LN) class V with persistent nephrotic proteinuria, resistant disease not responding to more than one of the recommended initial regimens, and for subsequent treatment of pure class V, or class III/IV intolerant of mycophenolate mofetil and azathioprine (AZA). CYC is also acceptable during pregnancy. We aimed to evaluate retrospectively efficacy of CYC in our cohort of LN patients.

Methods: Using electronic clinical and pathology database we searched 106 LN patients, treated in our nephrology unit since 2002, when we introduced CYC for LN, to 2012. Patients with class I, II and VI, and those who never received CYC were excluded from analysis. Study group included 14 patients, 12 female and 2 male, median age 27.5 [17;39] years. 2 patients had class III, 6 - class IV and 6 - class V LN. Disease duration prior to switching to CYC was 60 [5;168] months, previous treatment included prednisonone in all, cyclophosphamide (CP) “pulses” in 4, mycophenolate mofetil/micophenolic acid (MMF/MPA) in 5, and AZA in 4 cases. Indications for CYC were non- responsiveness or intolerance of CP and MMF/MPA in 6, renal flare after CP and/or MMF/MPA initial and re-induction regimens in 4, and subsequent treatment in 4 patients intolerant of MMF/MPA and AZA. Initial dose of CYC was 200 mg/day [150;250], with dose adjustment to plasma concentration. Duration of therapy constituted 14.5 [1.84] month, duration of follow-up - 18 [1.84] months.

Results: 6 patients (42.8%) achieved and/or sustained complete remission, 6 (42.8%) - partial remission, and only in 2 (14.3%) cases CYC was non-effective. Changes in proteinuria and kidney function and distribution of efficacy in different LN classes are shown in tables 1 and 2.

In one case of LN class V after 5 years of treatment with sustained partial remission 2 nd renal biopsy did not show any signs of CYC-toxicity. 3 patients had 4 normal pregnancies and delivered healthy babies, in 1 case after delivery developed renal flare, successfully treated with MMF. There were no other flares in patients treated with CYC.

Conclusions: In our cohort of 106 LN patients 13% were treated with CYC. In 85.6% of cases complete or partial remissions were achieved/sustained with lowering of median proteinuria from 2.6 to 0.3 g/day and nicely preserved kidney function. The best results were seen in LN class V (100% of remissions, mostly complete), the worst - in class IV (only 66.6% of remissions, mostly partial).

MYCOPHENOLATE MOFETIL TREATMENT FOR RESISTANT LUPUS NEPHRITIS: A SINGLE CENTER EXPERIENCE

Arzu Veloglu1, Derya Guler1, Serdar Nalçaci1, Gurdal Birdal1, Hakki Arkan1, Mehmet Koc1, Haner Direskeneli1, Serhan Tugluk1 and Cetin Ozener1
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Introduction and Aims: Lupus nephritis (LN) is one of the major complications of systemic lupus erythematosus. Mycophenolate mofetil (MMF) is the prominent treatment for maintenance of remission, prevention of recurrence and progression to chronic renal disease. In our study, we evaluate the long term results of MMF treatment in patients with resistant LN.

Methods: Twenty-seven patients (23 female, four male; mean age 36.5±10.6 years) were included into the study. All patients received induction therapy with cyclophosphamide. SLEDAI scores, creatinine levels, estimated glomerular filtration rates, 24-hour protein excretions, C3 and C4 levels were collected both at the beginning and the last visit. Patients were compared according to previous maintenance immunosuppressive therapy. The end stage renal disease (ESRD) development and mortality rates were also recorded.

Results: Mycophenolate mofetil (MMF) showed WHO Class I LN in 14 patients, Class III LN in 10 patients, Class V in one patient and Class II in one patient. In one patient, renal biopsy was not performed because of the coagulation problem. Mean time of MMF treatment was 32.9 months. Mean MMF dose was 1592.6±651 g/day. The first and last SLEDAI scores and 24-hour protein excretion were significantly reduced by MMF treatment (6.7±1.05 vs. 1.9±0.51, p<0.001; 89±0.2 vs. 50±0.12 g/day, p=0.043, respectively). The data are summarized in Table 1. Sixteen patients were under previous maintenance immunosuppressive treatment. There were no differences between...
### SP335 Table 1. Clinical and Laboratory findings of patients

<table>
<thead>
<tr>
<th></th>
<th>Result</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial SLEDAI score</td>
<td>6.7±0.15</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Last SLEDAI score</td>
<td>1.92±0.51</td>
<td></td>
</tr>
<tr>
<td>Initial creatinine (mg/dL)</td>
<td>1.48±0.25</td>
<td>0.756</td>
</tr>
<tr>
<td>Last creatinine (mg/dL)</td>
<td>1.58±0.3</td>
<td></td>
</tr>
<tr>
<td>Initial eGFR (ml/min)</td>
<td>75.7±8.8</td>
<td>0.806</td>
</tr>
<tr>
<td>Last eGFR (ml/min)</td>
<td>74±7.9</td>
<td></td>
</tr>
<tr>
<td>Initial 24-hour protein excretion (g/day)</td>
<td>0.89±0.19</td>
<td>0.043*</td>
</tr>
<tr>
<td>Last 24-hour protein excretion (g/day)</td>
<td>0.50±0.10</td>
<td></td>
</tr>
<tr>
<td>Initial C3 (g/L)</td>
<td>1.04±0.13</td>
<td>0.977</td>
</tr>
<tr>
<td>Last C3 (g/L)</td>
<td>1.03±0.06</td>
<td></td>
</tr>
</tbody>
</table>

*p<0.05, Statistically significant

patients regarding to previous treatment. The mean follow-up time was 50.5 months. One patient died due to sepsis. ESRD was developed in three patients.

Conclusions: MMF treatment has provided an improvement in SLEDAI score and proteinuria in resistant LN patients. There was no deterioration in renal function. MMF is an ideal treatment for patients who were not on complete remission after induction therapy with cyclophosphamide.

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**SP336 RANDOM SPOT URINE PROTEIN/CREATININE RATIO: A RELIABLE METHOD FOR MONITORING LUPUS NEPHRITIS?**

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Introduction and Aims: Lupus nephritis (LN) is a common and severe manifestation of Systemic Lupus Erythematosus (SLE) that can lead to End Stage Renal Disease (ESRD) and death. There have been numerous reports on the use of random spot urine protein/creatinine (P/C) ratio to estimate 24-hour proteinuria in non-SLE Cronic Kidney Disease (CKD). However, few papers have been published regarding SLE patients and some of those authors wrote that random spot urine P/C ratio is unreliable to monitoring proteinuria in SLE GN patients. According to Kidney Disease Outcomes Global Improving (KDIGO) clinical practice Guidelines for Glomerulonephritis, random spot urine P/C ratio should be used for monitoring LN. The aim of our study was to evaluate the agreement of urine P/C ratio in untimed specimens with proteinuria measured by 24 h urinary collection in patients with SLE.

Methods: A prospective observational study was performed. A total of 53 paired (106) spot and 24-hour urine collections were evaluated, as part of routine monitoring of their disease activities. Statistical analyze was performed by SPSS 20.0 Statistical Analysis.

Results: Paired-samples T test didn’t revealed significant differences between the two assay methods (p = 0.216) and a statistically significant correlation was observed between them: Pearson coefficient 0.847 (p < 0.001). After stratifying by degrees of proteinuria, the correlation between 24-hour proteinuria and P/C ratio was maintained in the proteinuria range lower than 500mg/24h (Pearson 0.471, p = 0.006) and above 1000mg/24h (Pearson 0.917, p = 0.010), but this correlation was not observed between 500 and 1000mg/24h (Pearson -0.106, p = 0.718). When stratifying according to background of LN, paired-samples T test didn’t revealed significant differences between the groups.

Conclusions: Our study demonstrated a negative, not significant, correlation between urine P/C ratio and 24 h proteinuria for a range of 500 to 1000mg/24h. This finding is of greater importance and concern because this range is quite common among patients with LN in remission, in whom it is essential to monitoring and detect renal flares early. Until further clarification, to the best of our knowledge, we maintain reluctant to completely substitute the 24-hour collection by P/C ratio especially when (according to other activity parameters) a renal flare is suspected; as well as, before any change in therapy.

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**SP337 URINARY NEUTROPHIL GELATINASE – ASSOCIATED LIPOCALIN (uNGAL) AND URINE MONOCYTE CHEMOTRACCTOR PROTEIN-1 (uMCP-1) IN LUPUS NEPHRITIS**

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Introduction and Aims: Several small studies have indicated a role for urine neutrophil gelatinate – associated lipocalin (uNGAL) and urine monocyte chemoattractant protein-1 (uMCP-1) as markers of lupus nephritis (LN) disease activity. We therefore compared the urinary levels of these two biomarkers in SLE patients with biopsy-proven LN.

Methods: This was a prospective, cross-sectional observational study in which consecutive SLE patients with biopsy-proven LN attending the Nephrology/SLE Clinic were recruited. Two x10 ml samples of early morning urine were collected for urinalysis, urine protein creatinine ratio and for both uNGAL (ng/mg of urinary creatinine) and uMCP-1 (pg/mg of urinary creatinine). The last two were measured from frozen stored urine at end visit using an enzyme-linked immunosorbent assay (ELISA). Their renal function test, serum albumin, urinary parameters, lupus serology and renal SLEDAI-2K (global, renal, extra-renal) were also measured.

Results: Of the 100 patients recruited, 47 had active and 53 inactive LN. uNGAL levels (ng/mg creatinine) and uMCP-1 levels (pg/mg creatinine) were significantly higher in patients with active LN compared to those with inactive renal disease (p = 0.01 and p < 0.001 respectively). Both uNGAL and uMCP-1 levels were highly associated with SLEDAI-2K (renal) (uNGAL: r= 0.32, p = 0.001; uMCP-1: r= 0.39, p = 0.001). Both biomarker levels also correlated with SLEDAI-2K (global) (uNGAL: r= 0.19, p = 0.05; uMCP-1: r= 0.28, p = 0.006). However, there were no associations between uNGAL and uMCP-1 with SLEDAI-2K (extra-renal). Using receiver operating characteristic (ROC) curve, the area under the curve (AUC) for uNGAL was 0.83 (95% CI = 0.74 – 0.92, p = 0.001). With a cut-off value at 91.25 ng/ mg creatinine, uNGAL had a sensitivity of 0.89 and specificity of 0.67 for prediction of LN activity. Whereas, the AUC for uMCP-1 was 0.84 (95% CI = 0.75 – 0.92, p = 0.001). With a cut-off value at 4247 pg/ mg creatinine, uMCP-1 had a sensitivity of 0.89 and specificity of 0.61 for early diagnosis of LN activity.

Conclusions: Both uNGAL and uMCP-1 were highly correlated with LN activity. Since renal flares portend a worse prognosis for the renal outcome, serial measurements of one or both these noninvasive urinary biomarkers may be of great clinical value in predicting early flares of LN thus permitting earlier intervention.
**EXPERIMENTAL MODELS OF CKD**

**SP338**

**SECRETED PRODUCTS OF MACROPHAGES EXPOSED TO CALCIUM OXALATE CRYSTALS INDUCE EPITHELIAL-MESENCHYAL TRANSITION OF RENAL TUBULAR CELLS VIA RhoA-DEPENDENT TGF-β1 PATHWAY**

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Bangkok Thailand

Introduction and Aims: Kidney stone disease is associated with renal fibrosis by the unclear mechanisms. We hypothesized that calcium oxalate (CaOx), a major crystalline component of kidney stones, could induce secretion of fibrotic factors from macrophages leading to "epithelial mesenchymal transition/transdifferentiation" (EMT) of renal tubular cells.

Methods: EMT markers were examined by Western blot analysis and immunofluorescence study. Level of TGF-β1 in the "secreted products of CaOx-exposed macrophages" (CaOx-M-Sup) and cellular levels of the cascade signaling molecule RhoA as well as the ubiquitinated proteins were measured. Finally, a proteasome inhibitor (MG132) was applied to examine whether the intervention of ubiquitin-proteasome pathway (UPP) could prevent EMT and changes in RhoA induced by CaOx-M-Sup.

Results: Western blot analysis revealed an increased level of vimentin (mesenchymal marker) but decreased levels of E-cadherin and cytokeratin (epithelial markers) in MDCK cells treated with CaOx-M-Sup. Immunofluorescence study confirmed the increased level of vimentin and decreased level of cytokeratin, and also revealed the increased level of fibronectin (another mesenchymal marker). The data also showed decreased levels and disorganization of F-actin (cytoskeletal marker) and zonula occludens-1 (tight junction marker) induced by CaOx-M-Sup. ELISA demonstrated the increased level of transforming growth factor-β1 (TGF-β1), the well-defined EMT inducer, in CaOx-M-Sup. Downstream signaling of TGF-β1 was involved as demonstrated by the decreased level of RhoA. Interestingly, pretreatment with MG132 could restore RhoA to its basal level, most likely through UPP. Moreover, MG132 successfully sustained cytoskeletal assembly and tight junction, and could prevent the cells from EMT.

Conclusions: Altogether, these data demonstrate for the first time that CaOx-M-Sup could induce EMT in renal tubular cells by TGF-β1 signaling cascade via RhoA and UPP. This may be, at least in part, the underlying mechanism for renal fibrosis in kidney stone disease.

**SP339**

**25-HYDROXYVITAMIN D CAN REGULATE MINERAL METABOLISM IN A CKD MODEL OF 1α-HYDROXYLASE KO MICE**

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1Nephrology Research Department IRBLleida, University Hospital Arnau de Vilanova Lleida Spain, 2Department of Physiology Nijmegen Centre for Molecular Life Sciences Nijmegen The Netherlands

Introduction and Aims: Supplementation with 25-hydroxyvitamin D (25D) is used in CKD patients without any knowledge of its efficacy and toxicity. Current recommendations are to supplement with 25D to achieve a certain threshold that could affect both, classical and non-classical actions of vitamin D in the body. However, their direct effect on calcium homeostasis (without conversion in calcitriol) is not fully understood. In the present work we studied the effect of 25D treatment on mineral metabolism in a model of 75% nephron mass reduction (oxn) in mice lacking 1α-hydroxylase (1oxKO).

<table>
<thead>
<tr>
<th>Bone formation rate</th>
<th>Osteoid area/bone area</th>
<th>Osteoblast perimeter</th>
<th>Osteoclast perimeter</th>
<th>Bone area/trabecular area</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n)</td>
<td>%/yr</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Healthy control (7)</td>
<td>548 (±241)</td>
<td>0</td>
<td>16.7 (±5.4)</td>
<td>17.2 (±5.7)</td>
</tr>
<tr>
<td>CKD control (3)</td>
<td>5.9 (10)</td>
<td>64 (±17)</td>
<td>27.1 (±4.4)</td>
<td>7.3 (±3.9)</td>
</tr>
<tr>
<td>CKD+R-641 (6)</td>
<td>622 (±396)</td>
<td>12 (±15)</td>
<td>16.3 (±4.9)</td>
<td>4.4 (±1.8)</td>
</tr>
</tbody>
</table>

**Methods**: A dose response study was carried out in 10-week-old SNX 1oxKO mice using 25, 50 and 100 μg/g of 25(OH)D3 to compare its efficacy activating VDR with that of a single dose of 1.25(OH)2D3 (50 pg/g).

**Results**: Sham and SNX 1oxKO mice receiving vehicle were both hypocalcemic. 1.25D raised blood Ca+2 levels near normal values (11.5±0.23mg/dl). Serum Ca2+ normalization was achieved with 25 ng/g (10.63±0.26mg/dl) of 25D. The highest dose provoked marked hypercalcemia (12.46±0.71 mg/dl). Serum phosphate (P) levels were low in untreated sham 1oxKO (ko sham: 5.75±0.56mg/dl) and, surprisingly, were not modified by nephrectomy. Treatment with 1.25D and the two lower doses of 25D significantly raised serum P to normal levels. As expected, KO mice presented severe secondary hyperparathyroidism (PTH >3000pg/ml). PTH suppression to normal levels (100-200 pg/ml) was achieved with 1.25D (297.6±7.95 pg/ml, n=7) and the 50 ng/g dose of 25D (317.17±100.74 pg/ml, n=7). Serum 25D increased in a dose dependent manner with 25D administration above the current recommendations to avoid vitamin D toxicity (25ng/g: 270.21±3.40 pg/ml, 50 ng/g: 336.95±230.52 pg/ml and 100 ng/g: 601.14±342.46 pg/ml). In the kidney, 1.25D effects increasing TRPV5 mRNA expression were similar to those achieved with 50 ng/g and 100 ng/g of 25D. Calcibindin-D28k mRNA and protein expression was up-regulated by 1.25D and also by any dose of 25D. In duodenum, 1.25D produced a 4.5 fold increase in TRPV6 mRNA levels and 25D increased TRPV6 levels between 1.5 and 2 folds. Calcibindin-D98k mRNA and protein levels were significant up-regulated with the two highest doses of 25D with a similar potency to that of 1.25D.

**Conclusions**: These results show that 25D administration can normalize serum Ca, P and PTH, with a potency similar to that of 1.25D without being activated by 1α. However, the concentrations of 25D required in blood are extremely high, and may cause toxicity.

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Introduction and Aims: Vitamin D deficiency (VDD) is highly prevalent in Chronic kidney disease (CKD) patients. Loss of kidney function reduces the production of 1α,25-dihydroxyvitamin D (1,25(OH)2D3), a hormone that regulates the levels of phosphate and calcium. Reduced vitamin D levels are associated with an increased risk of cardiovascular disease (CVD) and osteoporosis. Many studies have focused on the effector link of renal inflammation, but self-defense mechanisms of podocytes are poorly studied. The aim of the study was to investigate the effect of VDD on podocyte expression and fibrosis development in a model of IR-AKI.

Methods: Male Wistar rats (180–200g) were randomly divided into four groups (n=8 each): control (C) and ischemic (IR) fed a standard diet; VDD and VDD+IR, fed a low-Vitamin D diet. On day 28, IR and VDD+IR rats were sacrificed at 45-minute clamping of both renal arteries. On day 90, we measured inulin clearance (GFR). Mean arterial blood pressure (MAP), renal blood flow (RBF) and calculated renal vascular resistance (RVR). We also measured serum levels of 25-hydroxyvitamin D (25(OH)D3), creatinine (Cr), urea and PTH. Histology, Western Blot and Immunohistochemical studies were performed.

Results: VDD+IR rats suggest progressive renal injury. Downregulation of podocyte expression is a possible marker of chronicity. Our study shows a very plausible role of VDD in this pathway as a potential stimulus for fibrosis.

Conclusion: VDD+IR may be considered as a risk factor for CKD progression.

Introduction and Aims: The increased proteinuria/fibrosis and fibronectin/collagen IV expression in C57BL/6 and SDF-1+IR rats suggests progressive renal injury. Downregulation of podocyte expression is a possible marker of chronicity. Our study shows a very plausible role of VDD in this pathway as a potential stimulus for fibrosis.

Conclusion: VDD+IR may be considered as a risk factor for CKD progression.

Introduction and Aims: The increased proteinuria/fibrosis and fibronectin/collagen IV expression in C57BL/6 and SDF-1+IR rats suggests progressive renal injury. Downregulation of podocyte expression is a possible marker of chronicity. Our study shows a very plausible role of VDD in this pathway as a potential stimulus for fibrosis.

Conclusion: VDD+IR may be considered as a risk factor for CKD progression.
focal-segmental glomerulosclerosis and progressive renal failure. The aim of this study was to test the antiproteinuric and nephroprotective efficacy of RAS antagonists in this mouse model.

Methods: C57BL/6 mice with Nphs2<sup>flox/R140Q</sup> Cre<sup>+</sup> genotype were injected with Tamoxifen or vehicle for 5 days to induce hemizygosity for R140Q mutant podocytes. The animals (8 per group) were treated prophylactically with the ACE inhibitor ramipril (R), the AT1 receptor blocker candesartan (C), the combination of ramipril and candesartan (R+C) or the non-RAS antihypertensive amlopidine (A), all administered untreated with either tamoxifen induction (sick controls) or vehicle injections (healthy controls). Weight, blood pressure and proteinuria were monitored once weekly. Biochemical and histopathological changes were examined after 4 weeks.

Results: Blood pressure was elevated in sick animals and more markedly reduced by RAS antagonists than by amlopidine (mean arterial pressure: healthy controls, 85; sick controls, 96, R, 69; C, 66; R+C, 50; A, 81 mm Hg). Proteinuria was markedly attenuated in animals treated with RAS antagonists (by 76% in C, 77% in R and 78% in R+C relative to sick controls) but not in those receiving amlopidine. After 4 weeks, R + C were normo-albuminemic (R, 27, C, 30, R+C, 31, A, 24 g/L, sick controls, 19; healthy controls, 32 g/L) and serum creatinine was increased less than in untreated animals (R, 0.12; C, 0.12; R+C, 0.14; A, 0.13; sick control, 0.16; healthy control, 0.11 mg/dL). All animals treated with RAS and amlopidine showed no glomerular sclerosis indices (R+C, 0.91; sick controls, 1.47; healthy controls, 0.25). The average number of podocytes per glomerulus was reduced by 50% in sick animals but was preserved in R+C animals (R+C, 73; A, 62; sick controls, 79; healthy controls, 75). Within glomeruli, a marked decrease in podocyte mass was observed in sick animals. Western blot analysis showed a substantial loss of podocin protein in all induced animals irrespective of pharmacological treatment.

Conclusions: In mice carrying the most common human podocin mutation, administration of RAS antagonists markedly attenuates proteinuria and podocyte loss and delays glomerulosclerosis despite persistently increased intracellular degradation of mutant podocin protein. Our findings suggest that RAS blockade provides effective pharmacological nephroprotection in this hereditary podocytopathy.

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**SP345**  
PODOCYTE DYSFUNCTION IN CYSTINOSIS IS ASSOCIATED WITH INCREASED PODOCYTE MOTILITY AND PODOCYTURIA

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**Introduction and Aims:** Cystinosis is an autosomal recessive disorder caused by mutations in the CTNS gene that encodes a lysosomal cystine transporter and results in high cystine levels in the patients’ lysosomes. A major consequence of cystinosis is the development of severe renal disease, characterized by general proximal tubular dysfunctions and progressive end-stage renal failure. Despite the general belief that renal proximal tubular cells are the primary targets in cystinosis, several lines of evidence, such as the presence of glomerular proteinuria and morphologic podocyte changes, point to early podocyte dysfunction in this disorder.

**Methods:** Blood pressure was elevated in sick animals and more markedly reduced by RAS antagonists (mean arterial pressure: healthy controls, 85; sick controls, 96, R, 69; C, 66; R+C, 50; A, 81 mm Hg). Proteinuria was markedly attenuated in animals treated with RAS antagonists (by 76% in C, 77% in R and 78% in R+C relative to sick controls) but not in those receiving amlopidine. After 4 weeks, R + C were normo-albuminemic (R, 27, C, 30, R+C, 31, A, 24 g/L, sick controls, 19; healthy controls, 32 g/L) and serum creatinine was increased less than in untreated animals (R, 0.12; C, 0.12; R+C, 0.14; A, 0.13; sick control, 0.16; healthy control, 0.11 mg/dL). All animals treated with RAS and amlopidine showed no glomerular sclerosis indices (R+C, 0.91; sick controls, 1.47; healthy controls, 0.25). The average number of podocytes per glomerulus was reduced by 50% in sick animals but was preserved in R+C animals (R+C, 73; A, 62; sick controls, 79; healthy controls, 75). Within glomeruli, a marked decrease in podocyte mass was observed in sick animals. Western blot analysis showed a substantial loss of podocin protein in all induced animals irrespective of pharmacological treatment.

**Conclusions:** In mice carrying the most common human podocin mutation, administration of RAS antagonists markedly attenuates proteinuria and podocyte loss and delays glomerulosclerosis despite persistently increased intracellular degradation of mutant podocin protein. Our findings suggest that RAS blockade provides effective pharmacological nephroprotection in this hereditary podocytopathy.

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**SP347**  
LACK OF MURINE DOUBLE MINUTE (MMD)-2 IN PODOCYTES CAUSES AUTOPHAGIC CELL DEATH AND FOCAL SEGMENTAL GLomerulosclerosis

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<sup>1</sup>Renal Division, Medizinische Klinik und Poliklinik IV, Universität München Munich Germany, <sup>2</sup>Department of Pathology & Immunology, Washington University School of Medicine in St Louis MO USA

**Introduction and Aims:** Podocytes are terminal differentiated epithelial cells of the glomerular filtration barrier that can hardly be replaced upon loss. Like neurons, they seem to survive many years or even decades and it remains a miracle, how they manage to stand the many hemodynamic, toxic, and immunologic insults that occur during lifetime. The E3-ubiquitin ligase murine double minute (MMD)-2 is a non-redundant element of NF-κB signaling and the master negative regulator of tumor suppressor gene p53- mediated cell cycle arrest. We have recently shown that MDM2 blockade can prevent adriamycin-induced podocyte loss, proteinuria, and glomerulosclerosis. In these studies, MDM2 blockade restored p53 and prevented podocyte mitotic catastrophe, because podocyte mitosis leads to podocyte detachment and death. The role of the intense MDM2 expression in non-stressed podocytes, however, is unknown today. We hypothesized, that MDM2 would be required to prevent p53 overactivation, a state that may cause premature senescence or even podocyte death.

**Methods:** We generated and phenotypically characterized podocyte-specific MDM2-knockout mice (Podocin<sub>Cre</sub>/Mdm2<sup>-/-</sup> mice). Revealed lack of MDM2 in podocytes upon immunostaining of renal sections and by glomerular isolate qPCR. Nephritis/WT-1+ podocyte counts were identical in 3 weeks old mice of both groups. The podocyte/glomerulus ratio increased with aging in the heterozygous control mice while it declined in podo-MDM2 KO mice by week 14 of age. Relative podocytepentya in podo-MDM2 KO mice resulted in proteinuria and progressive focal segmental glomerulosclerosis. Electron microscopy of podo-MDM2<sup>-/-</sup> renal tissue displayed the typical abnormalities of glomerulosclerosis but also specific ultrastructural changes in the podocytes, such as massive vacuolization and ER abnormalities suggesting involvement of excessive autophagy and autophagic podocyte death.

**Conclusions:** In contrast to the pathogenic (mitogenic) role of MDM2 in podocyte injury, podocyte need MDM2 for homeostasis, and excessive autophagy. MDM2 seems to be an essential regulator of podocyte injury and homeostasis.

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**SP348**  
UP-REGULATION OF TRPC6 IN PODOCYTES ASSOCIATED WITH THE DEVELOPMENT OF GLomerular HYPERFILTRATION IN RATS WITH 5/6 Nephrectomy

Takatsuji Iwakata<sup>1</sup>, Hajime Hasegawa<sup>2</sup>, Kaori Takayanagi<sup>2</sup>, Taisuke Shimizu<sup>1</sup>, Shokichi Naito<sup>1</sup>, Togo Aoyama<sup>1</sup>, Takashi Sano<sup>1</sup>, Yasuo Takeuchi<sup>1</sup> and Kouji Kamiya<sup>1</sup>

<sup>1</sup>Nephrology in Internal Medicine Kitasato University School of Medicine Sagamihara Kanagawa Japan

**Introduction and Aims:** Glomerular lesion induced by in vivo administration of specific antibody against mouse nephrin protein are investigated.

**Methods:** Thirty microgram of expression vector containing nephrin cDNA of full length, immunoglogulin (Ig) motiis 1-8 or fibronectin motiis are administered 4 times every 2 weeks into 9 New Zealand White rabbits. Control vectors were also administered into 3 rabbits in the same manner. Purified rabbit IgG obtained at 8 wks are administered once into C57BL/6N mice, intravenously. Urinary protein excretion and pathological findings of mouse kidney are evaluated.

**Results:** In mice with 1-4mg IgG produced by full-length nephrin cDNA showed massive proteinuria from day 1 with a dose-dependent manner. All 6 mice with 4mg IgG and 6 out of 7 mice with 2mg IgG produced by full-length cDNA showed a glomerular lesion of FSGS. Remaining 8 mice with 1-2 mg IgG produced by full-length cDNA had a minor glomerular abnormality. None of 12 mice with 4mg IgG produced by Ig motiis 1-8 and 18 fibronectin motif cDNA showed a significant proteinuria.

**Conclusions:** Polyclonal specific antibody against mouse nephrin protein induces glomerular FSGS lesion and nephritic syndrome in mice.
SP349  MODEL FOR IDIOPATHIC FSGS: PROTEINURIA AFTER INJECTION OR OVEREXPRESSSION OF CARDIOTROPHIN-LIKE CYTOKINE 1 IN MICE

Virginia J. Savin1, Mukut Sharma1, Changli Wei3, Jochen Reiser3,

Introduction and Aims: Idiopathic focal segmental glomerulosclerosis (FSGS) is associated with recurrence after transplantation due to a circulating permeability factor or factors (N Engl J Med. 334:878-883, 1996). We have shown the effects of expression of Cardiotrophin like cytokine 1 (CLC-1 or CLCF1), a member of the IL-6 family, as a candidate for the active substance. CLC-1, like FSGS patient plasma, increases albumin permeability (Pμ) of isolated glomeruli and appears to act via its known receptor complex and activation of the JAK/STAT signaling pathway. Monoclonal antibody to CLC-1 markedly diminished the effect of recombinant FSGS patient plasma from patients with idiopathic FSGS and may play an important role in creation of a murine model of human recurrent FSGS.

Methods: All studies were done in C57BL6 mice. rCLC-1 (R&D Systems) was injected intraperitoneally (IP), one dose, 10 μg /kg, or infused by minipump for 28 days. 40 μg /kg/day. A construct containing CLC-1 was administered by electroporation in the hind limb of mice. Measurements included urinary albumin/creatinine, pα2K and pST3A in peripheral blood cells (PBC) and in kidney homogenate. Glomerular histology was assessed.

Results: Albuminuria was induced promptly by rCLC-1 after injection or electroporation. Peak albuminuria occurred by 7 days of expression and was 3-5 fold increased vs. baseline. IP administration of rCLC-1 increased pα2K and pST3A of PBC within 15 min. WT-1, and Crif1 for mitochondrial dysfunction in podocytes. We evaluated the expression score of desmin were all significantly increased in 5/6 nephrectomized (N) mice, similarly, gene expression of TRPC6 was significantly increased in N (100.5±5.8) vs. WT-1 and antibodies confirmed co-localization of both antigens, and indicated an increase in the number of TRPC6 positive podocytes in N. Additionally, double immunostaining with TRPC6 and synaptopodin also showed an increase in TRPC6 expression above the capillary wall in N associated with blunted immunoreactivity and disruption of synaptopodin staining along the capillary. Changes in gene expression of TRPC6 in podocytes were also studied by use of in situ hybridization.

Conclusions: In the present study, introduction of TRPC6 in the development of glomerular sclerosis resulted from GHF. Electroporation introduced CLC-1 and appears to act via its known receptor complex and activation of the JAK/STAT signaling. We assumed that urinary losses of PACAP bound to ceruloplasmin in NS might lead to PACAP deficiency, leading to thrombocytosis and increased platelet reactivity. The aim of this study was to investigate plasma PACAP levels in relation to blood platelet counts and aggregability in patients with congenital NS (CNS). Methods: Four patients with CNS of the Finnish type, aged 0.5-19 months were tested. Plasma and urinary levels of PACAP were measured semi-quantitatively by western blot. In two patients, platelet aggregation tests were performed by a platelet aggregometer before and after bilateral nephrectomy. Hematopoietic stem cells were isolated from the same two patients and differentiated into colony forming unit (CFU) megakaryocytes.

Results: All patients had plasma PACAP deficiency (14-40% of control, p<0.001) and excessive urinary PACAP excretion. In three patients both kidneys were removed as a routine treatment of CNS. PACAP plasma levels progressively increased during the first days after nephrectomy and blood platelet counts normalized. In one patient, platelet aggregation tests were performed. In analogy to PACAP-deficient mice, an increased platelet aggregation response to collagen was found in nephrotic state, while platelets isolated after bilateral nephrectomy showed normal reactivity towards collagen. In two patients hematopoietic stem cells were isolated before and after bilateral nephrectomy and there was no difference between conditions with and without addition of recombinant PACAP.

Conclusions: Urinary PACAP losses leading to blood PACAP deficiency explain increased platelet count and aggregability via stimulating megakaryocytes. This mechanism is likely to underlie arterial thrombosis in CNS.

SP350  URINARY LOSS OF PACAP AS A CAUSE OF INCREASED RISK OF THROMBO-EMBOLIC DISEASE IN CONGENITAL NEPHROTIC SYNDROME

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Introduction and Aims: Thrombotic complications occurring in up to 15% of patients represent a severe burden in nephrotic syndrome (NS). The underlying mechanisms are mainly unraveled in regard of venous thrombosis, while elevated blood platelet count and hyperaggregability increase the risk of arterial thrombosis. A role of the neuropeptide PACAP (pituitary adenylate cyclase-activating polypeptide) as an inhibitor of megakaryocyte maturation and platelet function has recently been established. PACAP interferes with the regulation of apoptosis in megakaryocytes, via stimulation of NFκB signaling. We assumed that urinary losses of PACAP bound to ceruloplasmin in NS might lead to PACAP deficiency, leading to thrombocytosis and increased platelet reactivity. The aim of this study was to investigate plasma PACAP levels in relation to blood platelet counts and aggregability in patients with congenital NS (CNS).

Methods: Four patients with CNS of the Finnish type, aged 0.5-19 months were tested. Plasma and urinary levels of PACAP were measured semi-quantitatively by western blot. In two patients, platelet aggregation tests were performed by a platelet aggregometer before and after bilateral nephrectomy. Hematopoietic stem cells were isolated from the same two patients and differentiated into colony forming unit (CFU) megakaryocytes.

Results: All patients had plasma PACAP deficiency (14-40% of control, p<0.001) and excessive urinary PACAP excretion. In three patients both kidneys were removed as a routine treatment of CNS. PACAP plasma levels progressively increased during the first days after nephrectomy and blood platelet counts normalized. In one patient, platelet aggregation tests were performed. In analogy to PACAP-deficient mice, an increased platelet aggregation response to collagen was found in nephrotic state, while platelets isolated after bilateral nephrectomy showed normal reactivity towards collagen. In two patients hematopoietic stem cells were isolated before and after bilateral nephrectomy and there was no difference between conditions with and without addition of recombinant PACAP.

Conclusions: Urinary PACAP losses leading to blood PACAP deficiency explain increased platelet count and aggregability via stimulating megakaryocytes. This mechanism is likely to underlie arterial thrombosis in CNS.

SP352  MITOCHONDRIAL DYSFUNCTION IN PODOCYTE REDUCES ALPHA ACTININ-4 AND SYNAPTODIN IN PODOCYTE, WHICH INDUCES PROTEINURIA

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Introduction and Aims: Our previous report showed that Crif1deletion induce severe mitochondrial dysfunction in mice podocyte. And it resulted in massive albuminuria and effacement of foot process in mice. Actin cytoskeleton architecture and dynamics in podocyte are important constituents of the glomerular filtration barrier. There have been few studies about the relation of mitochondria and actin cytoskeleton in podocytes of glomerulus. We evaluated the changes of actin cytoskeletal proteins and architecture in mitochondrial injured podocyte.

Methods: We used immortalized mouse podocyte cell line. Crif1 silencing(si)RNA treatment was used for inducing mitochondrial injury. We divided podocytes into 3 groups; control podocytes, scramble(s)c RNA treated podocytes, Crif1 siRNA treated podocytes. We checked the expression of mitochondrial respiratory complex I, II, III, IV, α-tubulin, nephrin, α-actinin-4 and an increase of fragment mitochondria in confocal microscopy. Using confocal microscopy, we examined actin cytoskeleton architecture and mitochondria of podocyte. For evaluation of cell migration, we performed scratch assay. Results: Crif1 siRNA treatment reduced the expressions of mitochondrial respiratory complexes I, II, III, IV, α-tubulin, nephrin, α-actinin-4 and ZO-1, α-actinin-4 and an increase of fragment mitochondria in confocal microscopy compared to scrambled siRNA treated podocytes. Podocyte migration was increased in Crif1 siRNA treated podocytes. Conclusions: With the above results, it is speculated that mitochondrial dysfunction induced by crif1 inhibition reduces alpha actinin-4 and synaptodin in podocyte.
endothelial barrier promotion by FTY720. In the study, we investigated the effects of FTY720 on the levels of nitric oxide (NO) and the expression of hMSCs in renal tissue from subtotally nephrectomized rats.

Methods: Seven days after surgery, Sprague-Dawley rats were allocated to the following groups: Sham operate surgery, subtotally nephrectomy (SNX) + vehicle, and SNX + FTY720 (0.3mg/kg body wt). Rats were killed on week 12 after surgery and blood, urine, and kidneys were collected for analysis. Blood pressure was detected before killing. The renal structural changes were investigated by light and transmission electron microscopy. The expressions of hMSCs were detected by immunohistochemical staining, RT-PCR and Western blot.

Results: FTY720 significantly attenuated the rise in blood pressure, proteinuria, serum creatinine and urea nitrogen in SNX (p<0.05). FTY720 treatment prevented increased expression of interstitial matrix proteins such as collagen type I and collagen type III, fibronectin, and α-SMA in SNX kidneys. Immunohistochemistry showed the tissue localization of hMSCs in the renal tissue from subtotally nephrectomized rats, which suggested a potential value of FTY720 in preventing progression of chronic kidney disease.

Conclusions: FTY720 ameliorates endothelial injury in glomeruli and vasculature in kidneys from subtotally nephrectomized rats, which suggests a potential value of FTY720 in preventing progression of chronic kidney disease.
historical methods have been used to analyze the state of renal vasculature in fibrosis. The aim of this study was to evaluate functional in vivo tests of the renal microvasculature, such as non-invasive, longitudinal blood volume determination, in murine models of renal fibrosis.

Methods: We sequentially analyzed two models of renal fibrosis: murine unilateral ureteral obstruction (UUO, days 1, 3, 5, 7 and 10) and Alport mice (6 and 8 weeks old). We assessed renal blood volume (rBV) using in vivo contrast-enhanced micro computed tomography (μCT); visualized vasculature using ex vivo high-resolution μCT (spatial resolution 4 μm) after in vivo perfusion of the renal vasculature with a cast agent; and analyzed vascular permeability using extravasation of Evans blue.

Results: Kidney volume assessed by μCT showed expansion of obstructed UUO kidneys due to hydronephrosis (starting at day 1 and reaching maximum on day 3) and compensatory hypertrophy of the contralateral kidneys (obvious at day 7). The rBV slightly increased in contralateral kidneys on day 5 (+12%, p<0.01, n=4 per group) and remained stable thereafter, whereas rBV in obstructed kidneys was significantly decreased on day 3 (-33%, p<0.01) and further decreased until day 10 (-46%, p<0.01) in comparison to contralateral kidneys. In Alport mice, a slight decrease in kidney volume could be observed from week 6 to week 8. Compared to wild type littermates, Alport mice demonstrated a significantly reduced rBV at the age of 6 and 8 weeks (+41% and -53%, respectively, both p<0.01, n=5 per group). Results were validated using immunohistochemistry (CD31, VEGFR2, Meca-32). 2D slices and 3D volume renderings of high-resolution ex vivo μCT scans demonstrated a significant reduction of mainly small renal blood vessels in both models of renal fibrosis (UUO at day 10 and Alport at week 8) in comparison to healthy kidneys and wild type littermates. The extravasation of Evans blue was higher in obstructed UUO kidneys (+112%, p<0.01) and with high variability also in Alport mice (+143%, p<0.01).

Conclusions: We established methods for the in vivo assessment of the renal vasculature in mice. Renal fibrosis in both models was characterized by a progressive reduction of the overall number and functionality of renal blood vessels. These data not only lay the basis for better understanding of renal fibrosis progression but also for intervention studies targeted at maintaining the number and function of renal microvessels.
upregulate HO-1 when compared to tubular cells as shown by experimental models of glomerular injury in which potent HO-1 inducers such as cytokines and pro-oxidant radicals including superoxide (O2•−), hydrogen peroxide (H2O2) and peroxynitrite (ONOO−), are overproduced in the glomerular milieu; a robust HO-1 induction was consistently found not in glomerular cells but at tubular sites “downstream” of the glomerular capillary. This raises the question of whether HO-1 induction in glomeruli is subject to tight regulation. Here, we address this question in normal rat glomeruli using the natural HO-1 substrate/inducer, heme (hemin).

Methods: Glomeruli were isolated from wild type (WT), male, Sprague-Dawley (SD) rats, hmox1−/− SD, and SD with glomerular epithelial cell (GEC)-targeted HO-1 overexpression (GEC+/−). hmox1−/− rats were obtained using Zinc Finger Nuclease (ZFN) technology designed to target a specific HO-1 sequence within Exon 3. GEC−/− rats were obtained using Sleeping Beauty Transposon mediated transgenesis. Glomeruli from WT, hmox1−/− and GEC−/− rats were treated with defined concentrations of Heme (Hemin) for 18 h. Glomerular protein lysates were assessed for HO-1 levels by western blotting. HO-1 mRNA levels were assessed by quantitative Real-time PCR amplification. A robust HO-1 induction was routinely observed in WT rat glomeruli, a 60-70% HO-1 depletion was achieved compared to WT. In WT glomeruli, low Hemin (6-200 μM) concentrations increased HO-1 synthesis (mRNA and protein) in a dose dependent manner, up to 2-fold.

Results: Constitutive HO-1 protein expression was observed in wild type, hmox1−/− and GEC−/− glomeruli. In hmox1−/− rat glomeruli, a 60-70% HO-1 depletion was achieved compared to WT. In WT glomeruli, low Hemin (6-200 μM) concentrations increased HO-1 synthesis (mRNA and protein) in a dose dependent manner, up to 2-fold.

Conclusion: Heme-mediated HO-1 synthesis in glomeruli is regulated by HO-1 levels achieved, pointing towards a negative feedback regulatory mechanism. This mechanism is clearly operational in GEC in which, under injury conditions, may serve to prevent HO-1 protein from reaching toxic levels that may cause cytotoxicity due to the release of catalytically active Fe2+.}

**SP362**

**AUTOPHAGY INDUCTION PROMOTES ARISTOLOCHIC ACID-I-INDUCED RENAL INJURY**

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Introduction and Aims: Ingestion of aristolochic acid (AA) causes AA nephropathy first by inducing tubular apoptosis in the acute phase. Crosstalk between autophagy and apoptosis might orchestrate the fate of tubular cells in acute AA nephropathy. We tested this hypothesis by acute administration of AA-I-induced renal injury.

Methods: Autophagy was induced as enhanced Atg5 and LC-3-II expressions in the kidneys of AA-I-treated rats. Punctate LC3-II distribution was observed in AA-I-treated kidneys. Atg5 and Atg7 knockdown by using shRNA inhibitor E64 induced the accumulation of LC-3-II, which further promoted apoptosis as shown by enhanced PARP cleavage. Inhibition of autophagy by 3-methyl adenosine led to attenuating AA-I-induced apoptosis as indicated by decreasing PARP cleavage, nuclear condensation, and decreasing number of cells negative for acridine orange/ethidium bromide staining. Furthermore, knockdown of Atg5 by short hairpin RNA attenuated LC-3-II expression and PARP cleavage in NRS52E cells.

Conclusions: We suggest that an Atg5-dependent autophagy, which promotes renal tubular cell apoptosis, is induced in the acute phase of AA-I-induced nephropathy.

**SP363**

**ASSESSMENT OF ERYTHROPOIETIN EFFECTS IN THE PROGRESSION OF EXPERIMENTAL CHRONIC KIDNEY DISEASE**

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Introduction and Aims: The Erythropoietin (EPO) is an endogenous glycoprotein produced primarily in kidney and its main function is stimulate the production of blood cells to transport oxygen to the tissues. The EPO has been used primarily to treat anemia caused by chronic kidney disease. Recent studies have shown a renoprotective EPO effect on ischemic and chronic kidney disease. The mechanisms of renoprotection include inhibition of apoptosis, inflammation and induction of angiogenesis. Thus, the aim of this study is to evaluated the influence of EPO on progression of kidney disease in experimental chronic kidney disease.

Methods: Male Wistar rats weighing 280-300g underwent 5/6 nephrectomy and were divided into two groups: (NX) only nephrectomized(n=6) and (NX-EPO) nephrectomized(n=6) and treated with a weekly dose of erythropoietin (250U/kg/ip). All animals were sacrificed 8 weeks after surgery. Hematocrit, serum creatinine, proteinuria, indirect blood pressure measurement, glomerular score and tubular lesion and immunohistochemical analysis were assessed. For immunohistochemical of desmin expression, a semiquantitative 0-4 system, with 0 being negative and 4 the most positive stained, was used. The immunohistochemical expression of PCNA was determined by counting positive tubular cells in 10 randomly selected fields (400×).

Results: The NX-EPO group showed significant improvement in serum creatinine (NX 1.6 ± 0.4 versus NX-EPO 0.1 ± 0.1, P = 0.001) and protein/creatinine ratio (NX 11.2 ± 6.0 versus NX-EPO 4.1 ± 2.2, P = 0.021). Histopathological results demonstrate a lower rate of glomerular sclerosis (NX=33% versus NX-EPO=17%) and tubulointerstitial fibrosis (grade III NX versus grade I NX-EPO) according Banff classification.

Conclusion: The Erythropoietin prevents progression of kidney disease in experimental chronic kidney disease by improving of serum creatinine, proteinuria and attenuation of glomerular lesion score. We observed a lower expression of desmin in podocytes and lower expression of PCNA in tubular cells regardless of its effect on hematocrit and blood pressure.
of proinflammatory cytokines such as interleukin-6 and generated neutrophils recruiting producing NGAL (Neutrophil Gelatinase-Associated Lipocalin) release. Methods: 77 plasma samples were collected in a tertiary hospital; 61% of them (47 patients) had AKI and 39% (30 patients) had a normal renal function. We obtained samples for 26 septic patients (47% AKI), 23 transplant kidney patients (ischemia-reperfusion model; 70% AKI), 15 patients under colistin treatment (nephrotoxic model; 46% AKI) and 13 patients with several possible AKI risk factors (50% of them developed finally multifactorial AKI). Samples were tested for IL-6 and MAC using ELISA kit and NGAL were tested by means to immunofluorescence assay. Results: Plasma MAC level was statistically different in patients with AKI as compared to normal renal function controls, regardless of the etiology of AKI (501±247 mg/AU/ml vs 388±150 mg/AU/ml; p<0.015). Plasma IL-6 levels were significantly higher in a AKI patients compared to normal kidney function (10,47±2,8 pg/ml vs 7,37±3,0 pg/ml; p=0.02) and NGAL levels were also significantly higher in AKI patients (570,5±305 mg/g vs 292,5±233 mg/g; p<0.001). No relevant differences in the fibrinogen biomarkers were detected in the different etiological subgroups. Conclusions: Our data show that in AKI, regardless etiology, the complement system is activated, leading the pro-inflammatory cytokine stimulation (IL-6) and could produce releasing of NGAL from neutrophils.

**SP366**

**TIMP-1 INHIBITION AMELIORATES RENAL FIBROSIS IN TGF-β TRANSGENIC MICE**

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Introduction and Aims: We have previously shown that CBAxB6-TGFB transgenic mice are characterized by hepatic expression of Alb/TGFß transgene results in 10 fold elevation of circulating TGF-ß levels. These mice develop massive proteinuria, severe glomerulosclerosis, moderate interstitial fibrosis and premature uremic death by the age of 21 days. Analysis of renal matrix related molecules (MMPs, TIMPs, Smads, matrix extracellular matrix (ECM)) revealed striking increase solely in TIMP-1 mRNA expression (90 fold as compared to wild type CBA mice) (Kokeny et al, Clin Kidney J 2011, 4 (5):421-429). To confirm the role of elevation of TIMP-1 expression in the development of renal fibrosis we examined the effect of TIMP-1 inhibition in this model. Methods: Eight old mice old CBAxB6-TGFB transgenic mice (n=5) were treated daily with TIMP-1 neutralizing antibody (2 ug/day, R&D Cat: AP990) intraperitoneally for 5 days. CBAxB6-TGFB transgenic mice (n=4) were treated with a saline injection as a control during the same period (n=4). At the age of 14 days, urinary protein/creatinine ratio (PCR), serum creatinine, urea, and plasma TGF-ß levels were determined. Kidneys were collected for renal histology (glomerulosclerosis index (GSI) on PAS stained slides). Data were statistically analyzed using Mann-Whitney test. Results: Plasma TGF-ß levels and body weights of treated and control mice were comparable (9.5±1.36 vs 9.5±1.03 grams and 50±1.2 vs 57±1.4 mg/ml respectively). Renal hypertrophy, as characterized by relative kidney weight was decreased in the treated animals compared to controls (7.4±0.7 vs 9.2±1.5 mg kidney/g body weight, p<0.05). Urinary protein/creatinine ratio was significantly lower in treated mice (treated: 6.7±1.6 vs control: 14.2±5.9, p=0.05). TIMP-1 inhibition also lowered serum creatinine by 30% and serum urea by 50% in treated animals (1.4±0.1 vs 2.1±0.4 mg/dl and 51±25 vs 110±39 mg/dl, respectively, P<0.05) and ameliorated glomerular hypertrophy, mesangial proliferation and expansion (glomerulosclerosis index in treated: 1.50±0.25 vs control: 2.54±0.16, p<0.05). Conclusions: Our preliminary data demonstrate that inhibition of TIMP-1 significantly ameliorates the progression of TGF-ß induced renal fibrosis in this model.

**SP367**

**UP-REGULATION OF ALK1 IN MOUSE KIDNEY FOLLOWING URETERAL OBSTRUCTION**

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Introduction and Aims: Tubulointerstitial fibrosis, one of the common end points of chronic renal insufficiency, is characterized by an excessive accumulation of extracellular matrix (ECM) in the renal interstitium, myofibroblast activation, cell infiltration, tubular apoptosis and proliferation. Transforming growth factor-ß1 (TGF-ß1) is considered a fundamental profibrotic cytokine. ALK1 (activin receptor-like kinase 1) is a type I receptor for TGF-ß1 with a pivotal role in endothelial proliferation and migration. Others receptors such as ALK5 and endoglin are overexpressed in experimental models of renal fibrosis. Nevertheless the expression levels and the role of ALK1 in renal fibrosis are unknown. Methods: We performed unilateral ureteral obstruction (UUO) in mice, an obstructive nephropathy experimental model, in order to analyze the expression of ALK1 following 15 days UUO by western-blot and immunofluorescence, and the co-expression with other proteins such as α-SMA (myofibroblast marker) and CD68 (macrophage marker) in order to elucidate which cells expressed ALK1 following UUO. We also cultured renal fibroblasts from haploinsufficient (ALK1+/+) and control (ALK1+/-) mice in order to analyze the role of ALK1 in ECM protein (collagen I, fibronectin) expression. Results: ALK1 expression is increased following UUO. In non-obstructed kidneys the expression of ALK1 is restricted to glomerular cells, some interstitial fibroblasts and smooth muscle cells of small blood vessels. In obstructed kidneys, ALK1 expression is mainly located in the tubulointerstitial area. Double immunostaining with ALK1/ α-SMA and ALK1/CD68 showed that ALK1 is expressed in both myofibroblasts and infiltrated macrophages. ALK1 is expressed in cultured renal fibroblasts, and ALK1 heterozygous renal fibroblasts showed higher expression of collagen I and fibronectin, suggesting that ALK1 downregulates ECM protein expression. Conclusions: Summarizing, ALK1 upregulation following UOO may be considered as a protecive mechanism against renal fibrosis due to its ability to downregulate ECM protein expression.

**SP368**

**REGULATION OF TUBULAR CELL PHENOTYPE BY THE LIM PROTEIN HIC-5**

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Introduction and Aims: We have previously reported the role of the LIM protein, Hic-5 in the regulation of mesangial cell phenotype during progressive chronic kidney disease, and shown that it has an important role in controlling pathophysiological phenotype change in experimental glomerulosclerosis. During those studies, we also identified a subset of tubular cells that constitutively express this protein (Kidney International 2010). Therefore we undertook a series of in vivo and in vitro experiments to investigate its role in tubular phenotype regulation in health and disease. Methods: NRK52E rat tubular cells and MDCK canine tubular cells were transfected with a Hic-5 overexpression construct. Wild type cells and Hic-5 transfected cells were then compared in assays for proliferation, apoptosis, adhesion and cell motility. In separate experiments, rats were subject to unilateral ureteric obstruction (UUO) and sacrificed at 7, 14 and 21 days. Immunostaining for Hic-5 was undertaken. Results: NRK52E and MDCK cells do not express Hic-5 in culture, and have a differentiated (either proximal nor distal tubular) phenotype. Forced over-expression of Hic-5 in cells resulted in increased proliferation, decreased susceptibility to apoptosis, increased adhesion and reduced motility. In health, tubular cells of distal phenotype constitutively express Hic-5, but following UUO, this expression is down-regulated and lost by 14 days, associated with tubular cell apoptosis and progressive disease. Conclusions: Hic-5 regulates important phenotypical characteristics in a subset of tubular cells including proliferation, attachment and susceptibility to cell death. These findings, and the loss of expression during experimental UUO supports its role as a mediator of cell loss during tubular injury.

**SP369**

**CHRONIC EFFICACY OF LISISOPRIL IN IMPROVING KIDNEY BIOMARKERS, FUNCTION AND STRUCTURE IN UNX MALE ZSF1 RATS**

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Introduction and Aims: Diabetic nephropathy (DN) is a complex pathology leading to ESRD. Development of treatments that prevent ESRD requires translatable models and evaluation of biomarkers. UNx reduces GFR, increases proteinuria in animal models and humans. Therefore we aim to explore UNx as a mean of exacerbating disease in this model.
Methods: We used hypertensive and metabolic syndrome male ZSF1 rats that we submitted to unilateral nephrectomy (UNx, at 12w of age) to exacerbate DN and associated diseases. We characterized metabolic, renal and cardiac changes in ZSF1 rats within 12w post UNx and compared them to age-matched Sham ZSF1 rats. Urine and plasma parameters were measured for determining relevant biomarkers (BMs). Echography method was used for describing the evolution of kidney and heart size, and cardiac function. Impact of aging and UNx on kidney, liver, eyes and heart structure was determined by histology and IHC analysis. Sensitivity of the UNx, ZSF1 rat model to antihypertensive drugs (ACEI, Lisinopril/30mg/kg as Food Admix) was evaluated during chronic treatment of ZSF1 rats (for 3 months) on kidney BMs, function and structure.

Results: Our data showed that UNx did neither exacerbate SBP of ZSF1 rats nor change LV mass, cardiac function or heart rate up to 16W after surgery compared to age-matched Sham ZSF1 rats despite development of cardiac hypertrophy with aging. Glucose intolerance and insulin resistance was unchanged by UNx. UNx-induced further hyper TG, hypercholesterolemia and elevated NEFAs in plasma of ZSF1 rats and induced hepatocellular vacuolation. UNx increased right kidney size, kidney weight and KW/BW ratio compared to age-matched Sham ZSF1 rats. UNx reduced urine volume, Creatinine Clearance and deteriorated several plasma (BUN, KIM-1, Cyst-C, FGF-21, FGF-23 and b2M) and urine BMs (Albuminuria, Cyst-C, and TGFβ1). UNx increased severity of overall kidney lesions compared to age-matched Sham ZSF1 rats despite development of cardiac hypertrophy with aging.

Conclusions: Our data confirms that the ZSF1 rat model develops DN with similarities to human morphology and recapitulates features of metabolic syndrome observed in human. UNx worsened DN progression in male ZSF1 rats as compared to Sham. Lisinopril normalized albuminuria, reduced KIM-1, b2M, Vehicle) of UNx_ZSF1 rats already 3W after the start of the treatment, reduced LV mass and right kidney size. Lisinopril normalized albuminuria, reduced KIM-1, b2M, TGFβ1, and Cyst-C expression. Lisinopril reduced kidney fibrosis and induced hepatocellular vacuolation. Lisinopril significantly reduced diabetic renal injury (structure, functions and improvement of BMs), reduced BP, hypertrophy and dyslipidemia. Sensitivity of the ZSF1 UNx to kidney for exploring DN is confirmed.

Introduction and Aims: Emerging evidence suggests that renal tubular epithelial cells can undergo epithelial to mesenchymal transition (EMT) to become matrix-producing fibroblasts (myofibroblasts) under pathologic conditions. The aim of this study was to investigate the effect of our novel, first-in-class anti-fibrotic compound, PBI-4419, on renal EMT.

Methods: The effect of PBI-4419 on transforming growth factor-beta (TGF-β1) in HK-2 cells is inhibits TGF-β1-induced EMT, which is initiated by TGF-β1-induced E-cadherin and mesenchymal/pro-fibrotic markers, connective tissue growth factor (CTGF) and collagen I, was determined by quantitative real-time PCR. EMT was induced by TGF-β1 in HK-2 cells was assessed by mammalian two-hybrid assay. TGF-β1-induced EMT was assessed by western blot and expression of E-cadherin along with upregulation of CTGF and collagen I transcript expression. Results: TGF-β1 induced EMT was significantly inhibited by PBI-4419 (5 μM) as demonstrated by an increase of E-cadherin and the decrease of CTGF and collagen I expression. Interestingly, it was also observed that in the absence of TGF-β1, PBI-4419 alone supported an epithelial phenotype by upregulating E-cadherin and by downregulating basal expression of CTGF and collagen I. We further demonstrate the activity of PBI-4419 on EMT with renal tissues from 5/6-nephrectomized rats; markers for fibrosis (CTGF and collagen I) and a marker for myofibroblasts (α-smooth muscle actin; α-SMA) were assessed. CTGF, collagen I and α-SMA mRNA expression was significantly upregulated in the remnant kidney. Treatment with PBI-4419 resulted in a significant reduction in the expression of CTGF (60%, p<0.001), down to the control level of the sham animals), collagen I (60%, p<0.0001) and α-SMA (50%, p<0.05) in the remnant kidney.

Conclusions: In conclusion, these results support that PBI-4419 has the potential as a novel therapeutic agent in the prevention or reduction of fibrosis in kidney diseases by inhibiting EMT.

Introduction and Aims: Chronic hypoxia in the tubulointerstitium serves as a final common pathway in progressive renal disease. Circumstantial evidence suggests that HIF-1, which obviously expressed in the ischemic tubules, may be functionally suppressed in a CKD milieu. In this study, we hypothesized that indoxyl sulfate (IS), a uremic toxin, impairs cellular hypoxia response.

Methods: In vitro, the expression of HIF-1α, Chp/p300 interacting transactivator, with Glu/Asp-rich carboxy-terminal domain, 2 (CTD2) and HIF-1 target genes was measured by immunoblotting and real-time PCR. Binding of HIF-1 to the target gene promoters was evaluated by chromatin immunoprecipitation (ChiP) assays. Association of the cofactor p300 with HIF-1α was assessed by mammalian two-hybrid assays. mRNA stability of CITED2 was measured by actinomycin D treatment. The role of MAP kinase pathways was evaluated by using specific inhibitors. In vivo, the effect of IS on the expression of HIF-1 target genes was investigated in rats with adriamycin nephropathy as well as the remnant kidney, in the presence or absence of an oral adsorbent, AST-120. Additionally, the expression HIF-1 target genes was evaluated in the isoproterenol-induced heart failure (HF) model in rats treated with or without indole.

Results: In human proximal tubular cells (HK-2), IS reduced the hypoxia induction of HIF-1 target gene mRNA and protein. This effect was not accompanied by quantitative changes in the HIF protein level and was independent of the HIF-1α C-terminal transactivator domain (CTAD). Among factors which impede the recruitment of transcriptional co-activators to the HIF-1αCTAD, CITED2 was markedly upregulated by IS, via mechanisms of posttranscriptional mRNA stabilization involving the checkpoint cell signal-regulated kinase (ERK)1/2 pathway. In vivo, the incommensurate expression of HIF-target proteins was demonstrated in the ischemic tubules of several CKD models, such as adriamycin nephropathy and the remnant kidney, which was offset by an oral adsorbent of indole, AST-120, signifying the involvement of IS. Further, the induction of angiogenic, hypoxia-inducible genes was blunted in rats with experimental heart failure, when they were given indole in parallel.

Conclusions: Results of these studies uncover a novel role of IS in modulating the transcriptional response by HIF-1, and provide insight into molecular mechanisms underlying progressive nephropathies as well as the cardio-renal-anemia syndrome.

Introduction and Aims: Indoxyl sulfate is accumulated in the serum of uremic patients, accelerating the progression of kidney failure. In uremic rat kidney, the expression of nuclear factor (erythroid-derived 2)-2 like 2 (Nrf2) and its related genes is downregulated. The present study aimed to determine whether indoxyl sulfate affects Nrf2 expression in the kidney.

Methods: Effects of indoxyl sulfate on expression of Nrf2 were determined using human proximal tubular cells (HK-2 cells) and following animals: (1) Dahl salt-resistant normotensive rats (DN), (2) Dahl salt-resistant normotensive indoxyl sulfate-administered rats (DN+IS), (3) Dahl salt-sensitive hypertensive rats (DH), and (4) Dahl salt-sensitive hypertensive indoxyl sulfate-administered rats (DH+IS). AST-120, an oral sorbent which reduces serum level of indoxyl sulfate, was administered to uremic rats to determine its effect on the expression of Nrf2.

Results: Indoxyl sulfate downregulated Nrf2 expression in HK-2 cells. The indoxyl sulfate-induced downregulation of Nrf2 expression was alleviated by an inhibitor of nuclear factor-κB (NF-κB) (pyrroolidine dithiocarbamate), and small interfering RNA specific to NF-κB p65. DN+IS, DH, and DH+IS rats showed decreased expression of Nrf2 and heme oxygenase-1 (HO-1), an antioxidant gene and a target of Nrf2, and increased expression of 8-hydroxydeoxyguanosine (8-OHdG), a marker of reactive oxygen species in the kidneys compared with DN. Thus, indoxyl sulfate as well as hypertension suppressed expression of Nrf2 in rat kidneys. AST-120 increased the expression of Nrf2 and HO-1, and suppressed expression of 8-OHdG in the kidneys compared with control uremic rats.

Conclusions: Indoxyl sulfate downregulates renal expression of Nrf2 through activation of NF-κB.

Introduction and Aims: Uremic syndrome is characterized by a deterioration of kidney function due to the accumulation of uremic toxins. These are characterized by low molecular weight and different hydrophobicity; they can exist in free solution or bound reversibly to serum protein. Uremic toxins are particularly difficult to remove by conventional dialysis treatments and are the major causes of mortality in CKD patients. One of the uremic toxin is p-cresol, a fenol protein-bound lipophile, suggesting the need for advanced dialysis treatments.
by product of protein catabolism. It is produced by intestinal bacteria. Uremia causes a modification of intestinal flora, increasing the number of p-cresol bacteria producers. Furthermore, increase of plasmatic p-cresol concentration leads to development of CKD. p-cresol cytotoxic effect in monocytes is well known, particularly in macrophages, but it’s still poorly understand what determines in epithelial renal cell. Our aim is to evaluate in vitro effect of p-cresol on renal tubular epithelial cell line (LOC), in terms of apoptosis and necrosis, to better understand the pathophysiological impact of this toxin.

**Methods:** We perform the detection of apoptosis and necrosis in LOC, incubated for 24 hours in medium with increasing concentration of p-cresol, by Annexin V Propidium Iodide Cytotoxicometric assay. We used scalar concentration of p-cresol, from 40 μg/mL (up level in uremic patient) to 2.5 mg/L. In addition, we evaluated Caspase-3 levels by ELISA kit and detect DNA Ladder, that showing the typical apoptotic DNA fragmentation. All experiments were performed 5 times.

**Results:** p-cresol concentrations ≥20 mg/L cause the necrosis of >60% of cells; instead at concentration ≤5 mg/L the percentage is comparable to control. We observed a positive trend, but no significant relationship between Caspase-3 levels and p-cresol concentration. DNA Ladder is present in cells treated with low concentration of p-cresol and decreases at increasing concentration of toxin, when the necrosis is almost the only type of cell death. We can better understand the pathophysiology of this phenomenon increasing the number of experiments.

**Conclusions:** In conclusion, our data show that p-cresol has a cytotoxic effect on LOC. In particular, p-cresol causes cellular death in renal tubular cells, determining necrosis in almost total cultured cells at the maximal concentration. At lower concentration, p-cresol determines cell death through apoptosis. This data is supported also by the detection of Caspase-3 activation. It will be interesting to extend the analysis considering muscular cells to estimate the damage of uremic toxin in muscle tissue (uremic atrophy) or studying a possible development of uremic syndrome in Cardiorenal Syndrome.
parenchymal edema did not contribute to ADC values. After sacrifice, ADC in both kidneys dropped to less than 50% compared to those measured in living animals. More importantly, the ADC of obstructed kidneys were significantly higher compared to non-obstructed kidneys. The ADC after sacrifice correlated closely with tubular dilatation, interstitial expansion and fibrosis.

**Conclusions:** Our data indicate that low ADC values measured by DW-MRI do not reflect fibrosis in vivo but rather non-random water movement in kidneys, i.e. perfusion, tubular flow and water reabsorption. Ex vivo, i.e. after cessation of non-random water movement, fibrotic kidney cortex is characterized by increased DW-MRI signal (i.e. higher ADC values) compared to non-fibrotic kidneys. This is most likely due to expansion of space which allows random water movement in fibrotic tissue, i.e. tubular dilatation, cell atrophy and widening of interstitial space. DW-MRI seems not to be a useful method for specific assessment of renal fibrosis.
Results: On the AL diet rats gained 73±30g over 16 weeks of observation. Rats on the 20%CR diet gained 31±14g and on the 40%CR diet lost 67±33g of weight (AL vs 20%CR; p=0.01, AL vs 40%CR; p<0.01, 20%CR vs 40%CR; p=0.01). 24 hr urine protein was +64±24mg in the AL, -3.5±2.6mg in the 20% cr and -2.4±4.2mg in the 40% CR (AL vs 20%CR; p=0.05, AL vs 40%CR; p=0.05). The % glomerulosclerosis was 22.9±10.7 in the AL, 2.2±24mg in the al, 2.2±24mg in the 20% cr and -2.4±4.2mg in the 40% CR (AL vs 20%CR; p<0.05, 20%CR vs 40%CR; p<0.05). The podocyte density (μm²) was for AL 1,323,799±568,892, 20%CR 1,249,867±56,960 and for 40%CR 677,429±37,081 (AL vs 40%CR; p=0.05, 20%CR vs 40%CR; p<0.05). The total podocyte volume (μm³) was for AL 701,368±267,563, for 20%CR 643,092±48,627 and for 40% CR 407,337±28,553 (AL vs 40%cr; p<0.05, 20%cr vs 40%cr; p<0.05). The glomerular tuft volume (μm³) was for AL 1,323,979±508,892, 20%cr 874,211±151 and for 40% cr 6,083±1,259 (AL vs 40%cr; p=0.05, 20%cr vs 40%cr; p<0.05). The GLEEP1 negative (non-podocyte) tuft volume (μm³) was for AL 622,611±275,885, for 20% cr 606,773±110,610 and for 40% CR 270,692±39,722 (20%cr vs 40% cr; p<0.05).

Conclusions: Moderate (20%) calorie restriction was not as effective as 40% CR but provided significant protection compared to AL fed rats. These data show that, in this model system, dietary intervention at a moderate level to maintain a stable weight can provide significant protection compared to AL fed rats. This data support the notion that dietary restriction can provide renoprotective benefits to animals with AL induced chronic kidney disease.

NGAL AND ANESTHETICS: PROTECTIVE ROLE OF SEVOFLURANE

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Introduction and Aims: NGAL (neutrophil gelatinase-associated lipocalin), a protein produced by neutrophils and the proximal renal tubule, is overexpressed in conditions of acute renal suffering, causing a more sensitive and specific diagnostic marker of the diagnosis in the AKY. The aim of this study was to analyze serum and urinary NGAL in patients undergoing neurosurgery and sedated with two different anesthetic procedures in order to assess any property nephrotoxic and/or renal protection by anesthetics.

Methods: The study was conducted on 20 patients divided by the anesthetic procedure used: total intravenous anesthesia (type A) and balanced anesthetics (intravenous + inhalation) (type B). The anesthetics drugs used in type A are propofol and remifentanil, in addition to type B was used Sevoflurane. All patients were performed preoperatively (T0), 1 hour (T1), 2 hours (T2) and 24 hours (T3) after the end of surgery, blood samples and urinary samples were taken to determine NGAL and creatinine.

Results: At time T2 we have found, in both groups, increases in serum and urinary NGAL (p = 0.002) compared to baseline. In addition, individuals undergoing anesthesia type B have blood levels and urinary NGAL significantly lower than those treated with anesthesia type A (p < 0.001). The serum creatinine remained unchanged, however, at all times of observation (p > 0.05).

Conclusions: The increased levels of NGAL indicates that exposure to anesthetics results in a renal insult. Moreover, this biomarker may have a prognostic role as the lowest levels were found in group B, or the group treated with sevoflurane, known volatile anesthetic with nephroprotective property.

INDOXYL SULFATE IMPAIRS MITOCHONDRIAL BIOGENESIS AND FUNCTION IN HUMAN ENDOTHELIAL CELLS

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Introduction and Aims: Endothelial dysfunction is the hallmark of the chronic kidney disease (CKD). The uremic toxin, indoxyl sulfate (IS), has recently been reported to induce endothelial dysfunction in patients with CKD. Although some evidence shows that IS causes oxidative stress to endothelium, the mechanisms by which IS causes endothelial dysfunction are yet to be examined. This study aimed to investigate the impacts of IS on the mitochondrial function and biogenesis in human endothelium.

Results: During four weeks all animals were characterized by good health and activity. The 4-week increments in body weight were for L:109±4, L+P:97±4 and W:102±4 % (inter-group differences not significant). Left ventricular – to – body weight ratio was the highest in the L group (2.37±0.08 mg/g) and significantly different from W (2.1±0.04 mg/g) but not from the L+P group (2.2±0.03 mg/g). The values for L and L+P groups were not significantly different. Kidney weights expressed as a percent of body weight were nearly identical in all groups (L: 0.43±0.01; L+P:0.43±0.01; W: 0.44±0.01 %). All measured values of urinary albumin excretion (UAE) were in the normal range for Sprague-Dawley rats; only in W group significant increase in UAE after 4 weeks was observed (from 0.23±0.07 to 0.55±0.14 mg/day). Renal tissue slices stained with hematoxylin-eosin did not indicate explicit signs of kidney damage in all groups; inter-group differences in the microscopic images of the renal cortex and medulla were not observed. After subcutaneous administration amino-preenols did not affect the function of renal excretory system of normal Sprague-Dawley rats.

Conclusions: Morphology and morphometric analysis showed no negative changes in renal structures caused by tested compounds, therefore we find them suitable as a component of liposomal drug carriers.
**Methods:** Human umbilical vein endothelial cells (HUVEC) were cultured with different treatments and were grouped as control, IS (125 μg/ml), IS + VitC (200μM), IS +N-acetylcysteine (NAC) (10μM) and IS+Resveratrol (10μM). In these groups, reactive oxygen species (ROS) production was calculated by flow-cytometry, mitochondrial membrane potential was estimated by the mean fluorescence intensity of rhodamine 123 and the mitochondrial DNA content was measured by quantitative real time PCR. Western blots were performed to assay the expression of the key mitochondrial biogenesis regulators, PGC1α, Tfam and NRF1.

**Results:** IS caused enhanced ROS production, reduced mitochondrial membrane potential and decreased mitochondrial DNA content in HUVEC cells. These effects were partially rescued by the antioxidants, VitC and NAC and by the known biogenesis stimulator, resveratrol. In response to IS, the expression of PGC1α in HUVEC cells was upregulated whereas those of Tfam and NRF1 remained unchanged.

**Conclusions:** Our results demonstrated that IS causes mitochondrial dysfunction in HUVEC cells by both oxidative stress and impaired mitochondrial biogenesis. We also offered novel insights that resveratrol protects endothelial mitochondria from IS-mediated injuries.

**SP383**

**THE SIGNIFICANT ROLE OF CURCUMIN IN EPITHELIAL-MESENCHYMAL TRANSITION OF RENAL TUBULAR EPITHELIAL CELLS**

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**Introduction and Aims:** Epithelial mesenchymal transition (EMT) is an essential process during embryogenesis and organ development, and is characterized by loss of epithelial cell morphology, markers and cellular adhesion, and appearance of mesenchymal properties such as migration and invasion. EMT is also involved in several adult pathologies, especially in cancer and fibrosis. EMT of tubular epithelial cells is known to play a key role in the process of renal fibrosis. In vitro, TGF-b1 can stimulate tubular epithelial cells to undergo myofibroblastic transition, and finally to become fibrogenic cells. Curcumin has been known to have an anti-inflammatory and antifibrotic effect in various organs such as heart, liver and lung, but the exact mechanisms are not clear yet. Moreover, there’s insufficient knowledge about the role of curcumin on EMT process. The aim of this study is to reveal the roles of curcumin on renal tubular EMT induced by TGF-b1.

**Methods:** Renal tubular epithelial cell line, HK-2 cells, were examined to assess the effect of curcumin on TGF-b1-induced EMT. Morphological and phenotypic changes were analyzed via confocal microscopy. Additionally, cell lysates were used to estimate epithelial (E-cadherin) or mesenchymal (a-SMA) markers, metalloproteinases, and various interleukines (ILs). Transcription factors, such as snail-1, were also measured by quantitative RT-PCR.

**Results:** Renal tubular epithelial cells showed characteristic features of EMT after TGF-b1 stimulation; loss of cadherin and disruption of cell-cell contact with a concomitant induction of mesenchymal marker, a-SMA. Moreover, both a migratory property and proliferative activity were observed. These changes, however, were attenuated significantly by an administration of curcumin. The expression of transcription factor, snail-1, was also suppressed markedly in a curcumin treated cells. Additionally, curcumin treatment caused a significant decrease of VEGF, IL-6, IL-10, IL-12 and MMP-3 level, but there was no significant change in IL-5, IL-8, IL-13 and MMP-9.

**Conclusions:** This study suggests that curcumin attenuates TGF-b1-induced EMT in renal tubular cells through the downregulation of transcription factor, snail-1 with affecting various ILs and MMPs. Considering that curcumin has been taken safely in a form of food, further study will be focused to evaluate the clinical effects of curcumin in patients with AKI or CKD.
RENAL HISTOPATHOLOGY

Introduction and Aims: Henoch-Schönlein purpura nephritis (HSPN) and immunoglobulin A nephropathy (IgAN) are considered to be a spectrum of one disease, and are indistinguishable immunohistopathologically. Recently, there has been emerging concern that crescents, the main histologic feature of IgAN, merely reflect active inflammation, thus may not useful in predicting long-term outcomes. Therefore we retrospectively evaluated whether the new Oxford classification of IgAN can be used to predict long-term outcome in adult HSPN patients.

Methods: We included 61 biopsy-proven HSPN patients between January 1991 and August 2010 in our institution. Pathologic findings were evaluated both by the International Study of Kidney Disease in Children classification and the Oxford classification. Primary outcome was defined as either a decrease of ≥ 30% in estimated glomerular filtration rate or progression to the end-stage renal disease.

Results: During a median follow-up of 49.3 months, 13 (21.3%) patients reached the primary endpoint. A Kaplan-Meier plot showed that renal-event-free survival was significantly longer in patients with < 50% crescents than in those with crescents in ≥ 50% of glomeruli (P = 0.003). Among the components of the Oxford classification, patients with endocapillary hypercellularity (E1) (P = 0.016) and tubular atrophy/interstitial fibrosis (T1/T2) (P = 0.018) had lower renal survival rates than those with E0 and T0. In a multivariate Cox model adjusted for clinical and pathologic factors, E1 (HR 8.9; 95% CI 1.47 to 53.8; P = 0.017) and T1/T2 (HR 8.74; 95% CI 1.40 to 54.38; P = 0.020) were independently associated with reaching a primary outcome, whereas the extent of crescentic lesions was not.

Conclusions: Our findings suggest that the Oxford classification can be used in predicting long-term outcomes of HSPN. A larger multicenter study with a longer follow-up is warranted to clarify the predictive value of pathologic features of the Oxford classification in the HSPN.

HISTOLOGICAL CHARACTERIZATION OF RENAL LESIONS AFTER THORACIC TRANSPLANTATION

Introduction and Aims: The prevalence of renal lesions after thoracic transplantation is increasing due to the aging of this population and increased patient and graft survival. The causes are multiple and the precise diagnosis through renal biopsy (RB) is essential. The aims of this study were to describe the histological lesions, to compare the lesions in lung transplant recipients (LTR) and heart transplant recipients (HTR), to determine the risk factors and the consequences of each lesions.

Methods: We conducted a retrospective monocentric study of all HTR (n = 16, 7.8%) and combined HLTR (n=1) since 2000, who had required RB. RB were all centrally reviewed. Clinical and biological characteristics were analyzed yearly after Transplantation.

Results: The most common histological lesion was interstitial fibrosis (91.7% of RB) with a mean surface of 35.9 ± 20.4%. Other frequent lesions were nephroangiosclerosis (24.7%), focal segmental glomerulosclerosis (6.9%), focal global glomerulosclerosis (4.5%), arteriolar nephrosclerosis (2.4%), and vascular lesions (1.2%). The presence of arteriolar TMA was pejorative with a progression to end stage renal failure in 100% (vs 50%) of patients (p = 0.03). Chronic lesions (glomerular, vascular or interstitial) were also associated with a pejorative prognosis.

Conclusions: After thoracic transplantation, various kidney histological lesions can be observed. An accurate diagnosis by RB is necessary to optimize the clinical management. The biopsy should be done early after transplantation to prevent the installation of chronic lesions associated with a poor prognosis.
patients, pts (27 males, 34.15 ±12.23 years old) with different kidney disease five years after kidney biopsy.

Methods: Tissue KIM-1 expression was determined immunohistochemically (kit, R&D Systems Inc, Minneapolis, MN, USA) and KIM-1 staining was scored semi-quantitatively by estimating the percentage of cortical tubules expressing KIM-1 per field. Tubulointerstitialitis (TIN) inflammation, atrophy and fibrosis per field were scored 0-3. Kidney function (MDRD formula) and proteinuria/day were evaluated at the time of biopsy (GFR0), and 6, 12, 24, 36 and 60 months later.

Results: Pathological analysis revealed minimal change glomerulonephritis (GN) in 3 pts, mesangial proliferative GN in 9 pts, IgA GN in 6 pts, membranous and membranoproliferative GN both in 7 pts, focal glomerulosclerosis in 11 pts, lupus nephritis in 10 pts, proliferative GN in 8 pts. Significantly positive correlations between KIM-1 tissue expression and TIN inflammation (r= 0.459) and TIN fibrosis (r=0.317) as well negative correlations with GFR0 (r = -0.572), GFR6 (r = -0.442), GFR12 (r = -0.394), GFR24 (r = -0.398), GFR36 (r = -0.412) and GFR48 (r = -0.434) not with proteinuria/day were found. Meanwhile, stepwise multivariate regression analysis pointed TIN inflammation as the best predictor of kidney function 0, 6, 18, 24, 36, 48 and 60 months and KIM-1 tissue expression (p=0.016) along with TIN inflammation (p=0.013) only 6 months after kidney biopsy.

Conclusions: KIM-1 tissue expression significantly predict kidney function only 6 months after biopsy when the effects of protocol therapy is the strongest. So, this could be the support of the tissue KIM-1 pathophysiological function hypothesis as it is the marker of tissue repair possibly.

GLOMERULONEPHRITIS IN THE ELDERLY PATIENTS A COMPARATIVE STUDY

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Introduction and Aims: The aim of our study is to determine the epidemiological, clinical, biological, histological and etiological specificities of glomerulonephritis in elderly patients.

Methods: For this, we have undertaken a retrospective study during the period 1975 to 2005 in department of nephrology, comparing two groups : group A of a 110 patients aged between 16 and 55 years old. 2005 in department of nephrology, comparing two groups : group A of a 110 patients aged between 16 and 55 years old. 2005 in department of nephrology, comparing two groups : group A of a 110 patients aged 65 years old, to a group B of a 110 patients aged between 16 and 55 years old.

For this, we have undertaken a retrospective study during the period 1975 to 2005 in department of nephrology, comparing two groups : group A of a 110 patients aged between 16 and 55 years old. 2005 in department of nephrology, comparing two groups : group A of a 110 patients aged 65 years old, to a group B of a 110 patients aged between 16 and 55 years old.

Results: The prevalence of renal failure after thoracic transplantation (TmT) is increasing due to the aging of this population and increased patient and graft survival. Accurate measurement of renal function in this population is not usually performed. The aims of our study were to describe the value of different formulas to estimate the glomerular filtration rate (eGFR, ml/min/1.73m2) and to describe the evolution of renal failure before and after renal biopsy (RB).

Methods: We conducted a retrospective monocentric study in 36 adults TmT requiring RB. To analyze the performance of eGFR, we used a Bland Altman analysis. To compare the changes in the eGFR by CKD-EPI (difference of slopes before and after RB), we analyzed the slopes by a linear mixed model.

Results: In the absence of measured GFR, CKD-EPI formula was chosen as a reference. At the time of TmT, there is a significant eGFR overestimation by MDRD and Cockroft and Gauld (CG) formula (bias ±17.5 and +12.8). The MDRD formula was more accurate than CG (SD 3.8 vs. 7.92). At the time of the RB, eGFR was lower compared to pre-transplant values. Furthermore, it was underestimated using MDRD (bias ±19) and overestimated using CG formula (bias ±1.9). MDRD formula was more accurate than CG (SD 2.4 vs. 5.2). Nephropathologist referral (defined as the day of the RB) modified the evolution of renal function. There is a decline in eGFR before RB (81.29 vs 32.17) and a stabilization afterward (33.51 vs 44.9 at the last follow-up). The equations of the regression line of eGFR before and after RB were ± 0.13 ± 0.40 Time and ±0.02 ± 0.59 Time respectively. These slopes were numerically different with a slower decline of eGFR after RB.

Conclusions: In a population of TmT, it is necessary to validate the existing eGFR formulas and to derive new formulas. MDRD formula is more accurate than CG. The change in GFR after TmT is characterized by a worsening of renal function leading to the realization of a RB. Nephrologist support allows stabilization of the degradation of renal function. Early referral may therefore improve the renal outcome in this population.
amylloidosis using duodenal biopsy, amyloidosis was found in 3 of them, while other pathologies were discovered in the remaining 7. Sensitivity was 95% and specificity 100% in the diagnosis of amyloidosis by duodenal biopsy. No complications related to duodenal biopsy were observed in any of the patients.

**Conclusions:** It is still unclear what the optimal alternative method is in the practice of nephrology for the diagnosis of amyloidosis. According to the findings of this study, duodenal biopsy, with a high sensitivity and specificity, may be a reliable first option in the diagnosis of amyloidosis prior to performance of the invasive renal biopsy.

**Methods:** We report 144 patients with MM complicated renal impairment in the period June 1974-April 2008.

**Results:** There were 64 women and 80 men with a sex ratio of 0.8. The average age of patients at the time of the discovery of nephropathy was 63.16 years (range: 31-82).

Initial An IR is present in 131 cases (90.9%). The mean creatinine clearance was 13.76 ml/min (range: 2.09-82.09). We found normal renal function in 13 patients (9%), a moderate IR in 22 patients (15.2%) and IR terminal in 34 patients (25.9%). The average 24-hour proteinuria was 2.39 g / 24H. Mean serum calcium was 2.51 mmol / l (range: 1.45-3.97). Anemia was found in 115 cases (80.9%). Thrombocytopenia in 33 cases (25.5%). The rate of β2 microglobulin is always greater than 3.5 mg/l. A hyperproteidemia was found in 62 cases (43.3%). The hypogammaglobulinemia was observed in 43.9% of cases. Nephrotic syndrome was found in 13 patients (9%). The protein immunoelectrophoresis showed a blood and urine IgG kappa myeloma in 30 patients (2.4%). IgG lambda in 35 patients (28.2%). IgA kappa in 10 patients (8%). IgA lambda in 19 patients (15.3%). IgD lambda in 3 patients (2.4%). IgM kappa in one patient, myeloma with kappa light chains was observed in 10 patients (8%) and lambda light chain myeloma in 16 patients (12.9%). The PBI is positive in 39 patients (50.6%). The bone marrow plasma cell infiltration average is 49% (range: 6-100). The IRA complicates the MM in 54 cases (37.5%) with dehydration as precipitating factor in 41 cases (75.9%), hypercalcemia in 30 cases (55.5%), injection of iodinated contrast product in 5 cases (9.2%), infection in 16 cases (29.6%). Cylinders myeloma nephropathy was found in 110 cases, renal amyloidosis in 16 cases, the disease Randall in 5 cases and chronic kidney glomerular without histological evidence in 12 cases. Hundred and ten new patients have benefited from chemotherapy (82.6%) including 103 patients underwent melphalan-prednisone. Once the diagnosis of renal disease, 34 patients required treatment and extracranal changes in 26 cases have reached the terminal stage. The median survival was 30.45 months. A renal response is achieved in 16 patients (25.3%).

**Conclusions:** A better understanding of the pathophysiological mechanisms and early treatment of precipitating factors or supplemented if necessary by hemodialysis and chemotherapy have improved the overall prognosis of multiple myeloma with renal impairment but with a large disparity in treatment response.

**Introduction and Aims:** Multiple myeloma (MM) is a malignant plasma cell proliferation and bone marrow accompanied by secretion of monoclonal immunoglobulin. Renal involvement is common. Different types can be observed. The most common are: tubulopathy myeloma (30-40%), AL amyloidosis (10-30%), disease complicated by significantly higher MGV. 2. Further studies are needed in order to assess the long term graft function of transplanted kidneys with higher MGV.

Light microscopy obsolescence of 17/26 glomeruli was observed, the remaining showing only a mild expansion of mesangial matrix. Tubulo–interstitium showed areas with various degrees of fibrosis, mononuclear infiltrates and presence of large hyperchromatic nuclei with irregular outlines in epithelial cells lining proximal and distal tubules (Figure 1A). Electron microscopy evidenced irregular distribution of chromatim within the enlarged nuclei of the tubular epithelium (Figure 1B), but no viral particles or electron-dense deposits. A diagnosis of KIN was made, and therapy with anti-angiostatin agents and low dose anti-aldosteron agent was started. After 12 months of follow-up, no progression of renal insufficiency was observed and urinalysis was still normal.

**Conclusions:** This case suggests that KIN is probably an underdiagnosed condition, because it can occur also in absence of the traditional clinical presentation. Therefore, young adults with paucisymptomatic CKD of unknown origin should be considered for routine renal biopsy to obtain a correct diagnosis that provides information in order to avoid any empirical use of harmful drugs and to encourage living donor transplant, since no recurrence of the disease has hitherto described.

**Introduction and Aims:** Karyomegalic interstitial nephritis (KIN) is a rare entity characterized by giant cells in the interstitium. The etiology of this condition is unknown. The classical form of KIN is characterized by proliferation and bone marrow accompanied by secretion of monoclonal immunoglobulin. Renal involvement is common. Different types can be observed. The most common are: tubulopathy myeloma (30-40%), AL amyloidosis (10-30%), disease complicated by significantly higher MGV. 2. Further studies are needed in order to assess the long term graft function of transplanted kidneys with higher MGV.

Light microscopy obsolescence of 17/26 glomeruli was observed, the remaining showing only a mild expansion of mesangial matrix. Tubulo–interstitium showed areas with various degrees of fibrosis, mononuclear infiltrates and presence of large hyperchromatic nuclei with irregular outlines in epithelial cells lining proximal and distal tubules (Figure 1A). Electron microscopy evidenced irregular distribution of chromatim within the enlarged nuclei of the tubular epithelium (Figure 1B), but no viral particles or electron-dense deposits. A diagnosis of KIN was made, and therapy with anti-angiostatin agents and low dose anti-aldosteron agent was started. After 12 months of follow-up, no progression of renal insufficiency was observed and urinalysis was still normal.

**Conclusions:** This case suggests that KIN is probably an underdiagnosed condition, because it can occur also in absence of the traditional clinical presentation. Therefore, young adults with paucisymptomatic CKD of unknown origin should be considered for routine renal biopsy to obtain a correct diagnosis that provides information in order to avoid any empirical use of harmful drugs and to encourage living donor transplant, since no recurrence of the disease has hitherto described.

**Methods:** Into the retrospective study medical records from cadaveric kidney donors harvested between 2005 and 2010 were included. In all cases MGV was evaluated in kidney biopsies performed immediately before transplantation ("zero biopsies"). The results are presented as a median and 95 CI.

**Results:** Analyzed group consisted of 34 cadaveric kidney donors who died due to intracranial hemorrahge. The aim of the study was to evaluate MGV in kidney donors died due to intracranial hemorrhage.

**Conclusions:** Kidneys harvested from patients who died due to intracranial hemorrhage [3 females and 17 males; age 49 years (42-51), kidney weight 191.0g (174.1-208.7) and serum creatinine concentration 104 μmol/l (81-236)] were used. Kidney donors who died due to intracranial hemorrhage [18 females and 16 males; age 49 years (42-51), kidney weight 191.0g (174.1-208.7) and serum creatinine concentration 104 μmol/l (89-174)] were used. The control group consist of 20 patients who died due to brain trauma [3 females and 17 males; age 49 years (42-51), kidney weight 191.0g (174.1-208.7) and serum creatinine concentration 104 μmol/l (81-236)]. The control group consist of 20 patients who died due to brain trauma [3 females and 17 males; age 49 years (42-51), kidney weight 191.0g (174.1-208.7) and serum creatinine concentration 104 μmol/l (81-236)]. The control group consist of 20 patients who died due to brain trauma [3 females and 17 males; age 49 years (42-51), kidney weight 191.0g (174.1-208.7) and serum creatinine concentration 104 μmol/l (81-236)].

**Methods:** Into the retrospective study medical records from cadaveric kidney donors...
INFLAMMATION AND MACROPHAGE INFILTRATION IN CHRONIC KIDNEY DISEASE

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1UMF Craiova Romania, 2“Carol Davila” Nephrology Hospital Bucharest Romania

Introduction and Aims: Recent data indicate that chronic inflammation can influence the production of various growth factors in different stages of renal fibrosis lesions. The aim of our study was the description of the immunoexpression of macrophage infiltration both in fibrosis and inflammatory onset, in cases with various stages of chronic kidney disease.

Methods: The study was conducted on 36 renal biopsies, obtained from patients who underwent renal biopsy procedures for clinical purpose, between 2008 - 2011 and followed for a period of 17±11 months. Glomerular sclerosis (GS), inflammatory infiltrates and interstitial fibrosis were assessed in classical histological stainings as Thricromic (Goldner-Szekely) according to the following criteria: GS was evaluated as the percentage of sclerotic glomeruli in each sample, inflammatory infiltrates were qualitatively graded using a scale of 0–3 (0= no pathology; 1= <25% involvement, mild; 2= 25–50% involvement, moderate; and 3= >50% involvement, severe), interstitial fibrosis was assessed by morphometric analysis of Thricromic staining and expressed as percentage of the area, the images being prior processed in Adobe Photoshop in order to extract the tubular basement membrane from the analysis. The expression of interstitial fibrosis with a mean of 54±11.7% compared with the group that didn’t (p = 0.01). In the patients group with increased serum creatinine during follow-up, there was observed the expression of a larger number of CD-68 positive cells compared with the group that didn’t (p = 0.04). An important aspect observed in this study was the association of a higher expression of interstitial fibrosis with a mean of 5.5 ± 3.2 cells/field compared with the group that didn’t (p = 0.02). EnPGN decreased significantly, while that of MN increased significantly.

Conclusions: This study observed macrophage infiltration as an important marker in histopathological diagnosis in association with the assessment of inflammatory and fibrosis lesions, as well as with the vitamin D treatment.

CHANGING SPECTRUM OF BIOPSY PROVEN PRIMARY GLOMERULAR DISEASES OVER PAST 15 YEARS: A SINGLE CENTER STUDY IN CHINA

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Introduction and Aims: The prevalence of Chronic kidney disease (CKD) is reported 10.8%–11.8% in Chinese population. With the development of economics and the longer life expectancy, the spectrum of CKD etiology kept changing. Primary glomerular diseases (PGD) are still the most common renal diseases in China. To investigate the changing pattern of PGD in China, we retrospectively analyzed consecutive native biopsies performed in our hospital from 1997 to 2011.

Methods: The patients were grouped according to a 3-year interval, 1997-1999 (period 1), 2000-2002 (period 2), 2003-2005 (period 3), 2006-2008 (period 4), 2009-2011 (period 5), and divided into three age groups (<20, 20-59, ≥60 years old). 8909 qualified cases were enrolled in this study.

Results: Among 8909 specimens, 6337 (71.13%) were diagnosed as PGD. While this prevalence decreased significantly from 77.61% in 1997-1999 to 66.73% in 2006-2008. IgA nephropathy (IgAN) was the most common PGD (36.66%), without any significant difference in 5 periods (P=0.185). IgAN was the most common PGD both in patients between 20-59 years old group (45.58%) and in <20 year-old group (19.29%) as well. Membranous nephropathy (MN) was the most frequently found PGD in patients at age ≥60 years old (39.64%). The frequency of MN increased significantly from 6.48% in 1997-1999 to 22.79% in 2009-2011 (P<0.001). The proportion of elderly patients increased significantly from 3.18% in 1997-1999 to 15.21% in 2009-2011 (P<0.001). The prevalence of EnPGN decreased since 1997.

Conclusions: PGD remained the most common renal disease in China, although with a descending trend. In different age, the spectrum of PGD is different. The frequency of EnPGN decreased significantly, while that of MN increased significantly.
EXTRACORPOREAL DIALYSIS: TECHNIQUES AND ADEQUACY - A

SP397 IMPROVEMENT IN TECHNOLOGY: EVALUATION OF THE BIOFEEDBACK ON TMP ON TWO DIALYSIS SYSTEMS

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Introduction and Aims: The biofeedback on TMP, as UltraControl (UC, Gambro), enhances and automatically adjusts the convective volume in hemodiafiltration online (OL-HDF). Moreover, the results of recent RCTs on postdilution OL-HDF, such as CONTRAST and TURKISH, suggest that OL-HDF with high convective volume can improve the patient survival. This study evaluated the convective performances of UC in post-dilution OL-HDF on two dialysis machines: AK200 ULTRA S (AK) and ARTIS.

Methods: We enrolled 14 stable pts (63±12 yrs), already treated by OL-HDF, in a sequential design study of two weeks for each monitor. Both monitors automatically set the infusion volume by a biofeedback on TMP (described by Teatin et al. Blood Purif 2011), while AK measures the TMP value by 3 points formula (Pre-filter, venous and inlet dialysate pressure) and uses a TMP step of 25mHg, ARTIS works with 4 points (Pre-filter, venous, inlet and outlet dialysate pressure) and TMP step of 20mHg. For each patient the remaining technical parameters were kept unchanged. The infusion volume, TMP and Pre-filter pressure (PPF) were hourly collected. All the pts were treated with 2.1 m2 Polyflux H (Gambro). The descriptive analysis was based on the mean ± standard deviation. Inferential statistics included two tailed t-test for paired data, considering a probability value of less than 0.05 as significant.

Results: No differences were found on main dialytic parameters, such as Qb (37±10 vs 370±12 ml/min, p=0.978), treatment time (265±16 vs 266±16 min, p=0.334) and total weight loss (1.8±0.7 vs 1.8±0.7 L, p=0.739), between the two periods. The ARTIS system reached a smooth higher infusion volume (27.0±2.5L vs 25.8±2.3L, p<0.01) compared to the AK200. The ARTIS system reached a smooth higher infusion volume (27.0±2.5L vs 25.8±2.3L, p<0.01) compared to the AK200. UltraControl reached high convective volumes (>20 L) in postdilution OL-HDF with AK and ARTIS machine. The introduction of 4 points TMP measuring and a smaller increment TMP step resulted in more optimize TMP setpoint, leading to an increase of infusion volume and reduction of the intra-patient variability on ARTIS machine. Therefore UltraControl system on ARTIS seems to be the best technique for Postdilution OL-HDF.

SP398 DESIGN, REALIZATION AND PRELIMINARY EXPERIMENTAL EVALUATION OF A NOVEL MAGNETIC FILTER FOR UTILIZATION IN MAGNETICALLY-ASSISTED HAEMODIALYSIS

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Introduction and Aims: Although Haemodialysis (HD) has become a mature replacement therapy it still has disadvantages such as slow toxin-removal kinetics (imposed by the underlying diffusion/convection processes) and non-selective action (undesired toxins cannot be distinguished from biomolecules that should be preserved). The so-called Magnetically Assisted Haemodialysis (MAHD) introduces fast kinetics and selective action. Specifically, MAHD is based on core-shell conjugates (Cs) of two ingredients: a ferromagnetic particle (FP), the core that ensures the fast kinetics and a biocompatible substance (BS) of high affinity for specific toxins, the shell that among others guarantees selectivity. The Cs should be administered to the patient timely prior to the MAHD session, so that they will collect toxins while circulating in the cardiovascular system. Ultimately the Cs are removed, together with the collected toxins, by the so-called Magnetic Filter (MF) that is incorporated at the extracorporeal circulation line (ECL). Here we introduce a novel MF.

Methods: Among others, the design of the MF was based on two main requirements: (a) production of intense magnetic force to achieve high efficiency on the removal of Cs and (b) absolute safety protecting the patient from the reentry of Cs into the cardiovascular system. Software packages (Finite Element Method Magnetics and Origin*) were used for the simulation of the magnetic field produced by the employed permanent magnets.

Results: Based on the above requirements a prototype MF was realized: a compact disc of diameter 13 cm with 10 permanent magnets (NdFeB, grade N42) of cylinder form (diameter 5 mm, height 5 mm) embedded uniformly along its periphery wherein a track also exists suitable for the adjustment of the rigid tube of a modified ECL. The MF was experimentally tested with physiological saline as blood substitute in which Fs of iron (Fe) or iron oxide (Fe3O4) were dispersed. The MF removed completely the Fs of Fe in a single round, while it needed a second round for the Fs of Fe3O4.

Conclusions: The MF introduced here can remove efficiently and safely Fs of Fe and Fe3O4 from an ECL. This opens interesting perspectives for its utilization in near-future in vitro experiments in the dialysis machine.

SP399 CONTROL OF PLASMA PHOSPHATE ON THRICE WEEKLY IN-CENTRE HAEMODIALFILTRATION

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Introduction and Aims: Adequate control of plasma phosphate without phosphate binders is difficult to achieve on a thrice weekly haemodialysis schedule without compromising nutritional intake. The use of frequent nocturnal dialysis has been shown to be an effective strategy but this is not practical in the in-centre setting. A thrice weekly nocturnal dialysis shift has recently been established in our centre and since inception 14 patients have participated in the program. Over 1000 individual sessions have been carried out to date.

Methods: The duration of dialysis was increased from a median of 4.5 hours to 8 hours, Qb was reduced to 200ml/min and Qd reduced to 300ml/min. All patients continued on post-dilution haemodiafiltration with a dialysate calcium concentration of 1.75mmol/l and potassium adjusted according to pre-dialysis levels. Dialysis adequacy and bone chemistry were reviewed at monthly QA meetings. A reduction in plasma phosphate was anticipated so all phosphate binders were stopped before the switch to nocturnal dialysis.

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Results: Within 1 month of commencing on nocturnal dialysis the weekly K/UV had increased from to 2.23±0.23 to 2.66±0.23 (p<0.001) and plasma phosphate had reduced from 1.76±0.50mmol/l to 1.20±0.33mmol/l (p<0.01). Despite all phosphate binders being stopped in these patients continued to have a drop in plasma phosphate to 1.7mmol/l and in several patients it has been necessary to increase dietary phosphate in order to keep the pre-dialysis plasma phosphate within the normal range.

Conclusions: To our knowledge this is the first time control of phosphate without the use of binders has been reported on a three-weekly in-centre based dialysis program. In addition to the improvement in the phosphate control there has been a significant financial saving from the cessation of binders.

SP400 THE EFFECTS OF DIFFERENT DIALYSIS TREATMENTS ON GYMIC EXCERIUS AND INFECTION IN PATIENTS WITH END-STAGE RENAL DISEASE WITH AND WITHOUT TYPE 2 DIABETES MELLITUS

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Introduction and Aims: It is known that hemodialysis discards out blood glucose, and that hemodynamic change during session induces stress hormones and inflammatory cytokines. The aim of this study was to evaluate the glycemic excursions and the changes of various inflammatory parameters in type 2 diabetic patients affected by end-stage renal disease undergoing bicarbonate dialysis (BHD) and hemodiafiltration (HDF) compared to euglycemic patients. Methods: Twenty patients (11 affected by type 2 diabetes mellitus, and 9 not diabetic patients) were evaluated. We measured, before and after dialysis, these parameters: body mass index (BMI), glycated hemoglobin (HbA1c), fasting plasma glucose (FPG), fasting plasma insulin (FPI), HOMA-IR, lipid profile, homocysteine (Hcy), high sensitivity C-reactive protein (hs-CRP), fibrinogen, lipoprotein (A) (Lp(a)), metalloproteinases-2, and -9 (MMP-2 and MMP-9), interleukins 6 (IL-6), and 8 (IL-8), and soluble receptor for advanced glycation end products (sRAGE). All patients underwent glucose continuous monitoring system, using The iPro Continuous Glucose Monitor System (Medtronic MiniMed) starting just before the bicarbonate dialysis, and ending five days later, after the HDF dialysis. Results: We observed a significant decrease of glycemic excursions during BHD respect to HDF. We also observed a statistically significant decrease of MMP-9 (p<0.001) after bicarbonate dialysis, but not after HDF. Considering only type 2 diabetic patients, we observed a decrease of sRAGE with bicarbonate dialysis (p<0.01), but not with HDF. Moreover, in type 2 diabetic patients, there was a significant decreasing inter-compartmental resistance due to cellular membrane and/or capillary endothelium. This resistance results in significant post-dialytic rebound or reduced solute removal. Exercise during dialysis is suggested to remove solute from remote inaccessible compartments owing to better perfusion of remote skeletal muscles and decreased inter-compartmental resistance. In this clinical research, we have compared the toxin removal outcome by high flux HD, stand-alone HDF and intra-dialytic exercise during high flux HD. Methods: Recruited patients underwent 3 parallel dialysis sessions: (1) HD, (2) HDF, (3) HD with exercise (HD-Ex). Dialysis prescription was same for all the three sessions. HD and HDF sessions were conducted using Fresenius 400S and Gambro AK200 ULTRA machine, respectively. All HDF sessions were performed in pressure-control mode. In HD-Ex, exercise was prescribed for 35 min in three bouts of 10 min with 5 min gap between successive bouts using static cycler (Monark 861E). Blood samples were collected and analyzed for concentrations of urea, creatinine, and β2-microglobulin at three time points: t = 0 min (pre-dialysis), t = 240 min (end-dialysis) and t = 360 (post-rebound). The percentage rebound is calculated to judge the quantum of removed solutes. Intra-dialytic blood samples were also collected every 30 mins. Results: Total 9 stable patients (5 males) on maintenance hemodialysis were studied. The convective volume achieved in HDF was 20 ± 2.9L. K/UV achieved was 1.46 ± 0.27 and 1.50 ± 0.29 for HD and HD-Ex respectively. The percentage rebound for urea was 14.9 ± 3.23 (HD), 14.38 ± 5.29 (HDF), and 13.03 ± 4.07 (HD-Ex) for creatinine was 23.5 ± 4.00 (HD), 23.53 ± 5.10 (HDF), and 21.99 ± 4.05 (HD-Ex); and for β2-microglobulin was 29.28 ± 8.45 (HD), 24.56 ± 2.51 (HDF), and 26.03 ± 5.69 (HD-Ex). The results are presented as mean ± SD. Intra-dialytic serum urea, creatinine and β2-microglobulin levels were significantly higher in the intra-dialytic period for HD-Ex than HDF and HD. There were no adverse events in any of the treatment sessions. Conclusions: The results of the post dialysis solute rebound indicate that HD-Ex than HD and HDF in terms of small solute clearance. For middle molecules like total solute or β2-microglobulin, HDF is superior in clearance compared to HD and HD-Ex, but HD-Ex outperforms HD. The increased serum solute concentration during HD-Ex session suggests that exercise mobilizes the solutes from remote inaccessible compartments to intravascular compartment and hence, contributed to increased removal during dialysis. Intra-dialytic exercise can enhance solute removal and can be a routine part of dialysis treatment.

SP405 TRANSIENT LOSS AND COMPLETE RECOVERY OF THE POPULATION OF PLATELETS DURING THERAPEUTIC PLASMA EXCHANGE

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Introduction and Aims: In therapeutic plasma exchange (TPE) thrombocytopenia is observed in some patients. Usually this is ascribed to the unintentional removal of Platelets (Plts) with the plasma that is rejected at the centrifugation stage. Except for this possibility other mechanisms could be at play: mechanical stress (MS) experienced

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Introduction and Aims: Efficacy of high flux hemodialysis (HD) and convective based dialysis, namely, hemodiafiltration (HDF) is restricted by inter-compartmental resistance due to cellular membrane and/or capillary endothelium. This resistance results in significant post-dialytic rebound or reduced solute removal. Exercise during dialysis is suggested to remove solute from remote inaccessible compartments owing to better perfusion of remote skeletal muscles and decreased inter-compartmental resistance. In this clinical research, we have compared the toxin removal outcome by high flux HD, stand-alone HDF and intra-dialytic exercise during high flux HD.

Methods: Recruited patients underwent 3 parallel dialysis sessions: (1) HD, (2) HDF, (3) HD with exercise (HD-Ex). Dialysis prescription was same for all the three sessions. HD and HDF sessions were conducted using Fresenius 400S and Gambro AK200 ULTRA machine, respectively. All HDF sessions were performed in pressure-control mode. In HD-Ex, exercise was prescribed for 35 min in three bouts of 10 min gap between successive bouts using static cycler (Monark 861E). Blood samples were collected and analyzed for concentrations of urea, creatinine, and β2-microglobulin at three time points: t = 0 min (pre-dialysis), t = 240 min (end-dialysis) and t = 360 (post-rebound). The percentage rebound is calculated to judge the quantum of removed solutes. Intra-dialytic blood samples were also collected every 30 mins. Results: Total 9 stable patients (5 males) on maintenance hemodialysis were studied. The convective volume achieved in HDF was 20 ± 2.9L. K/UV achieved was 1.46 ± 0.27 and 1.50 ± 0.29 for HD and HD-Ex respectively. The percentage rebound for urea was 14.9 ± 3.23 (HD), 14.38 ± 5.29 (HDF), and 13.03 ± 4.07 (HD-Ex) for creatinine was 23.5 ± 4.00 (HD), 23.53 ± 5.10 (HDF), and 21.99 ± 4.05 (HD-Ex); and for β2-microglobulin was 29.28 ± 8.45 (HD), 24.56 ± 2.51 (HDF), and 26.03 ± 5.69 (HD-Ex). The results are presented as mean ± SD. Intra-dialytic serum urea, creatinine and β2-microglobulin levels were significantly higher in the intra-dialytic period for HD-Ex than HDF and HD. There were no adverse events in any of the treatment sessions. Conclusions: The results of the post dialysis solute rebound indicate that HD-Ex than HD and HDF in terms of small solute clearance. For middle molecules like total solute or β2-microglobulin, HDF is superior in clearance compared to HD and HD-Ex, but HD-Ex outperforms HD. The increased serum solute concentration during HD-Ex session suggests that exercise mobilizes the solutes from remote inaccessible compartments to intravascular compartment and hence, contributed to increased removal during dialysis. Intra-dialytic exercise can enhance solute removal and can be a routine part of dialysis treatment.
by cells during the relatively intense centrifugation and biochemical shock (BS) exerted from the replacement medium can deconstruct Pts. To explore these issues, we studied intact Pts (IPts) of TPE patients with standard clinical techniques and advanced microscopes. 

**Methods:** During the TPE sessions the 15 patients studied here were given a combination of colloids and crystalloid media (Human Albumin 5%, Hydroxyethyl Starch 6% and saline NaCl 0.9%). The Cole® Spectra and Spectra Optia® units were employed. For the determination of the TPE dose and replacement medium volume the standard Nadler and Allen formula was used. The IPts investigations was conducted comparatively in samples drawn simultaneously from the venous and arterial branches at both the beginning and end of the TPE session. In addition to the standard clinical tests two powerful Microscopes, the Scanning Electron (SEM) and the Atomic Force (AFM) were employed.

**Results:** Discrepancies were observed in the registration of Pts across the extracorporeal circuit. Specifically, the combined clinical and microscopy data revealed that in 5 out of 15 TPE patients the Pts exhibited a statistically significant (p<0.05) intense reduction in the venous branch and complete recovery in the arterial branch in the samples obtained at both the beginning (venous: 80.6±114.0x10^3/μL and arterial:221.8±49.1x10^3/μL) and end (venous:44.8±41.5x10^3/μL and arterial:199.6±29.3x10^3/μL) of the TPE session. No statistically significant (p>0.05) difference between the beginning and end of the TPE session in both the venous (beginning:80.6 ±114.0x10^3/μL and end:44.8±41.5x10^3/μL) and arterial (beginning:221.8±49.1x10^3/μL and end:199.6±29.3x10^3/μL) branches was observed.

**Conclusions:** In some cases across the extracorporeal circuit Pts may transiently be deconstructed due to MS and BS. A possible consequence is to observe discrepancies in the complete blood count since automated analyzers do not count particles of size below a threshold such as granules of deconstructed Pts. The transiently deconstructed Pts can be efficiently reformed while circulating in the biochemically fertile environment of the patient cardiovascular system.

**ELEVEN KEY AREAS OF RENAL NURSE RESPONSIBILITY - THE FOUNDATIONS OF QUALITY PATIENT DIALYSIS OUTCOMES**

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**Introduction and Aims:** Renal nurses develop their expertise over time and in the exercise of their professional skills deliver the essence of safe, competent, and compassionate care. The knowledge, attitude and skills of a nurse develop progressively where complexities of clinical procedures and experiences are intertwined.

**Objective:** This study identifies whether Quality Patient Dialysis Outcomes (QPDO) were directly affected by eleven key areas of nurse responsibility used when evaluating and Pearson’s moment correlation were used to build relationships.

**Methods:** 59 Staff Nurses were appraised evaluating SC while 525 hemodialysis patients were evaluated using the QPDO parameters. Univariable linear regression and Pearson’s moment correlation were used to build relationships.

**Results:** Data indicated both increase and decrease trends in relation to staff competency. Competencies related to Health Education (112.6, Communication (114.7, Records Management (114.6, Safe and Quality Nursing Care (113.5), and Management of Resources (113.5) demonstrated increase trends. Competencies related to Research (1-35.2), Quality Improvement (1-12.3), and Legal Responsibility (1-6.8) were relatively decreased as the period of competency evaluation progressed. It was notable that QPDO related to RV/V, Albumin, Hemoglobin, and Hematocrit Levels were directly proportional to increasing extent of SC, p<0.05 and phosphorus levels were directly associated to areas where staff were demonstrated an increasing trend, p<0.05. Additionally, as the nurses progressed to becoming expert a direct correlation to the QPDO was notable. The study became the foundation for staff training and developing a competency appraisal framework in renal nursing practice thereby promoting quality assurance procedures while attaining QPDO.

**Influencing Variables of Chronic Hemodialysis Patients after Single Dialysis Sessions**

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**Introduction and Aims:** High concentration of asymmetric dimethylarginine (ADMA), an endogenous inhibitor of nitric oxide synthase (NOS), is found in patients with chronic kidney disease and correlates with vascular disease and cardiovascular mortality. The aim of the study was to investigate the effect of two different type of dialyzer on plasma ADMA and NOS concentration after single HD session.

**Methods:** Twenty-six HD patients were randomly divided into two groups depending on the type of dialyzer (synthetic ELISIO 190M, Med Flux and cellulose based SureFlux 170N, Low Flux dialyzer). In the blood samples collected before HD and after HD, endogenous NOS and ADMA level was estimated using ELISA kit. The results were compared with the results of 11 CKD patients in the pre-dialysis phase and 12 healthy subjects.

**Results:** In CKD patients, before HD, NOS and ADMA level was comparable to the pre-dialysis group but in contrast to the control group NOS level was significantly lower and ADMA level significantly higher. After HD, both NOS and ADMA level decreased. Change in NOS and ADMA level depending on the dialyzer is shown in table 2.

**BASELINE RENAL CYSTS VOLUME PREDICTS THE RECOMBINANT HUMAN ERYTHROPOIETIN REQUIREMENT IN AUTOSOMAL DOMINANT POLYCYSTIC DISEASE**

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**Introduction and Aims:** Prevalence of anaemia in patients with autosomal dominant polycystic kidney disease (ADPKD) increases according to the severity of chronic kidney disease (CKD). However, little is known about the relationship between kidney structure modification and recombinant human erythropoietin (rHu-EPO) requirement in these patients (pts). Aim of this study was to evaluate the role of renal function as measured by endogenous nitric oxide synthase and asymmetric dimethylarginine level in chronic hemodialysis patients after single dialysis sessions.
cysts and kidney size on rHu-EPO requirement in severe CKD and naive chronic hemodialysis (HD) patients.

Methods: A total of 43 pts with ADPKD and anemia treated with alfa-erythropoietin (rHu-EPO) were enrolled (16 pts with CKD Stage 4 and 28 naive chronic HD pts); the total volume of the four largest cysts (cysts-Vol) and the mean antero-posterior renal diameter (AP) were prospectively followed up for 18 months with kidney ultrasound.

Results: Mean age was 65±13yrs. At baseline, AP was 19.4±2.1 cm, cysts-Vol 407±36 cm³. During the 18months follow up, haemoglobin (Hb) was 10.8±0.7 g/dl, rHu-EPO dose was 14403±7518 UI/week, and rHu-EPO/Hb ratio was 1379±780. In fully adjusted model, baseline cysts Vol and AP predict EPO dose and EPO/Hb ratio and explain a large amount of variability.

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Conclusions: Cysts volume is useful to predict prospectively the rHu-EPO requirement. This assumption is valid even in chronic dialysis patients, where the renal function is completely lost.

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ONLINE HEMODIALFILTRATION: DIALYSIS QUALITY IMPROVEMENT

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Introduction and Aims: Haemodialysis (HD) treatment had over many years improved the survival rate of patients with end-stage renal disease (ESRD). However, conventional HD prescription has high rates of morbidity and mortality with poor quality of life. Online haemodiafiltration ( HDF) offers the most physiologic clearance profile for a broad size range of toxic molecules together with better haemodynamic stability. Our aim was to investigate, in a prospective randomized study, the effect of online HDF on dialysis clinical and biochemical outcomes and patient’s quality of life.

Methods: Seventy two patients, with 58% males and mean age of 54±12 years, had similar comorbidities, AV Fistula rate (80%), blood flow rate (324±30 ml/min), dialysis adequacy (0.94±0.08), biochemical results and duration on HD (51±3 months). They were randomized into two groups. Group 1 (n=36) was maintained on conventional HD and group 2 (n=36) treated by online HDF and both were followed up for 24 months. Prescription of HD and HDF included similar 4h dialysis duration performed 3 times/week using high-flux dialysers. The reverse osmosis treated water that was used for both groups contained <0.1 CFU/ml and <0.01 endotoxin unit/ml. Group 2 received an average of 18.9±2.4 L/4h as post-dilution replacement fluid. Assessment was based on clinical, laboratory and patient’s questionnaire survey outcomes. The scoring system of the questionnaires ranged from 0-10. Statistical analysis was performed using Medcalc software version 10.4.0.

Results: The results of this study show the effective role of online HDF on improving the clinical outcomes, adequacy of dialysis and laboratory results. Patients were much more satisfied with online HDF when compared with patients treated with conventional HD. Data are summarised in the following table.

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<table>
<thead>
<tr>
<th>Parameter</th>
<th>Online HDF</th>
<th>HD (Control)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP (mmHg)</td>
<td>106±5.4</td>
<td>112.7±9.5</td>
<td>&lt;0.0002</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>68±1</td>
<td>69±1</td>
<td>NS</td>
</tr>
<tr>
<td>Hypotension during dialysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cramps</td>
<td>93±7</td>
<td>39±12</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Itching</td>
<td>99±13</td>
<td>26±12</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Skin colour</td>
<td>22±21</td>
<td>10±1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cu/V</td>
<td>1.26±0.15</td>
<td>0.94±0.12</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Phosphorus (mg/dL)</td>
<td>4.5±0.4</td>
<td>4.6±1.5</td>
<td>&lt;0.035</td>
</tr>
<tr>
<td>Calcium (mg/dL)</td>
<td>8.9±0.5</td>
<td>8.4±0.3</td>
<td>NS</td>
</tr>
<tr>
<td>PTH (pg/ml)</td>
<td>386±143</td>
<td>532±281</td>
<td>&lt;0.015</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.60±3.3</td>
<td>3.30±0.37</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td>10.3±0.5</td>
<td>9.9±0.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Beta-2-microglobulin (mg/L)</td>
<td>22.4±3.8</td>
<td>36.6±18.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Erythropoetin dose</td>
<td>78%</td>
<td>75%</td>
<td>NS</td>
</tr>
<tr>
<td>Fatigue (general)</td>
<td>95±7</td>
<td>29±9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fatigue (post dialysis)</td>
<td>91±9</td>
<td>19±4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Compliance</td>
<td>82±10</td>
<td>144±8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Body energy</td>
<td>79±17</td>
<td>13±17</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>General mood</td>
<td>88±14</td>
<td>10±3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Appetite</td>
<td>39±16</td>
<td>10±2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Taste</td>
<td>71±19</td>
<td>10±5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Social activity</td>
<td>82±9</td>
<td>15±8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sport activity</td>
<td>65±14</td>
<td>10±3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Professional activity</td>
<td>81±7</td>
<td>10±4</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Conclusions: In conclusion, our results show that online HDF treatment was associated with significant improvement in clinical outcomes, dialysis adequacy, biochemical results and quality of life of ESRD dialysis-treated patients.

SP406

EXTENDED NOCTURNAL HEMODIALYSIS: SINGLE CENTER EXPERIENCE

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1Nephrocare Barreiro Fresenius Medical Care Barreiro Barreiro Portugal

Introduction and Aims: Despite advances in dialysis, this therapy is still associated with high morbidity, mortality and costs.

Methods: The mortality, morbidity, hypertensive profile, bone mineral disease, anemia, efficacy of dialysis and nutrition were evaluated in 14 patients undergoing extended nocturnal hemodialfiltration (HDF) mean time 18,5 hours/week. Among this patients 5 were male, 1 had diabetes mellitus and 3 had cardiovascular disease. The software used was SPSS version 19.

Results: We report the results of an extended nocturnal hemodiafiltration (HDF) program in a group of 14 patients, mean dialysate flow was 275 mL/minute, mean blood flow 275mL/min, with dialysate concentrate of HCO3 32 meq/L, Ca2+ 3, Na+ 138, K+ 2 and glucose 100 mg/L. The mean age was 53.1± years ± 10,3. At admission, average time of renal replacement therapy was 7.4± 4.7 years. The follow-up period was 13.6 ± 2.5 months. During the follow up period one patient died and one received a kidney graft. In all patients there was an improvement of dialysis efficiency (kT/V 4.6 ± 6,1vs 0.7 ± 0.8 wk, p 0.000). Although hemoglobin levels (11.5 ± 0.8 vs 11.3 ± 0.7 g/dl, pns) remained unchanged, there was a significant reduction in erythropoiesis stimulating agent (ESA) consumption (121.1 vs 80.7 IU/kg/wk, p 0.000). Iron consumption (40.4 ± 23.5 vs 34.05 ± 37.9 mg/wk, pns) and ferritin values (434.2 ± 305.2 vs 392.9 ± 162.3 mg/ ml, p 0.003) significantly decreased and nutritional parameters improved (nPCR 1.1 ± 0.1 vs 1.2 ± 0.7 g/kg/d, p 0.000). Serum calcium levels increased (8.2 ± 0.7 vs 8.9 ± 0.4 mg/dl, p 0.000) and there was a reduction in phosphatemia (4.5±0.4 vs 4.6±1.5, p 0.035) with significant improvement in clinical outcomes, adequacy of dialysis and laboratory results. Patients were much more satisfied with online HDF when compared with online HDF when compared with patients treated with conventional HD. Data are summarised in the following table.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Online HDF</th>
<th>HD (Control)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight</td>
<td>81±7</td>
<td>10±4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Compliance</td>
<td>82±9</td>
<td>15±8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Professional activity</td>
<td>81±7</td>
<td>10±4</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Conclusions: In conclusion, our results show that online HDF treatment was associated with significant improvement in clinical outcomes, dialysis adequacy, biochemical results and quality of life of ESRD dialysis-treated patients.
Introduction and Aims: In order to overcome the disadvantages of hemodialysis with bicarbonate (HDB), several techniques of renal replacement therapy have been developed. These techniques have not become widespread because of their high costs. Thus the idea of developing a technique that would improve the safety of HDB without raising the cost is born. This technique was called biofiltration free acetate with substitution of sodium bicarbonate at 84‰ (BSA at 84‰). Methods: The BSA at 84‰ is a dialysis technique using a bath-free buffer (acetate or bicarbonate). The correction of metabolic acidosis of the patient is ensured by providing a solution of molar sodium bicarbonate (84‰) at the venous bubble trap of extra corporeal blood circuit. The generator used is similar to that used with the technique of HDB. The injection of the buffer solution is provided using an infusion pump with adjustable flow. The flow rate used is about 3.5 to 4.5 ml/kg/hour. The volume injected during a session of 4 hours varies between 900 and 1000 ml. This volume is ultrafiltered through the dialyzer membrane in addition to the desired weight volume. Therefore, it is possible to use the same filters as for HDB. Results: Studies shows that the BSA at 84‰ technique: * Improved clinical tolerance, reduced the frequency of hypotension and other clinical manifestations of intolerance in both patients with acute renal failure and chronic dialysis patients. * A good correction of metabolic acidosis, both at short and long term, without the risk of post dialysis hyperbasemia. This is most probably related to the balance established between intake and elimination of bicarbonate by the filter and the richness in the dialysate on chloride ion which is at the origin of a better correction of metabolic acidosis in intravascular by transfer of bicarbonate from extracellular to intracellular sector. However, the likely benefits of hyperchloremia should not lose sight of its deleterious effects: acidosis of extracellular medium and hemolysis. Moreover, the risk of hyperbasemia is not zero if the volume of bicarbonate molar infused is greater than 4.5 ml/ kg/hour. * A lower cost compared to the technique of HDB due to the low cost of the concentrate of biofiltration and the low amount of concentrate used in BSA at 84‰ (4-5 times vs 8-9 liters). The generalization of the technique, remains dependent on the marketing of a module of BSA at 84‰ integrated to conventional hemodialysis generator, may minimize the cost of dialysis in the order of 14 per session. Conclusions: The good clinical and hemodynamic tolerance of BSA at 84‰, the best correction of metabolic acidosis and its lower cost, give this technique a pride of place in the therapeutic arsenal of chronic renal failure.
SP412  AUTOSUB+: A SOPHISTICATED INNOVATIVE TOOL FOR A SIMPLIFIED OL-HDF PRACTICE

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Introduction and Aims: The optimization of convective volumes (Vconv) delivered in Post of HDF (POST) allows to remove the Medium Molecules (MM) and especially those with the highest Molecular Weight (MW). MM removal thanks to automated Vconv. The 5008 dialysis machine ( Fresenius) was, up to the recent launch of its new CorDiax version, equipped with a module AUTOSUB (AS) enabling convective volumes (Qco = Q+ UF; Qsub = Substitution Rate and UF=Ultrafiltration for Weight gain) to plasmatic water rate (Qpw). Recently AUTOSUB+ (AS+) uses an innovative technology regulating Qconv according to the harmonic analysis at the venous pressure sensor of the blood pomp generated vibrations according to the principle of “la transformer de Foucair”. The aim of our study was to compare Vconv obtained with AS versus AS+ in POST.

Methods: 24 patients (Age: 73.6 ± 11.9; AVF=19 and Cather=5) were included in this monocentric crossover study. They were treated during a 240min/session on the same day of 2 consecutive weeks with 3 different Qb (mL/min) groups: Qb300, Qb350 and Qb380. AS was set with hematocrit (ht) given by the BVM and the level of hemolysis, htpo and hemoglobin. Statistical analysis (StatView) was performed with Student’s paired test for mean values of AS and AS+. Correlation between ht and TP with the global Filtration Ratio (FR=Vconv/Total Blood Processed) was also analysed.

Results: No significant difference between the two methods for Vconv. Table1: Vconv (L/session) obtained with AS versus AS+ according to 3 different Qb

<table>
<thead>
<tr>
<th>Qb300mL/min</th>
<th>Qb350mL/min</th>
<th>Qb380mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>24.8±3.1</td>
<td>27.8±3.0</td>
<td>28.8±2.4</td>
</tr>
<tr>
<td>23.9±1.2</td>
<td>27.2±1.9</td>
<td>28.5±2.1</td>
</tr>
</tbody>
</table>

No correlation between ht (34.7±3.14%) and AS or AS+. The most important correlation between TP and AS+ (R=0.8; P<0.001) versus AS+ (R=0.5; P=0.12) explains the better dispersion of Vconv with AS+ (versus AS). AS+ is no more dependent on the great variations of TP from one patient to another (6.7 ± 5.7g/dL). The interception of the 2 regression lines between TP and FR for AS and AS+ was 0.988 ± 0.006 and 0.995 ± 0.008 respectively.

Conclusions: AS+ using innovative technological approach allows, without any knowledge of ht and TP, identical Vconv to those generated by AS. In practice, using the default values of ht and TP decreases the accuracy of AS. In these conditions, optimizing Vconv without any biological value, makes AS+ a real innovation in the automation and simulation of OL-HDF. This study confirms the relevance of AS+ since when the training of Vconv is correctly set with the BVM ht values and with the latest patient’s TP values. Finally, AS remains as an effective tool for practicing POST both efficient and safe for those not yet equipped with the 5008 CorDiax machine.

SP413  CITRATE DIALYSIS FLUID AND CALCIUM MASS BALANCE

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Introduction and Aims: Citrate-containing concentrates have in recent years been introduced for use in hemodialysis. Citrate entering the blood will form complexes with calcium and some of the protein bound calcium will then be released to maintain the equilibrium between protein bound and free ionized calcium. Both free and citrate bound calcium can pass the dialysis membrane which increases the calcium transport from blood. We investigated 3 different Qb, each with 4 subsegments. The following parameters were used: Initial total calcium plasma concentration 2.4 mM (mmol/l), blood flow rate 300 ml/min, dialysis fluid flow rate 500 ml/min, urea Koa 1000 ml/min, calcium concentrations in dialysis fluid without citrate 1.0, 1.25, 1.5 and 1.75 mM, and citrate levels in the dialysis fluid 0.25 – 2 mM.

Results: The need for extra calculation in the dialysis fluid increases almost linearly with the citrate level. Each mM of citrate requires an additional 0.15 mM of calcium to maintain the same calcium mass balance. Other settings of blood and dialysis fluid flow rates, urea, Koa, and total calcium concentrations in plasma gave the same result.

Conclusions: For each mM of citrate in the dialysis fluid the calcium level should be increased by 0.15 mM to maintain the calcium transport during the treatment.

SP414  “THE LAST WILL BE FIRST...”, A FLEXIBLE APPROACH FOR RESTARTING HOME HEMODIALYSIS

Martha Ferreirasi1, Maria C. Di Vico1, Federica N. Vgotti1, Maria Deagostini1, Stefania Scognamiglio1, Valentina Consiglio1, Roberta Ciani1, Irene Monò1, Elena Mongiardi1 and Giorgina B. Piccoli1
1Department of Clinical and Biological Sciences, University of Turin SS Nefrolepia, ASOU san Luigi Gonzaga Orbassano Torino Italy

Introduction and Aims: The present revival of interest in home haemodialysis (HHD) is due to lower costs and more frequent/efficient or “intensive” treatments.

Nevertheless, HHD is still underdeveloped and development strategies are needed. Aim of the study is to report on the results obtained in the period 2010-2012 with a new flexible HHd program, open also to elderly patients and HHd program type.

Methods: The program is characterized by flexibility of training (duration and number of caregivers); implementation of daily dialysis, and individualized schedules; personalization of controls; easy access to hospital facilities; no discrimination for age or comorbidity. The study reviews the patient’s chart, as for ESRD, comorbidity, reasons of choice, reasons of drop-out.

Results: In the period of 2010 (start of the program) 2012, 19 patients were enrolled, 2 are waiting to join the program; 12 were sent on HHD (1 died), 1 will start in February 2013. Six patients dropped out from training, 3 for unavailability of the partner; 2 for difficulties in the a-v fistula; 1 for housing problems (presently hosted by relatives); 4/6 perform self-care dialysis in the center. The patients who dropped out from the training were younger (median: 44.5 (24-63)) only 1 had comorbidity (vascular). The patients who completed the training were older (median 58 (38-76), 2/3 only without comorbidity (multiple in 4: 6 cardio-vascular, 3 diabetes, 2 collagen diseases, 2 neoplasia, 3 other); 10 patients had contraindications (in 3 temporary; BMI ≥ 33, 1 recent angioplasty) for wait-listing a kidney (or kidney-pancreas) graft. Main reasons for choice: easier care, less need for hospitalization (80% of patients) for spending more time together (5 cases); easier travelling (3 cases). The partner was the wife/husband in all but 1 case who employed a payed nurse. Dialysis is started with incremental schedules, usually together with the training. Training lasted 3-12 months; schedules ranged from 2 to 7 sessions/week, 2.5-6 hours/session (last median equivalent renal clearance: 14.5 ml/min).

Conclusions: When HHD is offered with a flexible, open selection, it may represent a good choice for elderly patients and for patients with multiple comorbidities (often considered as the last candidates for HHD), not suitable for a kidney graft. Working and family reasons, in particular in elderly couples, are the main driving forces for this choice. Attention to “the last ones”, and flexibility in facing their needs, may improve the development of HHD.

SP415  CITRATE REDUCES COMPLEMENT AND LEUKOCYTE ACTIVATION IN VITRO IN HUMAN BLOOD

Viktoria Hancock1, Shan Huang1, Anders Nilsson1, Gunilla Grundström1 and Kristina Nilsson Eckdahl1
1Therapeutic Fluid Research Gambro Lundia AB Lund Sweden, 2School of Natural Sciences Linnaeus University Kalmar Sweden

Introduction and Aims: Acetate as acidifier in haemodialysis fluid is known to induce negative effects, such as nausea and increased inflammatory response. Although modern haemodialysis fluids contain relatively low levels of acetate compared with previously used fluids a few decades ago, the levels are far from physiological – raising concerns in particular for the older, more co-morbid and more vulnerable dialysis population. Haemodialysis fluid where acetate is substituted, in part or completely, by citrate was developed recently and has so far only been used to a limited extent in haemodialysis. Citrate containing dialysis fluids have shown promising results in terms of improving clearance and treatment tolerance. In the present study, the biocompatibility of citrate was examined by investigating the effects of citrate on complement and leukocyte activation in human whole blood.

Methods: Human whole blood from healthy donors was mixed with small aliquots of citrate to final concentrations of 0 to 6 mM citrate. After 1 hour of incubation at 37°C, complement activation was measured as generation of C3a, C5a and terminal complement complex C5b-9 (TC), and leukocyte activation was measured as up-regulation of CD11b expression on granulocytes.

Results: Complement activation was significantly reduced in the presence of citrate. C5a and TCC showed a reduction of 38% and 27%, respectively, already in the presence of 0.25 mM citrate compared with control without citrate, and the reduction was further enhanced at higher citrate concentrations up to 74% and 70%, respectively, in
the presence of 6 mM citrate. C3a showed significant reduction only at the highest concentrations of citrate, by 41-59% in the presence of 4-6 mM citrate. Leukocyte activation was reduced significantly in the presence of 1.5 mM citrate and above, measured as a reduction of CD11b by 19% with 1.5 mM citrate up to 78% at the highest citrate concentration, 6 mM.

Conclusions: In conclusion, citrate is a potent reducer of leukocyte and complement activation in human whole blood in vitro. Complement and leukocyte activation was significantly reduced by very low citrate concentrations (0.25 mM and 1.5 mM, respectively), similar to those currently employed in citrate haemodiafiltration.

Mathematical modelling indicates that during a typical dialysis treatment with a fluid containing 1 mM citrate the blood returning to the patient contains about 0.66 mM citrate. The systemic citrate concentration is dependent on the patient’s citrate metabolism; mathematical modelling indicates a systemic concentration of 0.1-0.4 mM citrate after 4 hours of dialysis, which is in agreement with our measured systemic concentrations of around 0.3 mM citrate post-dialysis. Our results reveal that substituting acetate for citrate in dialysate fluids might contribute to a more biocompatible dialysis by reducing activation of the innate immune response.

Methods: Over a two-year period (1/2011 – 12/2012) 293 pts underwent CRRT in our hospital. After exclusion of pts treated with both CRA and standard methods (ST, heparin or nothing) during the CRRT period, pts who did not undergo main surgery, and cases of CRRT duration <2 days, we considered 63 pts for our purposes.

The choice of anticoagulant was made for clinical reasons (active bleeding or high hemorrhagic risk). For each group we evaluated: age, hospital length of stay (LOS), CRRT duration, hospital mortality (HM), hemoglobin values at start (Hb-S) and stop of CRRT (Hb-E), number of blood transfusions administered during the CRRT period (CRRT-BT) and number of blood transfusions administered during the whole hospital stay (LOS-BT). Statistical analysis was made with Student’s T test.

Results: In CRA group there were 50 pts, for a total of 506 CCRT days; mean age 72.8 years (M 74%); mean LOS 36 days, mean CRRT duration 10.2 days, HM 40%; mean Hb-S and Hb-E respectively 8.8±0.8 g/dl and 8.0±0.7 g/dl (p<0.05), mean total BT 1.08, mean tot-BT 1.48. In CRA group there were 13 pts, for a total of 132 CRRT days; mean age 68.5 years (M 77%); mean LOS 26.7 days, mean CRRT duration 10.2 days, HM 69.2%; mean Hb-S and Hb-E respectively 8.6±0.7 g/dl and 7.6±0.7 g/dl (p<0.05), mean total BT 1.07, mean tot-BT 1.45. In CRA group were significantly lower in CRA group than in STD group.

Conclusions: In our experience critically ill surgical pts requiring extracorporeal blood pump standard 4-hour dialysis thrice a week under various membranes (CVVHD) with CRA. This approach would ensure significantly lower need of blood transfusion and more stable values of Hb during CRRT. Moreover, the Hb is much lower in CRA group in absence of significantly different LOS and CRRT duration.
Introduction and Aims: Former it was recognized that removal performance of low molecular weight protein of PD was higher than HD. However, higher performance dialysis membrane called as super high flux membrane was developed in recent years. The super high flux membrane has higher solute removal characteristics than high flux membrane, especially low molecular weight protein. Thus, we carried out a comparative evaluation of solute removal between HD, PD and on-line HDF using super high flux membrane.

Methods: It is targeted at three chronic maintenance dialysis patients who are enforcing a PD+HD combined therapy. HD using super high flux dialyzer FB-210UAlphα-eco (Nipro Corporation, Osaka, Japan) for 4 hours and pre-dilution on-line HDF, whose replacement volume was 60 liters for 4 hours using MFX-21Ueco (Nipro Corporation, Osaka, Japan) and PD were treated. The object solute was used as urea nitrogen, creatinine, inorganic phosphorus, beta-2 microglobulin, alpha-1 microglobulin, and albumin. and dialyzate drain was computed among HD and HDF by storing partially and all PD dialyze drain was collected for 4 times per day. The solute removal amount of each therapy was calculated with solute concentration and the amount of drain.

Results: The average removal amount of three patients by each blood purification therapy per one day was compared. In PD, when the average value of solute removal was 3263 mg, 508 mg, 199 mg, 21 mg, 22 mg, and 2993 mg at the order of UN, Cre, IP, beta-2MG, alpha-1MG, and albumin, respectively. In HD, it was 12017 mg, 2196 mg, 849 mg, 234 mg, 174 mg, and 3488 mg, respectively. In HDF, it was set to 12638 mg, 2412 mg, 932 mg, 208 mg, 150 mg, and 2676 mg, respectively. When it calculated what time there would be one HD treatment and one HDF treatment compared with PD, it differed for every solute. In HD, it became 3.7 times, 4.3 times, 4.3 times, 11.2 times, 7.8 times, and 1.2 times by each solute. On the other hand, in HDF, it became 3.9 times, 4.7 times, 4.7 times, 9.9 times, 6.7 times, and 0.9 time in a similar manner.

Conclusions: The removal amount of low molecular weight protein under HD and on-line HDF with a super high flux membrane were much larger than that under PD for one day. Moreover, since the removal amount of low molecular weight protein by these therapies with one session was equivalent to 7 day sessions of PD therapy. So at the time of HD and PD combined therapy, choosing the super high flux membrane strongly supports the lack of removal amount by PD, not only small molecular substance but also low molecular weight proteins.

### ZERO EMISSION DIALYSIS CLINIC - A CONCEPT STUDY

Juergen Kastl1, Maria Merello1, Carlo Boccato1 and Guido Giordana1
1NephroCare Coordination EMEALA, Fresenius Medical Care Deutschland GmbH, Bad Homburg, Germany

Introduction and Aims: Haemodialysis treatment is an energy resource demanding treatment, requiring 15–20 kWh total energy per treatment, which is significant CO2 emissions. With the concept study we demonstrated that it is possible to run a dialysis clinic carbon neutral.

Methods: We analysed two clinics in Germany and Portugal, representing typical dialysis clinics in different climate zones. We selected the state of the art technologies to increase energy efficiency. To achieve carbon neutral operations, we calculated the needed energy compensation and arranged suitable photovoltaic panels on the roof of the building. The concept study was performed with the help of our project partner DENA (German Energy Agency).

Results: Comparison of the two existing dialysis clinics in the two different climate zones:

<table>
<thead>
<tr>
<th>SP420</th>
<th>ZERO EMISSION DIALYSIS CLINIC - A CONCEPT STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Portugal (Coimbra)</td>
<td>Germany (Cologne)</td>
</tr>
<tr>
<td>Size of the dialysis clinic</td>
<td>2,123 m²</td>
</tr>
<tr>
<td>No of treatment p.a.</td>
<td>22,576</td>
</tr>
<tr>
<td>Year of construction</td>
<td>2005</td>
</tr>
<tr>
<td>Energy consumption per square meters (m²) and year (a)</td>
<td>179 kWh/(m²a)</td>
</tr>
<tr>
<td>Energy consumption per dialysis station</td>
<td>13,138 kWh/(station x a)</td>
</tr>
<tr>
<td>Energy consumption per dialysis treatment</td>
<td>17 kWh/treatment</td>
</tr>
</tbody>
</table>

The energy efficiency of a standard dialysis clinic (1,000m²; single floor; 12,500 dialysis trp.p.a.; located in Germany, Cologne) can be reduced to 7 kWh/tr. using the following features: 1. Building envelope: a well-insulated envelope can save up to 40 % of heating- and cooling energy 2. Daylight concept: Daylight reduces the energy demand for lighting and cooling load for the HVAC systems. 3. Lighting concept: The electric power demand for lighting is minimized by an efficient lighting concept 4. Mechanical ventilation: a centralised ventilation system with a heat recovery rate of 85% can reduce ventilation heat losses 5. Chilled and heated ceiling with capillary tubes are linked to the heat pump system 6. Heat pump: A reversible heat pump (15 kWh) provides heating and cooling energy. It uses warm waste water from dialysis as a heating and cooling source. The carbon dioxide (CO2) emissions can be compensated by using a photovoltaic system. The photovoltaic system (112 kWp) on the building roof substitutes the exact amount of CO2, which is emitted by the building during operation.

Conclusions: The concept study demonstrated that it is possible to run a dialysis clinic in complete CO2 neutral way.

### PAPERLESS DIALYSIS PATIENT MANAGEMENT SAVES THOUSANDS OF TREES EVERY YEAR

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1NephroCare Coordination EMEALA, Fresenius Medical Care Deutschland GmbH, Bad Homburg, Germany

Introduction and Aims: We want to calculate and demonstrate the environmental impact of modern data management systems in dialysis.

Methods: We analyzed the paper saving options of a patient data management system (EuCliD) in a multinational dialysis network.

Results: EuCliD is a database which unifies medical and economic information. Since it is specially designed for dialysis it enables us to constantly analyze the collected data for further improvement. At the end of 2012 more than 600 clinics of our multinational dialysis network are equipped with this data collection system. Our target is to provide dialysis treatments achieving an internally developed “gold standard”. The focus on data collection and its analysis has always been a priority for a multinational commercial dialysis network. Before the introduction of EuCliD relevant data like the prescription, therapy plans and diagnostic reports was printed on paper. With the increase of dialysis patients, the amount of documents raised resulting in a
Introduction and Aims: To define dialysis efficiency, mainly parameters from past dialysis sessions have necessarily to be used. Those parameters are for example Kt/V, blood flow, dialysis time and urea clearance. But in the results of these parameters there is more or less no information for a prospective creation of a higher efficiency in the next dialysis session. Furthermore, the quantification of parameters which are lowering the dialysis efficiency below the prescribed aim is demonstrated.

Methods: The dialysis efficiency of 236 patients was examined, using blood flow, dialysis time and urea clearance. Lowering dialysis efficiency parameters were examined: total recirculation, postdialytic rebound, the distribution volume, the relation between prescribed and effective blood flow and clearance as well as the effect of the vascular access (catheter or shunt).

Results: In 387 dialysis sessions of the 236 patients, the average prescribed blood flow was 288 ml/min (±41 ml/min), the calculated average effective blood flow however, was 246 ml/min (±72 ml/min). Thus only 85% of the prescribed blood flow was realized. The difference becomes even clearer, if the maximum values of the frequency distribution are compared. The maximum of the prescribed blood flow was 300 ml/min while the maximum effective blood flow reached only 220 ml/min. Analogous to the blood flows, the clearance values produced the following picture: The average clearance prescription was 232 ml/min (±29 ml/min) and the effective clearance which really became valid in the dialyser was 197 ml/min (±37 ml/min), being 15% below the prescription. Similar to the blood flows, the scattering of the effective clearance is much larger, as the standard deviation shows. With an average dialysis time of 4 hours and 20 minutes, the average prescribed Kt/V value was 1.59 (±0.30) while the average effective, therapeutically active Kt/V was only 1.23 (±0.33). Thus the effective Kt/V was 33% below the prescribed values. The difference between the prescribed Kt/V and the therapeutically active Kt/V is depending on the blood flow, the clearance, the distribution volume, the recirculation and the rebound. The average recirculation of the 236 patients was 19%. Only 39 patients had no recirculation and 32 patients a total recirculation under 10%, but 55 patients had a total recirculation between 25 and 30% (total recirculation = sum of preand cardiopulmonary recirculation). The average distribution volume of the patients was 351 (±64). The average postdialytic urea rebound was 6.03 mg/dl. Patients with catheter showed inconstant values for Kt/V, clearance and blood flow from session to session.

Conclusions: The prescribed dialysis is mostly reduced by patient related parameters. To improve the efficiency it seems to be more important to respect and to improve the patients individual situation rather than the change of external parameters.
Introduction and Aims: Studies have demonstrated that measuring the dialysis dose by using individualized Kt adjusted for gender and body surface area (BSA) allows for better discrimination of adequacy than Kt/v. To evaluate Kt as an indicator of dialysis dose, to compare the degree of compliance with different indexes and to identify factors involved in the administered dialysis dose.

Methods: This retrospective study included 103 patients (66%/male, average age 62 ± 12 years, 53.4% with diabetic nephropathy; 35% BMI:30; 66% with arteriovenous fistula (AVF)) who were on conventional hemodialysis treatment with nephrologist, dialysis staff and patients involved. Monthly average Kt values by gender and BSA were recorded during one year. Kt/v, 2nd generation daugardias and Percentage Urea Reduction (PUR) were calculated every two months. Compliance with different recommendations (Kt ≥ H:4.5L/M2BSA, Kt/v ≥ 1.3A:1.6, PUR ≥70%) was determined when influencing factors were analyzed.

Results: The average Kt dose was 46.8 ± 6.1 L, the average Kt/v was 1.5 ± 0.2 and the averagePUR was 2.1 ± 7 %. 81.1% of patients received an optimal dose of Kt/v adjusted for gender and 73.8% of patients presented PUR ≥ 70%; 54% of patients reached a minimum Kt of 45L although only 38% of them reached the target Kt adjusted for gender and 31% adjusted for BSA. Univariate analysis showed that Kt was higher in patients with higher weight values, lower age, male gender, non-diabetic, with AVF, higher blood flow (Qb) and longer time in dialysis. Kt/v was higher in male patients, patients with lower BMI and longer time in hemodialysis. Kt-BSA was higher in patients with AVF, lower age and higher Qb. Multivariant analysis showed significant results for Kt with body weight and Qb, for Kt/v with BMI and for Kt ASC with Qb.

Conclusions: 1) Kt appears to be the most exacting marker of dialysis dose. While only 81% of patients received a minimum Kt dose adjusted for gender, only 38% reached the target Kt adjusted for gender. 2) Kt adjusted to BSA appeared to be still more exacting than Kt adjusted for gender. Due to the high prevalence of obesity in our sample, studies are needed to determine the optimal Kt adjusted for BSA in our population. 3) Qb, effective time in dialysis and vascular access are factors influencing the adequate dialysis dose.

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**SP427**

**MEROPENEM PHARMACOKINETICS IN CRITICALLY ILL PATIENTS ON CONTINUOUS HEMODIAFILTRATION**

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Introduction and Aims: In critically ill patients with severe infection, adequate administration of antibiotics is crucial. Therefore, evidence of antibiotic pharmacokinetics for critically ill patients should be accumulated. Meropenem (MEPM) is an antibiotic with broad spectrum, and has been often used as first-line therapy for critically ill patients in Japan. However, pharmacokinetics of MEPM in septic patients undergoing continuous hemodiafiltration (CHDF) has not been fully elucidated.

Methods: We evaluated the pharmacokinetics of MEPM to clarify the optimal dose and times of infusion in patients on continuous standard CHDF in Japan. Eight patients with multiple organ failure and anuria due to sepsis who needed CHDF treatment were injected 0.5 gram of MEPM twice daily. Among 8 patients, 4 patients used polysulphone (PS) membrane and 4 patients used polymethyl methacrylate (PMMA) membrane, and blood concentrations of MEPM were sequentially evaluated. In all 8 patients, condition of CHDF was blood flow rate of 100 mL/min, dilution flow rate of 300 mL/hour, and replacement flow rate of 300 mL/hour, respectively. Time above MIC was evaluated, and whether blood concentrations differ between PS and PMMA was also evaluated.

Results: Time above MIC (% of MIC) of MEPM more than 50 % is usually thought to be effective and sufficient to sterilize bacteria. In our study, drip infusion of MEPM 0.5g twice daily under CHDF therapy as mentioned above could achieve effective therapeutic dose (% > MIC more than 50 %) if the MIC of bacteria against MEPM was below 4 μg/mL. Blood concentrations of MEPM did not differ between PS and PMMA.

Conclusions: For patients on CHDF condition as mentioned above, injection of 0.5 gram MEPM twice daily was thought to be effective to eradicate bacteria if the MIC of MEPM for bacteria were below 4 μg/mL.
SODIUM AND ULTRAFILTRATION PROFILING: IMPACT OF AN ALTERNATIVE MODEL IN HEMODIALYSIS HYPOTENSION

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Introduction and Aims: To study the impact of two different models of ultrafiltration rate and sodium concentration in hemodynamic stability during hemodialysis, in patients with end stage renal disease (ESRD).

Methods: Six patients, which experienced frequent episodes of hypotension during haemodialysis, were included in the study. Two models were scheduled, each one for four sessions. The first one with constant sodium concentration in dialysate (=145meq/L) and constant ultrasound rate (UFR). The second one with linearly increasing sodium concentration (from 140 to 150meq/L) and linearly decreasing UFR (sodium and ultrafiltration profiling). Signs and symptoms of blood volume reduction were evaluated and a total score of gravity was estimated for each session. The number of nursing interventions for blood volume preservation was also computed. Finally, patients’ thirst after each session, body weight difference between two consecutive sessions and blood pressure (BP) in next session were estimated.

Results: Nursing interventions were significantly fewer in sessions that profiling was used (p=0,035). The percentage reduction in BP in significantly lower in the 4th hour of the session when profiling was used (p=0,039). Thirst was reported to be significantly more in profiling model (p=0,030). Body weight difference between two sessions and BP in next session were not influenced by the model used.

Conclusions: Sodium and UFR profiling, with linearly increasing sodium concentration and linearly decreasing UFR, is a safe and efficient method for the prevention of blood volume reduction and hypotension during hemodialysis in ESRD patients.

EFFECT OF EMPIRICAL REDUCTION OF DIALYSATE SODIUM ON HYPERTENSION AND BODY COMPOSITION IN EGYPTIAN HEMODIALYSIS PATIENTS

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Introduction and Aims: Sodium balance plays a central role in dialysis treatment and should be considered when we study cardiovascular stability. A negative sodium balance may contribute to low cardiovascular stability during HD treatment, while, a positive sodium balance can reduce intradialytic symptoms but aggravates other symptoms as thirst, weight gain, hypertension and eventually development of cardiovascular failure. To reduce all these complications we must reach zero balance where amount of sodium removed during dialysis equals the amount accumulated during interdialytic period. Empirical reduction of dialysate sodium below plasma sodium enhances sodium removal by diffusion, and may lead to a reduction in total body sodium. However, this strategy is not so tolerant to some patients. Although most studies show that this approach results in improvements in blood pressure (BP), reductions in weight gain and fewer symptoms of thirst, others do not report such differences or find the reverse. The present study was aiming to study the effect of empirical reduction of dialysate sodium on hemodynamic stability during dialysis, body composition, inter-dialytic weight gain and hypertension in hemodialysis patients.

Methods: Twenty hypertensive patients with CKD stage 5-D on HD for more than six months were included in the study. They were subjected to the following: Confirmation of the dry weight by clinical examination and bioimpedance study, adherence to low sodium diet during all the period of the study, progressive reduction of dialysate sodium concentration after each two weeks (for a total of eight weeks). For every dialysate sodium concentration changes, the following data was collected: Pre, post and intradialytic BP, start and end plasma sodium, Symptoms and episodes of intradialytic hypotension (DIHII), Thirst score was completed every week. At the beginning and at the end of the study, measurement of all body water compartments was done using bioimpedance.

Results: By empirical reduction of dialysate sodium we achieved significant reduction of post dialysis plasma sodium, predialysis blood pressure, post dialysis systolic blood pressure, post dialysis diastolic blood pressure, Inter-dialytic weight gain and thirst score. The reduction in both predialysis plasma sodium and predialysis DBP was not significant. Also there was no change of any measurements of all body water compartments.

Conclusions: Optimization of the dialysate sodium prescription is necessary to assure favorable sodium balance and cardiovascular stability in HD patients. Empirical reduction of dialysate sodium in stable HD patients is well tolerated, safe, and beneficial. Empirical reduction of dialysate sodium to below predialysis plasma sodium level was tolerated in some patients. Further studies are required to find out the effect of empirical reduction of dialysate sodium in hypertension prone HD patients.
ON-LINE HEMODIAFILTRATION IMPROVES SURVIVAL OF PATIENTS ON MAINTENANCE HAEMODIALYSIS: A MULTICENTER COHORT EVALUATION

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Introduction and Aims: Hemodiafiltration (HDF) is the treatment modality that employs convection and diffusion in order to facilitate removal of small and larger molecular weight solutes. The clearance of large solutes is dictated by the ultrafiltration volume and the sieving coefficient. HDF with a substitution fluid volume ≥ 15 L was classified as high-efficiency HDF in the Dialysis Outcome and Practice Patterns Study (otherwise low-efficiency). Aim of this study is to evaluate if post-dilution on-line HDF improved patient survival compared to high-flux hemodialysis (HD).

Methods: The study was conducted in 13 dialysis centers; 4 in Bosnia and Herzegovina, 4 in Slovenia and 5 in Serbia. Patients were included if they were newly recruited patients or were ≤3 months on RRT. Study period was from January 1, 2007 to December 31, 2011. HDF high volume (HV) was defined as a substitution fluid volume higher than the median substitution volume applied (20.4 L), otherwise low volume (LV). Main statistical analysis was performed by using Cox regression, having all-cause mortality as outcome. Patients were censored by the date of kidney transplantation, new recruited patients or were ≤3 months on RRT. Study period was from January 1, 2007 to December 31, 2011. HDF high volume (HV) was defined as a substitution fluid volume higher than the median substitution volume applied (20.4 L), otherwise low volume (LV). Main statistical analysis was performed by using Cox regression, having all-cause mortality as outcome. Patients were censored by the date of kidney transplantation, newly recruited patients or were ≤3 months on RRT. Study period was from January 1, 2007 to December 31, 2011.

Results: 442 patients were included in the study. Baseline characteristics are reported in the figure. During the follow-up, 59 patients died, 17 were transplanted and 2 were lost to follow-up. After the adjustment for covariates only patients on HDF HV showed significant lower Hazard Ratio in respect to patients on high-flux hemodialysis (HD).

Conclusions: In conclusion, our data showed clear evidence of better patient survival on high volume post-dilution on-line HDF compared to high-flux HD.

REMOVAL OF GADOTERIC ACID (DOTAREM®) BY HEMODIALYSIS AND SAFETY IN DIALYSED PATIENTS

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Introduction and Aims: To evaluate the dialysability of gadoteric acid in patients with end-stage renal disease (ESRD) and requiring hemodialysis.

Methods: Phase I, monocentric, non-comparative, non-randomized, open-label clinical trial, including 10 evaluable patients (male or female, aged ≥18 years), presenting with ESRD who required hemodialysis for 4 hours, 3 times per week. Gadoteric acid (Dotarem®) was injected intravenously at a dose of 0.1 mmol/kg. The primary evaluation criterion was the decrease in serum gadoteric acid concentration after each hemodialysis session. To calculate the dialysability, blood samples were drawn simultaneously from the inflow and outflow lines of the circuit during the first hemodialysis session, and from the vascular access just before and after each of the three hemodialysis sessions. The 3 hemodialysis sessions started 1 to 2 hours, 2 days (i.e., 48 ±2h) and 4 days (i.e., 96 ±4h), respectively, following the gadoteric acid injection. The total gadolinium concentration was measured in the serum by inductively coupled plasma mass spectrometry (ICP-MS). The secondary evaluation criteria were the clinical safety (vital signs, injection-site tolerance) and laboratory assessments which were evaluated during a 4-day follow-up after gadoteric acid injection. Adverse events (AEs) and serious AEs were evaluated through a 3-week and 3-month post-injection period, respectively.

Results: All 10 subjects were Caucasian, of which 5 (50.0%) were female. Median (range) age was 64.0 (31-79) years. Median (range) weight was 70.6 (61-116) kg. During the first hemodialysis, the mean gadolinium clearance (mL/min) was 224.6 at 0.5h and 225.9 at 1.5h and the gadolinium serum concentration decreased over time by 88% to 93% and 97% at 0.5h, 1.5h, and 4h after start of dialysis, respectively. A second and third hemodialysis session allowed to further accelerate the removal of gadoteric acid from the body, with a decrease of at least 99.7% of gadolinium serum concentration (compared to the pre-dialysis value of the first session) after the third dialysis. No AEs at least possibly related to gadoteric acid were reported. No AEs occurred at the injection site during the observation period. There were no clinically relevant changes in mean laboratory values and vital signs. No cases of NSF have been reported so far.

Conclusions: The results of the study indicate that gadoteric acid was effectively removed by 3 hemodialysis sessions in patients with ESRD. The good general safety profile of gadoteric acid was also confirmed.

MONITORING ADVERSE EFFECTS OF ANTITUBERCULOSIS CHEMOTHERAPY IN CHRONIC HEMODIALYSIS PATIENT: PHARMACOVIGILANCE AND ROLE OF POISON CONTROL CENTER

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Introduction and Aims: Tuberculosis (TB) remains a public health problem in Morocco. It is more frequent, more severe and atypical in immunocompromised patients, including chronic hemodialysis patients in whom treatment is, moreover, a real challenge.

Methods: Prospective study from January 2010 to August 2012, including all chronic hemodialysis patients with TB. We analyzed the clinical data and therapeutic and side effects of antituberculosis treatment.

Results: Tuberculosis represents 22.9% of the cases of hospitalization for infection in hemodialysis patients in our department: These 14 patients: 8 men and 6 women, mean aged 48 years with mean duration in hemodialysis of 57 months, with 50% during the first 2 years. Extrapoluminal localization represented 71.4% of cases. A quadruple antituberculosis chemotherapy was prescribed in 57.1% of cases and a triple association in 42.8% of cases. We recorded 4 cases of acute hepatic cytolyis and a reversible confusional syndrome. Monitoring of isoniazide was systematically carried out in the laboratory of poison control center (PCC) and had found an overdose in 35.7% of cases.

Conclusions: Tuberculosis occurs mostly during the first 2 years of hemodialysis. The telltale signs are nonspecific. The location is especially extrapoluminal. The treatment is a real challenge in this population particularly exposed to a high risk of antituberculosis chemotherapy overdose, or, conversely, to therapeutic ineffectiveness by the influence of hemodialysis on the pharmacokinetics of these drugs. Thus, prescribing antibacillary in hemodialysis requires dosage precautions and close clinical and laboratory monitoring. The recourse to the PCC is often necessary for optimal therapeutic safety.
PERITONEAL DIALYSIS - A

SP436  MIS (MALNUTRITION-INFLAMMATION SCORE) IS EFFECTIVE AND CRUCIAL TOOL FOR PROGNOSTIC PREDICTION OF PERITONEAL DIALYSIS PATIENT

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Introduction and Aims: Malnutrition occurs in peritoneal dialysis (PD) patients commonly and may correlate with increased mortality. Several factors, such as protein loss into the peritoneal cavity, chronic inflammation, accumulation of uremic toxins, etc. could influence PD patients' nutritional status. Nutritional assessment of PD patients is a very important process to evaluate their nutritional condition. MIS is a useful tool to assess patients' nutritional status comprehensively. In this study, we validated the efficacy of MIS as a prognostic factor for PD patients.

Methods: 40 patients (male 11, female 29) were enrolled into the study. A mean age of the onset of PD was 78.5 ± 7.4 years. All patients had their nutritional status assessed with MIS and were classified into three subgroups corresponding to each score MIS. normal nutritional group (MIS 0-7), mildly impaired group (MIS 8-12), severely impaired group (MIS over 13) respectively. We analyzed patients' survival rates and compared it among three groups using the Kaplan-Meier analysis.

Results: Three year survival rates of the normal group, the mildly impaired group and severely impaired group were 72.9%, 71.0% and 35.2% respectively. And we found a significant difference in the mortality between the severely impaired group and the other two groups with a Log-Rank test (P=0.0312).

Conclusions: The results of this study indicated that MIS is one of the prognostic factors for PD patients. MIS is a comprehensive and quantitative nutritional assessment and consists of several components (medical history, physical examination, body mass index and laboratory parameters). According to the scores of each component, we can design therapeutic intervention for patients with malnutrition. MIS is a powerful predictor for PD patients.

SP437  THE EFFECT OF OMEGA-3 FATTY ACID SUPPLEMENTATION ON OXIDATIVE STRESS IN CONTINUOUS AMBULATORY PERITONEAL DIALYSIS PATIENTS

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Introduction and Aims: End stage renal disease (ESRD) is a condition that inflammation and oxidative stress plays an important role in damaging to tissues, especially in vascular system. The effect of omega-3 fatty acids is well documented in some inflammatory diseases via eicosapentanoic acid (EPA) and docosahexanoic acid (DHA) components of fish oil. The aim of this study was to investigate the effects of dietary omega-3 fatty acid supplementation on levels of lipid peroxidation and oxidative stress in ESRD patients.

Methods: This randomized controlled double-blind clinical trial consisted of 90 patients on CAPD. One group was treated orally with 3000 mg omega-3, per day for 8 weeks and the other two groups with a Log-Rank test (P=0.0312).

Conclusions: The results of this study indicated that MIS is one of the prognostic factors for PD patients. MIS is a comprehensive and quantitative nutritional assessment and consists of several components (medical history, physical examination, body mass index and laboratory parameters). According to the scores of each component, we can design therapeutic intervention for patients with malnutrition. MIS is a powerful predictor for PD patients.

SP439  FACILITATIVE EFFECTS OF TRANSPPLANTED ADIPOSE-DERIVED MESENCHYMAL STEM CELLS DURING REPAIR IN CHLORHEXIDINE-INDUCED PERITONEAL FIBROSIS RATS

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Introduction and Aims: Transplantation of adipose-derived mesenchymal stem cell (ADSC) has been suggested to repair the injured organs and tissues in various of the fields. Although the rat peritoneal mesothelial cells (RPMCs) improve the peritoneal fibrosis, it is still unclear the effect of ADSC to the peritoneal fibrosis. We established ADSCs and then examined the effect of transplanted ADSCs during peritoneal repair compared with that of cultured RPMCs using cell line previously established in chlorhexidine (CH)-induced peritoneal fibrosis rats.

Methods: To prepare the peritoneal fibrosis rat model, continuous-infusion pumps containing 8% CH gluconate in ethanol dissolved in saline were placed in the lower abdominal cavity in 45 male Sprague-Daley rats for 3 weeks. After removal of the pumps, RPMCs and ADSCs were injected into the peritoneal cavity at day 22 or 29. At day 35, morphological alterations and expressions of the tissue regeneration-related factors were examined.

Results: Transplantation of ADSCs both at day 22 and 29 facilitated the peritoneal repair RPMCs injected at day 29 accelerated peritoneal repair, however RPMCs injected at day 22 significantly suppressed the repair. The effect of ADSCs injection to peritoneal repair was dependent on the number of transplanted ADSCs. Expression of VEGF mRNA in the ADSCs injection rats was significantly elevated compared with that in the control rats. The levels of TGF-β and MMP-2 mRNA were inhibited by the ADSC injection. Those levels were significantly increased in the RPMCs injection rats at day 22.

Conclusions: It appears that ADSCs transplantation is a useful and new approach for repair of the peritoneal fibrosis contributing to the paracrine effects.

SP440  UPDATE ON THE EUROPEAN ENCAPSULATING PERITONEAL SCLEROSIS (EPS) REGISTRY

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Introduction and Aims: Encapsulating Peritoneal Sclerosis (EPS) is a rare but serious complication of long-term peritoneal dialysis (PD). Its aetiology is still...
unclear, but important risk factors include duration of PD and stopping PD (transfer to haemodialysis or transplantation). The overall incidence of EPS in Europe is uncertain and there is a lack of consensus on diagnostic criteria for EPS at an early stage. Because of the limited number of EPS patients in individual centres, a central registry is pivotal to record EPS cases thereby facilitating studies in this field. The European EPS Registry has been set up as a web-based database for EPS cases in Europe with the goal to achieve a greater understanding of this condition with regard to its epidemiology, pathophysiology, potential therapeutic interventions.

Methods: The Registry database was built in 2009 collaboratively by nephrologists and hosted by the Hans Mak Institute for Independent Quality Research in Nephrology. The diagnosis of EPS was defined by existing ISPD criteria, but also linked to a probability ranking to allow review of likelihood by expert physicians. The online database captures demographic data, CKD, RRT history, details of PD, membrane transport and adequacy, peritonitis history, treatment and outcomes from EPS itself. In 2011 the possibility of electronic submission of suspected EPS cases was launched in Europe at www.epsgrege.eu.

Results: The online database currently consists of 159 patients (63.5% male, median age 53.0 [38.25-63.0] years). Median PD duration was 65 [47-89.75] months. In 124 (78.9%) patients, a CT scan was performed for diagnostic purposes. The contribution per country included: Netherlands (61), Germany (53), Belgium (11), Spain (14), United Kingdom (9), Italy (6), Greece(2), Iceland (1), Hungary (1), France (1). Within the submitted cases in the Netherlands, 48 have been reviewed and 13 patients were classified as EPS, 19 with clinical EPS, 10 with suspected early EPS, and 6 patients with No EPS. Overall mortality of patients included was 37.1% with a mean time to death of 9.9 ± 14.9 months after EPS diagnosis.52 (32.7%) patients underwent surgery (enterolysis or peritonectomy) for EPS.

Conclusions: EPS is an important complication of PD therapy and collaborative approaches across Europe are essential to improve both clinical knowledge around diagnosis and investigations as well as research into causes and treatment. The European EPS Registry has recently been established as an online database. The international submission of EPS cases is successful and we encourage physicians to submit every suspected or proven case of EPS.

COMPETITIVE RISKS OF ENCAPSULATING PERITONEAL SCLEROSIS AND DEATH IN PERITONEAL DIALYSIS

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Introduction and Aims: Encapsulating peritoneal sclerosis (EPS) is an uncommon complication of peritoneal dialysis (PD), where the risk increases significantly with increasing time on therapy. We hypothesised EPS, 19 with clinical EPS, 10 with suspected early EPS, and 6 patients with No EPS. Overall mortality of patients included was 37.1% with a mean time to death of 9.9 ± 14.9 months after EPS diagnosis.52 (32.7%) patients underwent surgery (enterolysis or peritonectomy) for EPS.

Methods: We combined 3 large datasets (AnzData, Global Fluid Study, Scottish Renal Registry) with complete data on EPS occurrence and the denominator population. All incident patients aged ≥15 years were included and a competing risks survival analysis was used with outcomes of censored, EPS (prior to death) or death and robust standard errors. Comorbidity data was classified by either primary renal diagnosis (low comorbidity = glomerulonephritis, polycystic kidney disease, chronic pyelonephritis, high comorbidity = other) and diabetic status (all 3 datasets) or by Stoke comorbidity (other) and diabetic status (all 3 datasets) or by Stoke comorbidity. The contribution per country included: Netherlands (61), Germany (53), Belgium (11), Spain (14), United Kingdom (9), Italy (6), Greece(2), Iceland (1), Hungary (1), France (1). Within the submitted cases in the Netherlands, 48 have been reviewed and 13 patients were classified as EPS, 19 with clinical EPS, 10 with suspected early EPS, and 6 patients with No EPS. Overall mortality of patients included was 37.1% with a mean time to death of 9.9 ± 14.9 months after EPS diagnosis.52 (32.7%) patients underwent surgery (enterolysis or peritonectomy) for EPS.

Conclusions: Competing risks regression is an appropriate model for analysis of dialysis outcomes.

BUDGET IMPACT ANALYSIS OF PERITONEAL DIALYSIS VS. CONVENTIONAL IN-CENTER HEMODIALYSIS IN THE UNITED KINGDOM

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Introduction and Aims: The increasing prevalence of patients with end-stage renal disease (ESRD) is driving up the costs of dialysis care dramatically. The National Institute of Clinical Excellence (NICE) has projected significant cost savings by increasing the proportion of patients on peritoneal dialysis (PD). This study investigates the five-year budget impact on UK national healthcare spending on dialysis of changing the distribution of adult patients undergoing peritoneal dialysis and in-center hemodialysis (ICHd).

Methods: An Excel-based budget impact model was constructed to assess dialysis-associated costs when changing adult patients between PD and ICHd. The model incorporates the current modality distribution and accounts for UK dialysis payments, drug costs (including ESA), and the costs and probabilities of adverse events including access failure, access infection, pneumonia, and cardiovascular events. Data from the UK renal registry reports were used to estimate the UK adult dialysis population for the next five years. The baseline scenario assumed a stable distribution of PD (15%) and ICHd (82%) over five years; the remaining 3% is assumed to practice home hemodialysis. Alternative scenarios included: 1) the prevalence of PD increased by 1.5% each year for five years; 2) the prevalence of PD increased by 3.0% each year for five years; 3) the prevalence of PD decreased by 1.5% each year for five years. All three scenarios were accompanied with commensurate changes in ICHd. In addition, changes in submodality distribution for PD and ICHd were assumed in all three scenarios. Differences among scenarios were evaluated in terms of costs to UK National Health Services (NHS).

Results: Under the current UK national tariff, an increase in the prevalent PD population from 15% in 2013 to 21% or 27% in 2017 is predicted to result in five-year cumulative savings for NHS of £18.5 million and £63.6 million, respectively. If the prevalent PD population were to decrease from 15% in 2013 to 9.0% by 2017, the NHS payment for adult dialysis patients would increase by £71.5 million over the next five years (Table 1). Table 1. Cumulative costs by resource type (value in £1,000s).

Conclusions: The model is flexible in terms of sensitivity analysis and can be used as a tool to assist centers and physicians to determine how best to manage patient care.

LONG-TERM EFFECT OF LOW GLUCOSE DEGRADATION PRODUCT DIALYSIS SOLUTION ON THE MARKERS OF ENDOTHELIAL DYSFUNCTION AND PHENOTYPE OF HUMAN PERITONEAL MESOTHELIAL CELLS IN CONTINUOUS AMBULATORY PERITONEAL DIALYSIS PATIENTS

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Introduction and Aims: During continuous ambulatory peritoneal dialysis (CAPD), the peritoneum is exposed to bioincompatible dialysis fluids that cause denudation of mesothelial cells and tissue fibrosis. Recent studies showed that vascular events are preceded by endothelial dysfunction and increase in circulating markers of endothelial activation, including vascular cellular adhesion molecule (VCAM)-1 and intercellular adhesion molecule (ICAM)-1. Therefore, the authors conducted a prospective, observational study to investigate the effect of the low glucose degradation product (GDP) solution on the markers of endothelial dysfunction and phenotype of human peritoneal mesothelial cells (HPMCs) in CAPD patients.

Methods: Among new CAPD patients from May 2001 to April 2012 in our hospital, 74 patients (43 male, 27 diabetes, mean age 47±11 years) finished a 60-month protocol. They were assigned to one of the four groups, group D (Dianeal®, n=28, lactate-based high GDP solution), group P (Phynesian®, n=7, bicarbonate/lactate-based low GDP solution), group S (StaySafe®, n=28, lactate-based high GDP solution), and group B (Balance®, n=19, lactate-based low GDP solution). Blood chemistry including CRP, ICAM-1 and VCAM-1 were measured at months 1, 12, 24, 36, and 60. HPMCs were
INTRODUCTION AND AIMS: In September 2010 an increased number of sterile peritonitis cases were reported in Europe. Two lots of Nutrineal and One Dianeon lot were recalled due to concerns over high endotoxin levels. This study was designed to differentiate clinical characteristics and outcomes in PD patients with endotoxin-associated sterile peritonitis (eSP), bacterial peritonitis (BP) or no peritonitis (NoP) >12 months. Methods: An observational, retrospective, medical record review study was conducted in 12 dialysis centers in Hungary, The Netherlands, Portugal, the United Kingdom, 46 eSP subjects had sterile peritonitis and 38 NoP subjects were asymptomatic after exposure to a recalled lot, while 43 BP subjects had bacterial peritonitis. Clinical characteristics were analysed at baseline, index event and 12 months post index event. Statistical analyses were descriptive due to small sample size. Results: At baseline subject demographics, PD prescription, adequacy and residual renal volume were similar across cohorts but the peritonitis rate was 22% in the e-SP compared to 7% and 0% in the BP and NoP cohorts respectively. Diabetes was similar across cohorts. Congestive heart failure was more frequent in the NoP compared to the BP and eSP cohorts. 12 months post index event, D/P Cr decreased in the eSP, increased in the BP, and was unchanged in the NoP cohort compared to baseline. Mixed model results showed no statistically significant between-between group differences in Cr across cohort or over time. Results: Compared to baseline, Cr was unchanged in the NoP and eSP cohorts. Fungal and antibiotic resistant peritonitis occurred only in the BP cohort. 73% of subjects stayed on PD. 9% of eSP, BP and NoP subjects died, respectively. At 27/7 who started PD for their first RRT in single center, and evaluated their severity of other factors did not show significant relationships with DR. Results: As compared to the patients without proliferative DR, the patients with proliferative DR were significantly higher D/P Cr (0.62±0.11 vs. 0.72±0.10, p<0.04). Other factors did not show significant relationships with DR. Conclusion: The present study demonstrates that a proliferative DR is associated with an increased peritoneal permeability. We previously reported that DM nephropathy and higher peritoneal permeability at PD initiation are independent risk factors of death in the patients starting PD for their first RRT. Hence, strict follow up is needed in those patients.

INTRODUCTION AND AIMS: Bacterial peritonitis is a major complication of PD and a leading cause of technique failure. Recognition of bacterial pathogens by the peritoniathum is mediated in part by toll-like receptors (TLRs). Heme oxygenase-1 (HO-1) gene expression by LPS in macrophages is not only induced via a TLR-4 dependent mechanism, but also increased HO-1 activity has also been shown to have inhibitory effects on intracellular signaling, that is initiated by TLR-4 activation. This regulatory interplay between TLR-4 and HO-1 appears to form a negative feedback loop which might inhibit excessive activation of macrophage by LPS. However, The regulatory effects of HO-1 overexpression on LPS-induced inflammation, which plays a leading cause of technique failure, are unknown in HMCs, yet. So, the objectives of this study are examine the effects of overexpression of human HO-1 on LPS-induced inflammation in HMCs. Methods: HPMCs in overnight peritoneal effluent were completely isolated with centrifugation. We treated HPMCs with LPS (1μg/ml) and HO-1 inducer (b-hematin; 10μg/ml). To further investigate the pure effect of HO-1 on LPS-induced inflammation, Gene transfer of recombinant Adenovirus-harboring human HO-1 (Adv-HO-1 Gene) to HPMCs was done. The involvement of MAP kinase family (ERK and JNK) and nuclear factor(NF)-κB in these processes was also studied. Results: Our study suggest that HO-1 pathway is involved in LPS-induced TLR4 responsiveness and HO-1 may regulate LPS-induced inflammation in HPMCs. This study has implications for improving treatment of infection in PD patients and is the first to show the beneficial effect of HO-1 on attenuating LPS-induced inflammation in HMCs.

INTRODUCTION AND AIMS: Peritoneal dialysis (PD) is recommended as the first line treatment for the end-stage renal disease patients in terms of the integrated renal replacement therapy (RRT). However, PD patients with diabetes had higher mortality and higher rate of technical failure compared to the patients without diabetes. Sometimes a higher peritoneal permeability at PD initiation is reported as a risk factor for poor outcome in PD patients, and patients with diabetes are liable to have permeable peritoneum. Previous study demonstrated that an increased peritoneal permeability is associated with an increased increased vascularization and/or dilatation of peritoneal microvessels, especially in patients on long-term PD treatment. On the other hand, diabetic retinopathy (DR) is characterized by the formation of new vessels inside the retina showing abnormal architecture and permeability due to the long-term hyperglycemia. Therefore, these two situations seem to be similar, we might be able to infer a characteristic of the peritoneum from a state of DR. The aim of this study was to evaluate the relationship between peritoneal permeability and DR. Methods: This study retrospectively examined 34 patients (63 years old, male/female: 27/7) who started PD for their first RRT in single center, and evaluated their severity of diabetic retinopathy and the dalsyate to plasma creatinine ratio (D/P Cr) obtained from the last peritoneal equilibration test for the marker of peritoneal permeability. Results: As compared to the patients without proliferative DR, the patients with proliferative DR were significantly higher D/P Cr (0.62±0.11 vs. 0.72±0.10, p<0.04). Other factors did not show significant relationships with DR. Conclusion: The present study demonstrates that a proliferative DR is associated with an increased peritoneal permeability. We previously reported that DM nephropathy and higher peritoneal permeability at PD initiation are independent risk factors of death in the patients starting PD for their first RRT. Hence, strict follow up is needed in those patients.
patients were collected during the first day of an acute episode of peritonitis and on days 3, 7 and 30 (i.e. at least one week after antibiotic therapy withdrawal). All samples were examined for cell count, bedside culture and calprotectin concentration. In presence of fever or minor clinical pain, a PD fluid was transported then 100/ mm³ with or without a positive culture was used for diagnosis of peritonitis. Moreover we evaluated C reactive protein and blood leucocytes on the same days of PD effluent collection. Calprotectin levels were determined by means of a modified ELISA test with a threshold value of 156 mg/mL. Continuous fluid was not ultrafiltration in PET of 184 ± 162 mL and in miniPET of 370 ± 109 mL. The sodium dip in miniPET was 0.078 ± 0.030, and free water fraction was 0.59 ± 0.22. The mean value of estimated LpS was 0.54 ± 0.026 mL/min/ mmHg and PFA was 1.1 ± 0.9 mL/min. The fractional contributions of different types of pores to hydraulic permeability were: alphaU = 0.038 ± 0.042, alphaS = 0.836 ± 0.095, and alphaL = 0.124 ± 0.081, that resulted in the reflection coefficient for glucose of 0.066 ± 0.041 and OCG = 0.0029 ± 0.0010 mL/min/mmHg. The values of Pfs were as follows: 17.3 ± 5.0 mL/min for urea, 8.7 ± 3.5 mL/min for creatinine, 8.2 ± 2.5 mL/min for glucose; 5.1 ± 9.2 mL/min for sodium, and 10.4 ± 4.3 mL/min for phosphate. The initial values of LpS, OCG, and Pfs should be considered 1.67 times higher than the basic values.

Results: The three patients had good mean values of 156 mg/mL. Continuous fluid was not ultrafiltration in PET of 184 ± 162 mL and in miniPET of 370 ± 109 mL. The sodium dip in miniPET was 0.078 ± 0.030, and free water fraction was 0.59 ± 0.22. The mean value of estimated LpS was 0.54 ± 0.026 mL/min/mmHg and PFA was 1.1 ± 0.9 mL/min. The fractional contributions of different types of pores to hydraulic permeability were: alphaU = 0.038 ± 0.042, alphaS = 0.836 ± 0.095, and alphaL = 0.124 ± 0.081, that resulted in the reflection coefficient for glucose of 0.066 ± 0.041 and OCG = 0.0029 ± 0.0010 mL/min/mmHg. The values of Pfs were as follows: 17.3 ± 5.0 mL/min for urea, 8.7 ± 3.5 mL/min for creatinine, 8.2 ± 2.5 mL/min for glucose; 5.1 ± 9.2 mL/min for sodium, and 10.4 ± 4.3 mL/min for phosphate. The initial values of LpS, OCG, and Pfs should be considered 1.67 times higher than the basic values.

Conclusions: The extended version of sPET was able to provide relatively complete characteristics of the peritoneal transport membrane assumed in the 3p model. In our group of patients it yielded the 30% of patients with permeability characteristics of the peritoneal transport membrane assumed in the 3p model. Also peritoneal fluid absorption was closer to clinical assessments than to the value of 0.3 mL/min typically assumed in this model. Also peritoneal fluid absorption was closer to clinical assessments than to the value of 0.3 mL/min typically assumed in this model. Also peritoneal fluid absorption was closer to clinical assessments than to the value of 0.3 mL/min typically assumed in this model.

Introduction and Aims: Not much data is available about the impact of psycho-social factors like mental health, financial status, distance from the Unit, and education, on the long-term performance of patients in peritoneal dialysis. We developed a 12-point scoring system that incorporated 6 clinical and 6 psycho-social parameters, and assigned scores based on different levels of these parameters. Scoring system for CAPD Diabetes Mellitus No-0;Yes-1 Urine Output <400 mL-0, 400-600 mL-1, >600 mL-2 Serum Albumin<4.5-0.3.0-4.5-1,>4.5-2 Hemoglobin<11.0-0.7,11.0-17.0-2 Age<65yrs-0,>65yrs-1 Cal/Phosph Product<40-0,40-60-1,>60-2 Support Structure for Dialysis Living with family/partner-0, Caretaker/Nurse-1, Alone-2, Education College/more-0, School/graduate-1,Low-Inability Access to mother unit Easy(<100 miles)-0,Difficult (>100 miles)-1 Finances Fully reimbursed-0,Partly reimbursed-1 Self paying-2 Mental Health No/minimal depression-0,Mild Depression-1,Moderate/Severe Depression-2 Mobility No restriction-0,Minimal restriction-1,Moderate/severe restriction-2

Methods: All patients initiated on CAPD from Jan 2009 through June 2012 were included in the study and scores were computed. These patients were prospectively followed up 2 years and data on number of hospitalisations, episodes of peritonitis and exit site infections, technique failure and death were recorded. The scoring system was prospectively validated by separating the patients randomly into a validation cohort and a derivation cohort. Subsequently we also retrospectively applied this scoring tool to patients initiated on CAPD from Jan 2005 through Jan 2009.

Results: 119 patients were included in the prospective part of the study and underwent scoring at initiation of CAPD. A score of 14 or more had significant correlation with mortality (p<0.05), episodes of peritonitis (r=0.64,p=0.04) and technique failure (r=0.70,p<0.05). There was no association with Exit Site Infections (p>0.3). Patients were then randomly separated into a derivation cohort and a validation cohort and compared. In the retrospective arm of the study,179 patients were assessed. A score of 14 was significantly associated with hospitalizations(r=0.72,p<0.05)peritonitis (r=0.70,p<0.05),technique failure (r=0.73,p<0.05) and mortality (r=0.73,p<0.05). Upon separating into a derived score >30 and a validation cohort, there were no significant differences between the patients in either cohort. AUROC curves for predicting hospitalisations was 0.699 (95% CI 0.727-0.859);peritonitis was 0.811 (95% CI 0.758-0.888);AUROC for technique failure was 0.602 (95% CI 0.536-0.757);mortality was 0.815 (95% CI 0.769-0.899).The predictive power remained robust even after a 2 year follow up.

Conclusions: The scoring tool, prospectively and retrospectively, performed well in predicting more hospitalisations and episodes of peritonitis, technique failure and mortality. When retrospectively applied remained good. A score of 14 or more correlated well with adverse outcomes on CAPD.
was conducted to compare the clinical differences and the impact between patients with initial loss of and fast decline in RRF on long-term prognosis of CAPD patients.

Methods: According to the timing of anuria (<100ml/day) after the CAPD initiation, a total of 274 incident patients were divided into 4 groups: Group 1: anuria detected during the 1st peritoneal equilibrium test (n=41). The other 233 patients were stratified into 3 groups according to the RRF decline rate: group 2: slow decliners (n=78), group 3: intermediate decliners (n=78), and group 4: fast decliners (n=77). The maximum observation period was 120 months.

Results: No difference was noted in long-term prognosis between groups of 1 and 4 (p=0.60) but they had poor long-term prognosis compared to the other two groups (groups 2 and 3) (all p<0.05). By multiple logistic regression tests, group 1 was associated with higher percentages of HD for more than 3 months (OR: 5.67, 95% CI: 2.54-12.65), female gender (OR: 0.40, 95% CI: 0.18-0.90), and lower levels of nPCR at initiation (OR: 0.23, 95% CI: 0.10-0.91), while group 4 was significantly associated with congestive heart failure (OR: 4.12, 95% CI: 1.70-10.00), male gender (OR:3.18, 95% CI:2.71-5.50), and higher BMI (OR: 1.17, 95% CI:1.07-1.27). By Cox proportional analysis, group 1 (HR: 2.51), group 4 (HR: 2.10), age (HR: 1.04), and diabetes (HR: 2.39) were independent risk factors to long term mortality.

Conclusions: Although having the higher baseline RRF at the beginning of CAPD, fast decliners of initial anuria in the long-term mortality. Independent of age and diabetes, both fast decliners in RRF and initial anuria are two important factors associated to the poor long-term outcomes in CAPD patients.

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**Introduction and Aims:** Tunnel and exit site infections (TESI) portend a potential risk of peritonitis and demand peritoneal catheter removal, having a significantly contribution to Peritoneal Dialysis (PD) technique failure. Establishing risk profiles for TESI may have an important role in their prevention.

**Methods:** We developed a retrospective cohort study of all patients treated with PD in a single unit between 1990 and 2012. Main demographic, clinical and PD-related variables were compared between patients who suffered at least one episode of TESI and those remaining free from this complication. We applied univariate and multivariate analysis, including survival between catheter insertion and first episode of TESI (Kaplan-Meier), and produced adjusted risk profiles for this complication using multivariate survival models (Cox).

**Results:** The study population included 665 patients with mean age of 59 years, 58% male, 34% diabetics, mean Charlson’s score 3.8 and 32% of patients in automated PD. 169 patients (25%) suffered at least one TESI, of which 46 had >1 episode, yielding a total rate of 1 episode per 85 patient-months. Most infections were caused by Staphylococcus aureus (SAu) and gram negative bacteria, 47% and 34% of TESI respectively. On univariate analysis, SAu carriage, despite screening and treatment with mupirocin (p=0.001), PD start before year 2000 (p<0.001), time from catheter insertion and initiation of PD <30 days (p=0.003), time from catheter insertion and initiation of PD <30 days (p=0.003), and higher C-reactive protein (p=0.037) and lower hemoglobin levels (p=0.015) portended an increased risk of TESI during follow-up. Lower baseline GFR and PD secondary selection displayed similar but nonsignificant trends. We didn’t find a significant association with other variables, including age, gender, diabetes, Charlson’s score, obesity, PD modality and assisted PD. We also observed a significant association between BMI and TESI risk. We applied univariate and multivariate analysis, including survival between catheter insertion and first episode of TESI (Kaplan-Meier), and produced adjusted risk profiles for this complication using multivariate survival models (Cox).

**Conclusions:** Systematic screening and treatment of SAu carriers do not fully prevent an increased incidence of TESI in this subpopulation. An adequate delay between peritoneal catheter insertion and initiation of PD should be allowed to reduce the incidence of TESI. Patients suffering TESI also undergo increased peritonitis rates; this phenomenon cannot be explained solely by episodes of catheter-dependent peritonitis.

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**Introduction and Aims:** The peritoneal membrane undergoes major alterations in adult PD patients treated with acidic PD fluids with high glucose degradation product (GDP). The effects of the various reduced GDP fluids are unknown. Neither peritoneal membrane morphology in healthy children nor the transformation with chronic PD has yet been investigated, even though uremic children are largely devoid of preexisting tissue damage and thus particularly suited for such analyses.

**Methods:** We initiated an international PD biopsy study for repeated, standardized sampling of parietal peritoneum and of omentum in children. Until now specimens were obtained from 37 non-uremic controls (0.1-16.6 years), undergoing elective surgery for diseases unrelated to the peritoneum, and 87 biopsies from 81 children on PD (0.1-20.1 years), of which 90% were on bioincompatible fluids.

**Results:** In healthy controls the mesothelial cell layer was mostly intact and positive for CK5/6 but negative for cathepsin in some of the young children. Submesothelial fat was absent in infants and young children. Submesothelial adipose compartment zone reached down to the muscle fascia and was 269 (207-370) μm and thus even thicker than reported in adults. Relative capillary surface area decreased with age (5.8 (2.7-13.6), 4.2 (2.8-6.6) and 3.2 (1.6-4.6) % of peritoneal surface area in children below 6, 12 and 18 years). At PD onset mesothelial cell layer was intact in 63%, after 2-4 years in 31 and after more than 4 years of PD in 20% of the specimens. Submesothelial zone thickness and capillary density increased with time on PD, even in children on low GDP fluids, while peritoneal vessel morphology remained unaltered. ASMA positive, activated fibrin was present in 23% of the children on PD. CD45 and CD68 positive leukocytes and macrophages were largely absent in controls, present in 24% of the patients at PD onset and increased two to threefold with time on PD. Analyses of larger omental vessel analyses are pending. No biopsy-related complications were reported.

**Conclusions:** In conclusion, PD membrane biopsy sampling is well tolerated even in infants. Our findings in non-uremic children suggest substantial differences in peritoneal structure and major PD associated peritoneal membrane transformation in children with time on PD, even though most of them on bioincompatible fluids. Omics technology will be used to delineate the underlying molecular pathomechanisms.
Abstracts

LV Mass Index (g/m²) 190.4 ± 30.2 146.6 ± 32.7 <0.001
NT-proBNP (pg/mL) 3468 ± 981 1095 ± 502

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Introduction and Aims: Our aim was to evaluate the relationship between degree of fluid status and arterial stiffness measured by pulse wave velocity (PWV) in peritoneal dialysis (PD) patients.

Methods: Sixty PD patients were evaluated. Fluid status was determined by different methods including fluid overload measured by Body Composition Monitor (BCM), calf normalized resistivity (CNR), plasma N-terminal fragment of B-type natriuretic peptide (NT-proBNP) and extracellular to intracellular water ratio (ECW/ICW). Patients were stratified in normo- and hypervolemic groups according to their fluid overload (FO). CNR was calculated from resistance at 5 KHz using calf bioimpedance spectroscopy. Lower CNR indicates increased ECW in calf due to hypervolemia. Separate multivariate logistic regression models were used to evaluate the correlations of each fluid status indicators with PWV.

Results: Clinical, laboratory characteristics were given table 1. PWV was higher in the hypervolemic compared to normovolemic patients. Hypervolemic patients had higher NT-proBNP levels, a higher ratio of ECW/ICW and lower PWV. NT-proBNP level, ECW/ICW ratio, relative FO, and left ventricular (LV) mass index were positively and CNR negatively correlated with PWV (figure1). Relative FO (β=0.31, p=0.0009) and CNR (β=0.34, p=0.006) independently predicted PWV in multivariate analysis adjusted for age, duration of PD, body mass index and mean arterial pressure.

Conclusions: Arterial stiffness is increased in fluid-overloaded PD patients. Our results indicated that fluid status might is an independent predictor of PWV.

**SP457 25-HYDROXY VITAMIN D LEVELS ARE RELATED TO PARAMETERS OF RESIDUAL RENAL FUNCTION IN ADULT PERITONEAL DIALYSIS PATIENTS**

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Introduction and Aims: There is uncertainty about the importance of vitamin D supplementation in peritoneal dialysis (PD). 25-hydroxy vitamin D (25(OH)D) levels are low in dialysis patients, and seem to show some seasonal variance due to differences in nutrition and sun exposure. Up to now the association between residual renal function and serum 25(OH)D was investigated only in pediatric PD patients. The aim of the study was to analyze the relation between 25(OH)D and residual renal function parameters in adult PD patients.

Methods: Renal function parameters, as daily urine creatinine and urea excretion, weekly creatinine clearance (Crea-CI), urea clearance (Urea-CI), fractional excretion of urea (FE-Urea) and renal Kt/V, were analyzed in 32 adult PD patients together with serum 25(OH)D. All patients presented residual diuresis of at least 100 ml per day. 25(OH)D levels below 20 ng/ml were classified as deficiency and levels between 20 and 30 ng/ml as insufficiency. Furthermore, all patients were under high dose furosemide therapy of at least 250mg per day, and did not receive oral vitamin D supplementation. Vitamin D receptor agonists (calcitriol or paricalcitol) were given to control calcium-phosphorus-parathormone.

Results: PD patients (mean±standard deviation: age 63.1±17 years) presented diuresis of 1100±683 ml per day, Crea-CI of 49.3±1 L/week, Urea-CI of 25.5±15 L/week, FE-Urea of 0.54±0.16 and Kt/V of 0.68±0.47. Mean values of 25(OH)D were 13.9±7.7 ng/ml. Two patients presented 25(OH)D levels slightly above 30 ng/ml, five patients 25(OH)D insufficiency and the remaining 25 patients deficiency. Serum 25(OH)D correlated to renal creatinine excretion (r=0.35, p=0.049), renal urea excretion (r=0.42, p=0.02), FE-Urea (r=0.40, p=0.02) and Urea-CI (r=0.41, p=0.02), but not to diuresis, CI-Crea or Kt/V. Patients with higher 25(OH)D levels show relatively increased rates of urinary urea elimination even in relation to creatinine excretion.
Conclusions: Serum 25(OH)D levels were in the majority of cases in the range of deficiency. Several parameters of residual renal function were associated to 25(OH)D, especially parameters regarding urea elimination (daily urinary urea excretion, FE-Urea and Urea-G). Whether vitamin D supplementation will have an effect on residual renal function parameters has to be proven in further studies.

SP459  |  VITAMIN D STATUS IN INCIDENT PERITONEAL DIALYSIS PATIENTS AND THE EFFECTS OF ORAL SUPPLEMENTATION

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Introduction and Aims: It is known that vitamin D (vit D) deficiency is highly prevalent in uremic patients. Normalization is not always achieved despite oral vit D supplementation. In this study we evaluated vit D status, as serum levels of 25(OH)D3, in a cohort of 37 patients (22 males and 15 females, aged 64 ± 15 yrs) who were started on peritoneal dialysis in our Centre between September 2009 and December 2012. The effects of oral supplementation were investigated as well.

Methods: We measured 25(OH)D3, serum calcium and phosphate levels, alkaline phosphatase, intact PTH (iPTH) and pre-albumine, as an index of the nutritional status, at baseline and after treatment. Supplementation was carried out by using either weekly cholecalciferol or daily calcifediol. Deficiency or insufficiency were considered as 25(OH)D3-lower than 15 ng/ml or between 15 and 30 ng/ml, respectively.

Results: On baseline evaluation only 14% of patients had 25(OH)D3 levels above normal range, whereas 76% were deficient and 10% insufficient. There was no gender difference, while 25(OH)D3 was significantly inversely related to both age (p=0.011) and nutritional status (p=0.03). Upon treatment 69% achieved sufficiency, but deficiency (9%) or insufficiency (22%) still occurred. The addition of oral vitamin D yielded a significantly decrease in iPTH (p=0.03) independently of the use of other medications (9%) or insufficiency (22%) still occurred. The addition of oral vitamin D yielded a significantly decrease in iPTH (p=0.03) independently of the use of other medications (9%) or insufficiency (22%) still occurred.

Conclusions: In conclusion, this study performed in a subset of uremic patients to be started to peritoneal dialysis, confirms that vit D status is most often altered, more severely in older and malnourished patients. Oral supplementation with our protocols allowed normalization in most but not all patients. It is confirmed that 25(OH)D3 per se is able to decrease iPTH levels.

SP459  |  CHOLECALCIFEROL EFFECT ON PTH IN PERITONEAL DIALYSIS PATIENTS

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Introduction and Aims: The deficiency of 25(OH) vitamin D is a widespread problem in peritoneal dialysis patients. Unfortunately, in peritoneal dialysis patients only few studies evaluated the effects of nutritional vitamin D on mineral metabolism. The purpose of the study is to evaluate the long term effect of 25(OH)D vitamin D supplementation on PTH in peritoneal dialysis patients.

Methods: We performed a cohort study on 68 patients who had peritoneal dialysis for at least 6 months before starting a treatment with cholecalciferol for the subsequent 6 months. We evaluated the following parameters before and after the treatment with vitamin D: calcium, phosphorus, PTH, alkaline phosphatase, and 25(OH) vitamin D. Moreover, in both periods we evaluated therapy with drugs such as calcitriol, calcimimetics and calcium based binders. Statistical Analysis: All continuous variables were presented as the median values and interquartile range (IQR), while categorical variables were reported as number of cases. Normality of variable distribution was tested by Shapiro-Wilk W test. All non-normally distributed values were log transformed to better approximate normal distribution. Wilcoxon test were used to tested by Shapiro-Wilk W test. All non-normally distributed values were log transformed to better approximate normal distribution. Wilcoxon test were used to

Results: After six months of cholecalciferol treatment we observed a significant increment in 25(OH) vitamin D level (p=0.001) and a significant reduction of PTH value (p=0.028). The decrease of PTH values was significant associated only with cumulative dose of cholecalciferol (OR=1.609; p=0.041) and with calcitriol dosage (OR=1.961; p=0.05). In multivariable regression analysis, both cholecalciferol (OR=1.713;p=0.028) and calcitriol (OR=2.168; p=0.037) doses were independent predictors of PTH decrease.

Conclusions: We showed significant decrease of PTH values during six-month therapy with cholecalciferol.

SP460  |  SERUM PHOSPHORUS LEVELS, BUT NOT SERUM CALCIUM AND PTH LEVELS ARE ASSOCIATED WITH ABDOMINAL AORTIC CALCIFICATIONS IN PERITONEAL DIALYSIS PATIENTS

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Introduction and Aims: Vascular calcifications are important complications in patients receiving PD therapy. Simple and inexpensive techniques such as plan X-ray can be used to provide important information about vascular calcifications in CAPD patients. Disturbed mineral metabolism has been suggested to play a major contributing role for vascular calcification in ESRD patients. The aim of this study was to evaluate the relationship of abdominal aortic calcifications with biochemical data of mineral metabolism in CAPD patients.

Methods: We conducted a cross-sectional study in 38 stable patients (58.8 % males; mean age 55.5 ± 13.6 years; 23.6% diabetics and average duration of dialysis 28.36 ± 16.97 months) treated with CAPD for more than 6 months. Demographic and biochemical data were examined. Plan X-ray images of lateral lumbar spine from all subjects with abdomen empty from dialysate fluid were studied for calculation of semiquantitative vascular calcification scores as described by Kauppila. The severity of the anterior and posterior aortic wall calcification were graded individually on a 0-3 scale for each first four lumbar segments and the results were summarized to a score (zrange 0-24).

Results: Kauppila scores revealed 21 patients (55.2%) with presence of abdominal aortic calcifications (AAC ≥1) and 14 patients (36.8%) with scores higher than 7. The mean AAC score of the study population was 5.03 ± 3.85. We found that serum phosphorous levels increased significantly in patients with AAC score ≥1 comparing with patients without aortic calcification. AARC score =0, respectively 5.3± 0.3 mg/dl vs 4.2± 0.2 mg/dl (P<0.007). But there was no significant difference in serum iPTH and calcium levels in patients with and without AARC, respectively 427 ± 546 mg/dl vs 348 ± 116 mg/dl and 8.5 ± 0.4 mg/dl vs 8.2 ± 0.3 mg/dl. The reason of the lack of significant difference in iPTH levels probably is related to the presence of either high or low levels of iPTH (high turnover or low turnover bone disease) in the group with aortic calcification. To study further this association we excluded from analysis patients with AARC score = 0, and we found that serum phosphorous levels increased significantly in patients with severe AAC score ≥7 comparing with patients with mild AAC score 1- 6, respectively 5.6 ± 0.3 mg/dl vs 4.8 ± 0.3 mg/dl (P<0.01).

Conclusions: Our study demonstrates that abdominal aortic calcifications are highly prevalent in CAPD patients and strongly associated with serum phosphorus levels, but not with serum calcium and iPTH levels.

SP461  |  Sagittal abdominal diameter is an independent predictor of mortality in incident peritoneal dialysis patients

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Introduction and Aims: Visceral fat plays a crucial role in the development and the progression of cardiovascular disease. However, the impact of sagittal abdominal diameter (SAD), an index of visceral fat, on clinical outcomes has never been explored in dialysis patients. Therefore, we sought to elucidate the prognostic value of SAD on patient mortality in incident peritoneal dialysis (PD) population.

Methods: SAD was determined prospectively using lateral abdominal X-ray at the time of initial dialysis, and the association of SAD with mortality was evaluated in 418 PD patients.

Results: The mean SAD was 24.5 ± 4.3 cm. During a mean follow-up of 39.4 ± 21.3 months, 97 patients (23.2%) died. SAD was an independent predictor of all-cause (HR (hazard ratio) 1.081, 95% CI (confidence interval) 1.015-1.151, P = 0.015) and cardiovascular mortality (HR 1.119, 95% CI 1.022-1.225, P = 0.015). In addition, SAD provided higher predictive value for all-cause and cardiovascular mortality than body mass index (BMI). In subgroup analysis, higher SAD (≥ 24.2 cm) was significantly associated with all-cause mortality in men (HR 1.996, 95% CI 1.014-3.992, P = 0.045), women (HR 2.476, 95% CI 1.082-5.656, P = 0.032), younger patients (< 65 years/ HR 4.260, 95% CI 1.845-9.833, P = 0.001), and the lower BMI group (≥ 22.3 kg/m2). HR 2.033, 95% CI 1.056-3.914, P = 0.034).

Conclusions: SAD on lateral abdominal X-ray was an independent predictor of all-cause and cardiovascular mortality in incident PD patients.
ASSOCIATION OF ENDOTHELIAL DYSFUNCTION AND PLASMA ADMA LEVELS, CARDIAC FUNCTIONS AND METABOLIC PARAMETERS IN PERITONEAL DIALYSIS PATIENTS

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Introduction and Aims: Chronic kidney disease (CKD) is associated with endothelial dysfunction and increased cardiovascular events. Asymmetric dimethylarginine (ADMA) is accepted as a risk factor for coronary artery disease by causing endothelial dysfunction and vasoospasm. We aimed in the present study to investigate the relationship between flow-mediated dilatation (FMD) as an indicator of endothelial dysfunction and ADMA levels, echocardiographic and metabolic parameters in PD patients.

Methods: This is a cross-sectional study in which PD patients aged 18-80, with at least three month duration of dialysis and without active cardiac, infectious or malignant diseases, and clinically evident hypervolemia were included. FMD measurement, ADMA levels and echocardiographic parameters were recorded.

Results: Of the 55 patients included, the mean age was 53±15 years. Mean FMD level was 10.7±6.5. Mean ADMA level was 81.9±48.0 μmol/L. There was no statistically significant relationship between ADMA levels and FMD (p=0.073). We detected negative correlation of FMD with systolic and diastolic blood pressures (p=0.001 and p=0.001, respectively). Patients with hypertension had lower FMD values (p=0.012).

Conclusions: There is no significant relationship between ADMA levels and FMD. FMD was not related with ecocardiographic findings, laboratory results and parameters in PD patients. The major risk determinant for cardiovascular disease in peritoneal dialysis patients is the presence of hypertension.

THE SPECTRUM OF PODOPLANIN EXPRESSION IN ENCAPSULATING PERITONEAL SCLEROSIS

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Introduction and Aims: Encapsulating peritoneal sclerosis (EPS) is a life threatening complication of peritoneal dialysis (PD). Podoplanin, a glycoprotein expressed by mesothelial cells, lymphatic endothelial cells, and myofibroblasts in peritoneal biopsies from patients with EPS. The goals of the current study were to confirm the overexpression of podoplanin in EPS and describe the morphological pattern of podoplanin in a series of peritoneal biopsies from patients with EPS.

Methods: Included: 24 biopsies from patients with the diagnosis of EPS (n=5), patients on PD without signs of EPS (n=5), and control patients (uremic patients not on PD, n=5, non-uremic patients n=5). These were studied by quantitative Real-Time RT-PCR for the expression of podoplanin mRNA. In 24 peritoneal biopsies from patients with EPS, podoplanin and smooth muscle actin (SMA) were localized by immunohistochemistry.

Results: Biopsies from patients with EPS demonstrated significantly elevated levels of podoplanin mRNA (p<0.05). Four patterns of podoplanin distribution were distinguishable. The most common pattern (8 of 24) consisted of organized, longitudinal layers of podoplanin-positive cells and vessels in the fibrotic zone (‘organized’ pattern). 7 of 24 biopsies demonstrated a diffuse distribution of podoplanin-positive cells, accompanied by occasional, dense clusters of podoplanin-positive cells. Five biopsies exhibited a mixed pattern, with some diffuse areas and some organized areas (‘mixed’). These contained cuboidal podoplanin-positive cells within SMA-negative epithelial structures embedded in extracellular matrix. Less frequently observed was the complete absence of, or focal accumulations of podoplanin-positive fibroblasts outside of lymphatic vessels (podoplanin ‘low’, 4 of 24 biopsies).

Conclusions: In summary we confirm the increased expression of podoplanin in EPS, and distinguish EPS biopsies according to different podoplanin expression patterns which are associated with clinical parameters. Podoplanin might serve as a useful adjunct to the morphological workup of peritoneal biopsies.
Registry of Peritoneal Dialysis (Registre de Dialyse Peritonéale de Langue Française) between 01/01/2007 and 31/12/2011 and extracted the day-of-week they occurred; this was also done for peritonitis; in addition, we determined the day-of-week patients were transferred to HD.

**Results:** Day-of-week deaths: Monday: 434 – Tuesday: 419 – Wednesday: 454 – Thursday: 436 – Friday: 383 – Saturday: 359 – Sunday: 432. These non significantly different numbers represented from 11.9 to 14.5 % of all deaths, with no significant variation between the years observed. The main causes of death (in % of all deaths) were: non-PD related (66.2 to 70.2 %), coronary artery disease (14.5 to 17.7 %), peritonitis (2.7 to 5.6 %), malnutrition (2.7 to 6.6 %) and cancer (3.0 to 6.0 %), without a day-of-week effect. As to peritonitis, its occurrence was significantly (Spearmann’s rank coefficient = 0.785, p<0.001) different along the week (ranging from 328 to 836 cases or 13.0 % to 33.0 % relative to the mean number of treated patients per year, 2533).

Finally, among 1876 transfers to HD mainly caused by peritonitis, underdialysis and catherter dysfunction, 38 (4.7 %) were decided on a Saturday, and 165 (8.8 %) on a Friday while on the other days, there were 384 to 348. No difference was observed between France and Belgium.

**Conclusions:** In the largest European PD database, there was a day-of-week effect on the occurrence (or reporting?) of peritonitis as well as on the rate of transfer to HD, but none on death. It is possible that an endogenous circadian rhythm is involved in the timing of HD and might be explained by the continuous character of dialysis and ultrafiltration in PD as opposed to the discontinuous one in HD.

**SP467** SIGNIFICANCE OF PERITONEAL ISCHEMIA IN THE DEVELOPMENT OF PERITONEAL INSUFFICIENCY IN RATS UNDERGOING PERITONEAL DIALYSIS

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**Introduction and Aims:** In patients undergoing peritoneal dialysis (PD), peritoneal fibrosis is generally believed to be a principal factor to cause peritoneal insufficiency and further interruption of PD therapy. Recent works reveal that peritoneal fine arteriole stenosis is developed by long-term exposure to PD solution, suggesting possible involvement of peritoneal ischemia in the development of peritoneal insufficiency. The aim of this work was to study the significance of peritoneal ischemia as a deteriorating factor for the peritoneal damages in uremic rats with daily exposure to PD solution.

**Methods:** Renal failure was induced to male SD rats (6 weeks old) by administration of food containing 0.75% adenine for 4 weeks, and then human-use PD solution, Mid Peric® (400 mg/d). was injected into peritoneal cavity on 6 days a week for 4 weeks. Following peritoneal equivalent test (PET), visceral peritoneum was sampled for histological, immunohistochemical and molecular biological analysis in control (C), uremic (U) and intermittent installation of PD solution on uremia (PD) groups.

**Results:** In PET study, daily installation of PD solution in the uremic rats showed reduction of ultrafiltration volume (C:53±11, U: 38±9, PD: -6±2.2 ml), trans-peritoneal glucose transport (D:P/glucose: 0.2±0.1, PD: 0.17±0.04, 0.09±0.01), and an elevation of small solute permeability (D/P creatinine: 0.75±0.05, 0.9±0.02, 1.16±0.01). Peritoneal thickness and the number of TGF-β positive cells were both significantly increased in PD group comparing to U group. Because the number of peritoneal small vessels has been known to be increased in response to peritoneal ischemia, factor VIII positive cells and pimonidazole positive cells were measured to assess the severity of ischemia associated with installation of PD solution. As a result, both positive cells were increased by daily exposure to PD solution as compared to U group, suggesting increased number of peritoneal vessels in response to the peritoneal ischemia.

**Conclusions:** Present results might indicate that initiation of PD therapy worsened the peritoneal function. In compatible with previous report that peritoneal small vessels would be increased in the uremic cases and be increased more in cases with PD therapy in compensation to the fine arteriole stenosis, it was suggested that PD therapy itself might induce the stenosis of peritoneal fine arteriole and resultant ischemia, possibly leading to the peritoneal insufficiency.

**SP468** ZINC SUPPLEMENTATION ATTENUATES HIGH GLUCOSE-INDUCED EPITHELIAL-TO-MESENCHYMAL TRANSITION OF PERITONEAL MESOTHELIAL CELLS

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**Introduction and Aims:** Zinc (Zn) plays an important role in preventing many types of epithelial-to-mesenchymal transition (EMT)-driven fibrosis in vivo. But its function in the EMT of the peritoneal mesothelial cells (PMCs) remains unknown. Here, we studied the Zn effect on the high glucose (HG)-induced EMT in the rat peritoneal mesothelial cells (RPMCs) and the underlying molecular mechanisms.

**Methods:** RPMCs were isolated, cultured and passaged by enzymatic disaggregation, studied the Zn effect on the high glucose (HG)-induced EMT in the rat peritoneal mesothelial cells (RPMCs) and the underlying molecular mechanisms. But its function in the EMT of the peritoneal mesothelial cells (PMCs). RPMCs were incubated with high glucose (HG) for 24 h; then followed stimulation with 120 μM Zn for 24 h. RPMCs in the control group were just incubated with 120 μM HG for 48 h. RPMCs in the control group were just incubated with high glucose (HG). The expression of α-SMA, E-cadherin, collagen I, Snail, Nkx2, P-KNK, P-Smad 3 was detected by Western Blot. In addition, Elisa analysis was performed to investigate the change of TGF-β1 in the culture medium. Reactive oxygen species assay

**Conclusions:** RPMCs were isolated, cultured and passaged by enzymatic disaggregation, studied the Zn effect on the high glucose (HG)-induced EMT in the rat peritoneal mesothelial cells (RPMCs) and the underlying molecular mechanisms. But its function in the EMT of the peritoneal mesothelial cells (PMCs) remains unknown. Here, we studied the Zn effect on the high glucose (HG)-induced EMT in the rat peritoneal mesothelial cells (RPMCs) and the underlying molecular mechanisms. But its function in the EMT of the peritoneal mesothelial cells (PMCs). RPMCs were incubated with high glucose (HG) for 24 h; then followed stimulation with 120 μM Zn for 24 h. RPMCs in the control group were just incubated with 120 μM HG for 48 h. RPMCs in the control group were just incubated with high glucose (HG). The expression of α-SMA, E-cadherin, collagen I, Snail, Nkx2, P-KNK, P-Smad 3 was detected by Western Blot. In addition, Elisa analysis was performed to investigate the change of TGF-β1 in the culture medium. Reactive oxygen species assay

**SP469** DOES BODY MASS INDEX AFFECT PATIENT AND TECHNIQUE SURVIVAL IN PATIENTS UNDERGOING PERITONEAL DIALYSIS?

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**Introduction and Aims:** In this study, we aimed to investigate effect of body mass index (BMI) on patient and technique survival in patients underwent peritoneal dialysis (PD).

**Methods:** The study included 392 PD patients. Clinical outcomes were mortality and technique failure. Survival rates were estimated using the Kaplan-Meier method. Mortality risks were analyzed using the multivariate Cox regression model in which we included (a backward-wald manner) all the significant variables from the univariate analysis.

**Results:** There were 164 (41.8%) deaths. Forty-six (11.7%) patients underwent renal transplantation whereas 132 (33.7%) patients were transferred to hemodialysis. The estimation of overall patients and technique survival was 92.5 months and 107 months, respectively. Estimation of patient survival was 94.7%, 89.9%, 81.9%, 65.8%, 45.6%, 35.8%, and 29.5% at 1, 2, 3, 5, 8, 10, 13 years, respectively, shows univariate and multivariate analysis of risk factors for the patient survival. The multivariate Cox regression analysis was found that the patient survival rates were significantly associated with age, BMI, baseline serum creatinine and albumin levels, and total Kt/Vurea. The effect of BMI on patient survival did not change whether or not it adjusted for all confounders. No correlation between serum albumin level and BMI (r=0.008, p=0.877). All variables as potential risk factors for the patient survival were also assessed for technique survival in univariate analysis and technique survival rates were significantly associated only with BMI (p=0.015, RR: 1.05, CI: 1.01-1.09).

**Conclusions:** BMI was associated with unfavorable patient survival in PD patients underwent PD. Its effect was independent from albumin, which is a marker of nutritional status in the patient group. Moreover, it was shown that age, baseline serum creatinine and albumin levels, and total Kt/Vurea were associated to patient survival rates. BMI was also associated with unfavorable technique survival in PD patients.
Experiments were performed using the reactive oxygen species assay kit (Beyotime, Haimen, China) according to the manufacturer’s instructions.

**Results:** We found that Zn supplementation significantly inhibited TGF-β1 and ROS production, and reduced the HG-induced EMT in the RPMCs, likely through inhibition of MAPK, NF-κB and TGF-β/Smad pathways.

**Conclusions:** These results indicate that Zn can inhibit EMT in HG-induced RPMCs by inhibiting TGF-β1 production as well as MAPK, TGF-β/Smad pathways activation.

**Introduction and Aims:** Preservation of residual renal function (RRF) is one of the most important aims in peritoneal dialysis (PD). In the last decade, consensus was reached about the positive effect of RRF on outcomes. Avoidance of nephrotropic exposure is therefore strongly recommended in PD patients (pts). We conducted a retrospective observational study to investigate the trend of RRF in our PD pts during the first 6 months of follow up.

**Methods:** Data was collected from 37 adult pts admitted between 2009-2012. All patients were initiated on continuous ambulatory peritoneal dialysis (CAPD). PD modality was eventually changed to automated PD (APD) in accordance to the results of modulated peritoneal functional test. Glomerular filtration rate (GFR) was estimated by the arithmetic mean of urea and creatinine clearance. A 15% variation in GFR from baseline was considered a cut off value to define a significant change in RRF. We considered a GFR increment greater than 15% as an increase in RRF, a GFR reduction more than 15% as a decrease in RRF and any other GFR variation as a stable RRF. RRF was considered a GFR increment greater than 15% as an increase in RRF, a GFR reduction more than 15% as a decrease in RRF and any other GFR variation as a stable RRF. The relative OH% was not statistically significant.

**Results:** Baseline GFR was 6.6±2.7; 6 months GFR value was 6.8±3.5 and 7.6±4.5 respectively (p<0.05). Urinary volume at baseline was 1746±617, after 3 months a significant reduction occurred (1474±608, p<0.05). 17 pts (45%) showed an increase in RRF: 13 pts had an increase in GFR after 3 months, while the remaining 4 pts showed an increase after 6 months. Mean variation in GFR was 68%±58% (19%–222%), which corresponds to an absolute variation of 3.18±2.62 ml/min (0.9–11.2 ml/min). No association between the increase in RRF and age, gender, comorbidities or hydration status at baseline was found. No significant correlation was found between increase in RRF and baseline GFR, even though 12 pts (70%) with increased RRF had baseline GFR < 7 ml/min.

**Conclusions:** In the last few years many efforts have been made to find a strategy to further decrease the slope of RRF reduction in PD pts. Our preliminary results show that a clinically relevant increase in RRF during the first 6 months of follow up is indeed possible. It is reasonable to believe that the hemodynamic improvement expected after starting dialysis can be responsible for better heart performance and increased renal perfusion that can in turn lead to an increase in RRF. However, further investigation is needed to identify factors which may be related to an increase in RRF in PD pts.

**Introduction and Aims:** Antropometric formula of Watson is standard used to measure Urea Distribution volume (V Urea) and derived Kt/V Urea. Multifrequency Bioimpedance analysis is a new validated tool to measure patient body composition, hydration status and nutrition parameters. The aim of this study is to evaluate the difference between V Watson and the two methods and evaluate the impact on weekly dialysis dose (Kt/V), particularly in subgroups of risk patients.

**Methods:** We measured Urea distribution volume using BCM® (VBCM) in 54 stable Peritoneal Dialysis (PD) patients, and compared with Urea distribution volume using antropometric Watson formula (V Watson), and determined V Urea variation between the two methods (ΔV Watson/VBCM). We excluded BCM® determinations with quality < 90% and error > 35%. Using the two V Urea determinations, we calculated weekly Kt/V and also determined the variation between VUrea and Kt/VUrea (ΔKt/VUrea). We compared ΔVUrea in different subgroups of patients: Females, Diabetes, Elderly (age > 65 years), Anuric (Diuresis < 100ml), Overhydrated (BCM®, relative OH > 15%), Obese (BCM®, fat mass >25% in men and >30% in women) and patients with Protein Nitrogen Appearance (PNA) normalized for dry weight lower than 1 g/kg per day (nPNA<1).

**Results:** We studied 54 PD patients (50% female), with mean time on PD of 38 months. Twenty nine patients (54%) were in automatic PD (APD), 17 were diabetic (31.5%), 18 elderly (33%), 14 anuric (26%), V Watson was 3.11, higher than VUrea (p=0.001) and weekly Kt/VUrea was 0.21±0.27 higher than Kt/VUrea (p=0.001). When we compared ΔVUrea, in the different subgroups of patients, it was observed a median ΔVUrea 4.61 [2.1-6.1] in patients with nPNA<1 (p=0.001) and a median ΔVUrea 4.3 [0.8-5.3] in Obese (p=0.001). In the others subgroups we found a trend to higher ΔVUrea than VUrea but not reach significant values. In the regression model including age, residual renal function, and variables from BCM® model including age, residual renal function, and variables from BCM® model composition, the difference between the methods ΔVUrea was positively associated with age (b=0.011; 95%CI 0.005-0.015; p=0.006), fat mass (b=0.018; 95%CI 0.107-0.206; p=0.001), and negatively with lean mass (b=1.26; 95%CI -1.42 -1.10; p=0.001), while relative OH% was not statistically significant.

**Conclusions:** V Watson overestimates V Urea and leads to significant systematic underestimation of dialysis dose in PD patients. This is even more important in Obese patients. A combined in patients with BMI >30 additional and important information about body composition variables that significantly influence such error.
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**THE RELATION BETWEEN APELIN LEVELS, ECHOCARDIOGRAPHIC PARAMETERS AND CAROTID INTIMA MEDIA THICKNESS IN PERITONEAL DIALYSIS PATIENTS**

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**Introduction and Aims:** Inflammation, oxidative stress, and obesity are important features associated with pathogenesis of cardiovascular diseases. The incidence of cardiovascular diseases (CVD) is markedly increased and it is the most important cause of mortality in patients with chronic kidney disease (CKD). Apelin is an adipokine involved in a variety of physiological functions. Serum levels of Apelin increase in heart failure, it is associated with endothelial functions and take a role in the fluid homeostasis. Apelin may also be associated with increased mortality due to CVD. The aim of this study was to test whether Apelin levels might be associated with carotid artery atherosclerosis and left ventricular mass index (LVMI) in peritoneal dialysis patients.

**Methods:** Fifty peritoneal dialysis patients (25 male, 25 female, mean age 41.4±11.9 years, mean dialysis vintage 65.0±35.4 months) and 18 healthy individual (9 male, 9 female, mean age 41.7±6.8 years) were included in this cross-sectional study. All subjects underwent echocardiographic examination to assess LVMI and B-mode carotid artery doppler ultrasound examination to assess intima-media thickness of the common carotid arteries (CIMT). Serum Apelin concentrations were measured using a Human Apelin ELISA kit and CRP levels by immunonephelometric assay.

**Results:** There were no differences between patient and control groups with regard to demographic characteristics. In patient group, LVMI, CIMT, CRP and Apelin levels were elevated compared to control group. However, there was no association between Apelin, LVMI and CIMT. There was a positive correlation between Apelin and CRP, which was statistically marginally significant (p=0.05). When patients were divided in to two groups according to mean serum Apelin levels, LVMI, CIMT and CRP were higher in the high Apelin group but this difference did not reach statistical significance.

**Conclusions:** We observed an increased inflammation and target organ damage in peritoneal dialysis patients. However serum Apelin levels seem not to be associated with cardiovascular risk in this group of patients.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Patient group (n=50)</th>
<th>Control group (n=18)</th>
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<td>Right carotid intima media thickness (mm)</td>
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**PLASMA HYDROGEN SULFIDE IMPROVES ERYTHROCYTE ELONGATION INDICES IN PATIENTS UNDERGOING PERITONEAL DIALYSIS**

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**Introduction and Aims:** In ESRD patients increased mortality due to complications from cardiovascular disease is observed. Growing evidence, from experimental and clinical studies points, that oxidative stress may be implicated in the pathogenesis and complications of ESRD. Additionally, renal replacement therapy may aggravate the production of reactive oxygen species and long time of treatment may intensify depletion in antioxidant defense in vascular endothelium and erythrocytes leading to changes in red blood cell deformation. One of the important serum marker of oxidative stress is a product of lipid peroxidation malondialdehyde (MDA) concentration. The increase of free radicals is the reason of lipid peroxidation taking place in erythrocytes membranes including the...
oxidation of polyunsaturated fatty acids and phospholipids. It was demonstrated that hydrogen sulfide, synthesized in the endothelium, protects from hypoxia-reoxygenation injury via reaction with superoxide anion and hydrogen peroxide. Antithrombotic action of H₂S is directly related with prevention against hemin-mediated oxidative modification of LDL and decrease in release of oxidized phospholipids from atherosclerotic plaque. The present study was designed to evaluate probable links between plasma total hydrogen sulfide and malondialdehyde concentrations, as well as red blood cells deformation (elongation index, EI) and length of peritoneal dialysis.

Methods: Thirty four patients (14 women and 20 men) undergoing regular peritoneal dialysis treatment were enrolled in the study. The median age of patients was 69 years (range 21-77 years) and they underwent peritoneal dialysis from 1 to 141 months (median 23). The modified spectrophotometrical method by Fogo and Popowsky for measurement of total plasma sulfide was used in this study. This method is based upon the reaction of sulfide with N,N-dimethyl-p-phenylenediamine sulfate to form methylene blue. Red blood cells deformation was measured as elongation index with Shear Stress Diffractometer Rheodyn SSD (Myrenne Gmbh, Germany).

Results: Significant and positive Pearson’s correlation was observed between dialysis time and creatinine concentration (r=0.25; p=0.03), whereas H₂S concentration (r= -0.15; n.s.) and red blood cells elongation indices decreased with increased dialysis duration (r = -0.27; p=0.04). Hydrogen sulphide concentration correlated negatively with level of MDA (r = -0.25; p<0.05), while red blood cells EI increased with increase of hydrogen sulphide concentration (r =0.35; p<0.05).

Conclusions: Results shown in this study confirm that length of peritoneal dialysis may predispose erythrocytes to decrease in deformability especially at the shear stresses occurring in capillary vessels. Hydrogen sulfide or H₂S donors may play a key role in prevention of disturbances in the flow of erythrocytes through the capillary.

A NEW MARKER FOR ENDOTHELIAL FUNCTION IN PERITONEAL DIALYSIS PATIENTS: APELIN

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Introduction and Aims: The most important reason for mortality in end stage renal disease is cardiovascular diseases (CVH). Endothelial dysfunction (ED) is one of the most important steps in the pathogenesis of CVH. Apelin is a peptide found recently to have important roles in cardiovascular and endothelial physiology; and we planned in our study to examine the relationship between apelin and endothelial functions in peritoneal dialysis (PD) patients.

Methods: Forty two patients followed up in the PD unit of Haseki Training and Research Hospital were involved. Endothelial functions were evaluated ultrasonographically by flow mediated dilatation (FMD) percentage. Apelin levels and routine laboratory tests were studied from the blood samples obtained from patients.

Results: There was negative correlation between apelin and FMD percentage (r= -0.334, p=0.03). There was positive correlation between FMD percentage and triglyceride and very low density lipoprotein levels (r=0.310,p=0.046; r=0.304,p=0.05, respectively). Significant negative correlation was present between FMD percentage and systolic and diastolic blood pressure (r=0.565, p=<0.001; r=0.560, p=<0.001, respectively). FMD ratio was significantly lower in the group with hypertension, compared with the group without hypertension (9±5.8 vs. 14.9±6.6; p=0.01).

Conclusions: ED is closely related with hypertension and lipid profile in PD patients. Apelin may be used as a new marker for ED and a treatment alternative in PD patients.
**VASCULAR ACCESS**

**SP477**

**FISTULA PROCEDURE RATES (FPR) AND PRESCRIBED DIALYSIS BLOOD FLOW RATE (BFR): FINDINGS FROM THE DOPPS REGIONAL OUTCOMES AND PRACTICE PATTERNS STUDY (DOPPS)**

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**Introduction and Aims:** Interventions, both endovascular and surgical, are used to manage hemodialysis (HD) native AV fistulae. We postulated that dialysis facilities that routinely prescribe lower blood flow rates would experience lower FPR. Methods: DOPPS data were used from 3 study phases (2: 2002-04, 3:2005-08, and 4: 2009-11) to determine FPR. Rates were calculated as total numbers of fistula procedures reported during follow-up divided by fistula follow-up time during the study. Procedures included angioplasty, stent, surgical revision, banding, thrombectomy, thrombolysis, and other. Facility median BFR is based on initial study. Procedures included angioplasty, stent, surgical revision, banding, thrombectomy, thrombolysis, and other. Facility median BFR is based on initial study. Results: FPRs have increased over time in each DOPPS region, but facilities above the regional median BFR tended to have higher unadjusted (and adjusted, p < 0.01 - not shown) rates than those below the median. Conclusions: The purpose of this study is to develop a procedure for buttonhole puncture in which a scab is not formed at the buttonhole entry site on the skin, but rather an epidermal layer is formed on the same site. If this is achieved, the time needed for buttonhole puncture will be shortened and the opportunities for buttonhole tunnel tract infection might be reduced.

**SP478**

**NEW PROCEDURE THAT DOES NOT LEAD TO SCAB FORMATION AT BUTTONHOLE ENTRY SITE**

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**Introduction and Aims:** The purpose of this study is to develop a procedure for buttonhole puncture in which a scab is not formed at the buttonhole entry site on the skin, but rather an epidermal layer is formed on the same site. If this is achieved, the time needed for buttonhole puncture will be shortened and the opportunities for buttonhole tunnel tract infection might be reduced. Methods: In this method, the blunt needle is removed after hemodialysis is completed, bleeding is completely stopped, and the buttonhole entry site is disinfected with a diluted povidone iodine solution (0.1% povidone iodine solution prepared by diluting the 10% povidone iodine solution that is normally used to sterilize the skin.) This is based on a report that while the cytotoxic effect is minimal with the diluted povidone iodine solution, the bactericidal effect is paradoxically much stronger than with the pre-diluted solution. An anti-microbial dressing (Perme-Roll®) is then applied to the buttonhole entry site. This is a modified moist wound healing method. The difference between this modified method and normal moist wound healing methods is that with usual methods the wound is not sterilized at all before being covered with an anti-microbial dressing. With our method, in contrast, the buttonhole entry site is sterilized with the diluted povidone iodine solution, which has much a stronger bactericidal effect than the usual solution, before the anti-microbial dressing is applied. Prior to the next hemodialysis, the anti-microbial dressing is removed and the buttonhole entry site is disinfected with the diluted povidone iodine solution. Thereafter, a thin membrane that has naturally formed over the buttonhole entry site is pierced by an intermediately blunt needle, and the blunt needle is inserted into the tunnel tract. We have treated buttonhole entry sites with this method a total of 1020 times in 26 patients. Results: In 1011 of the 1020 treatments (99%), no scab formed at the buttonhole entry site. Instead, a thin membrane naturally formed. A histological test indicated that this was a layer of epidermal keratinocytes with inflammatory cell infiltration. In the rest of the treatments, a very small scab was created at the site. However, these scabs were easily removed with a plastic spatula. Conclusions: This method will shorten the time needed for buttonhole puncturing, since removal of a scab is no longer necessary. Moreover, this method might lead to decreased infection of the buttonhole tunnel tract, since the buttonhole entry site is covered at all times by some sort of protective barrier against bacteria (i.e., the anti-microbial dressing or the regenerated epidermal layer).

**SP479**

**FAR INFRARED THERAPY IMPROVES ARTERIOVENOUS FISTULA MATURATION**

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**Introduction and Aims:** Malfunction of arteriovenous fistula (AVF) is an important cause of morbidity and hospitalization in hemodialysis (HD) patients. The aim of this study is to evaluate the effect of far infrared (FIR) therapy on the maturation and patency of newly created AVF in patients with chronic kidney disease (CKD) stage 4 or 5.

**Methods:** Study design: Randomized controlled study. Setting and participants: Patients with eGFR between 5 and 20 ml/min/1.73m². Intervention: 40 minutes of FIR therapy three times weekly for a year. Outcomes: The primary outcome is the rate of AVF malfunction, which was defined as either (1) thrombosis without thrill for AVF not undergoing HD or (2) receiving any type of interventional procedure due to a lower KT/V (<1.2) for patients undergoing HD at one year. The secondary outcomes include (1) the cumulative primary assisted AVF patency with the definition as the time from the creation of AVF to the first episode of AVF malfunction, (2) physiologic maturation of AVF by the definition of Qa of AVF≥500 ml/min and diameter of AVF≥4mm at 3 months and (3) clinical maturation of AVF suitable for HD at 1 year.

**Measures:** Access blood flow (Qa) of AVF was measured by Doppler ultrasonography at 2 days, 1, 2, 3 and 12 months.
Abstracts of extracellular matrix deposition (p=0.003) and alpha-smooth muscle actin (α-SMA) cell number within the adventitia (p=0.02); most of these cells were myofibroblast (α-SMA+/Vimentin+). Phosphorylated PDGFβ receptor (p-PDGFRβ) was significantly increased within the adventitia of stenotic compared to native AVF (p=0.004), along with a marked increase in the phosphorylation of two key kinases in PDGFRβ signalling, Akt and ERK (p<0.0001 for both kinases). The myofibroblasts were the main cell type associated with the activation of p-PDGFRβ. At the same time, we observed a significant adventitial vessels rarefaction in stenotic AVF, as demonstrated by a reduced CD34 expression. The degree of adventitial fibrosis was directly correlated with the extent of adventitial α-SMA (R²=0.56; p=0.005) and inversely associated with adventitial CD34 expression (R²=0.56, p=0.01). In addition, we observed an increase in CD34+ α-SMA+ cells within the adventitia of failed AVF.

Conclusions: This study indicates that AVF failure is associated with an increased adventitial fibrosis, myofibroblast activation and capillary rarefaction, potentially associated with endothelial-to-mesenchymal transition. In this scenario, our data suggest that PDGFR signalling may play a pathogenic role and represent a potential therapeutic target.

**SP481**

DYSFUNCTIONAL, NON MATURING OR THROMBosed AVF: THE ROLE OF PERCUTANEOUS TRANSLUMINAL ANGIOPLASTY IN A LOCAL EXPERIENCE

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Introduction and Aims: Vascular access complications are one of the main causes associated with an increase in morbidity and mortality in patients on hemodialysis. The arteriovenous fistula (AVF) is considered the vascular access of choice and stenoses are the major cause of its dysfunction. Percutaneous transluminal angioplasty (PTA) has been widely recognized as a suitable technique for correcting such lesions. Our study retrospectively evaluates the clinical course and treatment outcome of performing PTA for dysfunctional, non maturing or thrombosed AVF in our experience.

Methods: Between Jan. 2008 and Dec. 2012, 101 PTA procedures were performed on 73 patients (49 men, 67%; median age 67 years, range: 27-89) with dysfunctional (63%), non maturing (7%) or thrombosed (30%) AVF. 63 wrist radiofemoral [25 with latero-terminal (L-T), 38 with termino-terminal (T-T) anastomosis] and 10 elbow fistulae with median age of 12 months (range 1 month-13 years) were treated. The Kaplan-Meier method was used to calculate the primary and secondary cumulative patency rates.

Results: In radiofemoral L-T AVF, stenoses were located in the iuxta-anastomotic segment in 11 patients (44%), in anastomotic area in 5 (20%), in the venous outflow in 5 (20%), in central vein in 1 (4%), in multiple areas in 3 (12%); in radiofemoral T-T AVF the distribution was similar (iuxta-anastomotic 47%, anastomotic 21%, outflow vein 16%, central vein 5%, multiple areas 11%). In elbow fistulae the stenoses occurred in the outflow vein in 7 patients (70%) and around the anastomotic region in 3 patients (30%). Angiographic and clinical success was 88%; 17 patients required 28 repeat PTA for recurrent stenosis/thrombosis. 8 patients had small extravasation that required no further treatment, 1 patient had microembolism in second interdigital artery during declotting of radiofemoral L-T thrombosed fistula, treated with urokinase infusion. Excluding initial failure, mean primary and secondary patency for AVF were 34.3 months (95% CI 26.4-42.1) and 41.1 months (95% CI 37.9-52.4); the primary and secondary cumulative patency rates at 12 months were 59% and 84% respectively.

Conclusions: PTA can effectively salvage dysfunctional, non maturing or thrombosed AVF. Since repeat angioplasty is often necessary to maintain function, careful surveillance is necessary. The concerted efforts of nephrologists and other specialists (interventional cardiologists/radiologists and surgeons) are the key to maintaining and prolonging vascular access survival.

**SP482**

ASYMMETRICAL DIMETHYLARGININE PREDICTS PROGRESSIVE STENOTIC DYSFUNCTION OF VASCULAR ACCESS DEMAND ANGIOPLASTY

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Introduction and Aims: Hemodialysis vascular access (VA) dysfunction is a major cause of morbidity among hemodialysis (HD) patients. Primary venous outflow occlusion and restenosis after percutaneous transluminal angioplasty (PTA) are two obstacles for the long term use of dialysis vascular access. Increased levels of circulating...
oxidative stress markers correlate with vascular endothelial dysfunction and development of cardiovascular events in uremia patients. It is not known whether these oxidative stress markers can be used as predicators for the progressive VA stenosis dysfunction and PTA.

**Methods:** Circulating levels of oxidative stress factors: hs-CRP (high-sensitivity c-reactive protein), MMP (matrix metalloproteinase)-2, MMP-9, Homocysteine, ADMA (asymmetrical dimethylarginine) and NO (nitrate oxides) were measured by immunosorbent assay (ELISA) in 159 HD patients (83 male, 76 female, mean age: 65 ± 12). All patients had been stabilized on renal replacement therapy for >6 months and were free of active infection. Patients were followed up clinically for up to 12 months to estimate the amount of the vascular access dysfunction (according to the clinical practice guidelines of National Kidney Foundation, the USA – Kidney Disease Outcome Quality Initiative 2006 for the VA ) need PTA intervention.

**Results:** During the 12 months observation, 24 patients (15.1%) need to undergo the PTA owing to dysfunction of access. Also during the follow-up period, restenosis occurred 12 patients (50% of 24 patients). In the comparison dysfunction with non-dysfunction vascular accesses, up to 27.3% of the patients with high levels of ADMA (>0.6207 μM, N=66) had been necessarily received PTA compared with 4.5% of those with low levels (≤0.6207 μM ; N=89; P<0.001). In multivariate analysis, plasma ADMA independently nearly seven times the risk of primary stenotic dysfunction of hemodialysis vascular access, (hazard ratio 7.13; 95% confidence interval 2.41 to 21.07; P<0.001). Kaplan-Meier analyses demonstrating proportion of patients without dysfunction VA. Patients are divided with a cutoff value of baseline ADMA of 0.6207 μmol/mL.

**Conclusions:** The results suggest a role for oxidative stress markers ADMA in the development of symptomatic dysfunction of VA and call for preventive strategies that target ADMA and endothelial dysfunction to decrease the risk for VA progressive stenosis.

**DOES BLOOD FLOW AFFECT VASCULAR ACCESS SURVIVAL?**

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**Introduction and Aims:** Adequacy of 4-hour, thrice weekly hemodialysis is achieved via good extracorporeal blood flow (Qb), especially in high-volume post-dilution haemodiafiltration where high Qb is essential for high substitution volumes. The aim of this study is to investigate if high Qb has an impact on arteriovenous fistula (AVF) or graft function in the long term.

**Methods:** Data were prospectively collected using the same database (EuClID) in 19 Portuguese dialysis units of the same network. Vascular access flows (Qa) were evaluated between 1 April, 2011 and 30 June, 2011 using the Fresenius Medical Care Blood Temperature Monitor (BTM) at 300 ml/min Qb. Cox Regression Hazard analysis was performed stratifying by vascular access type (fistula or graft) and by quartile of Qa, with access failure being defined as an event requiring surgical intervention. Censoring was for loss of follow-up or at study end (Jan 9, 2013).

**Results:** 1,043 patients (69.3±13.5 years old, 39.1% females, 32.8% diabetics), 811 with AVF and 232 with grafts were studied. The main characteristics by vascular access type are shown below: During 18-21 months of follow-up, 337 patients lost vascular access function (25.3% with AVF, 57.3% with graft). Stratifying Qa by quartile, Qa<701 mL/min and <1600 mL/min for AVF and grafts, respectively, was associated with significantly higher HR (p<0.001). After stratification by quartile of Qa and analyzing AVF and graft separately, recirculation was significantly associated with access survival only for AVF (HR: 1.942, 95%ci: 1.026-3.058; ref: per % point). A 2-fold higher HR for AVF failure was detected for Qb<312 mL/min and for Qb>414 mL/min versus Qb in the 350-357 mL/min range. For grafts, different Qb was not associated with a significant HR.

**Conclusions:** Lower Qb (<312 mL/min) is likely to indicate vascular access problems, as shown by the lower mean Qq (961±508 mL/min). However, the risk associated with Qb<414 mL/min (10% of patients) needs further investigation. In conclusion, this study showed that Qb up to 414 mL/min, which is still optimal for efficient post-dilution online HDF, is not associated with increased risk of AVF failure. For grafts, the Qb range considered (IQR: 342-401 mL/min) was not associated with an increased risk of vascular access failure.

**RANDOMIZED TRIAL COMPARING NEW CHITOSAN-BASED BANDAGE WITH KALTOSTAT HEMOSTATIC DRESSING TO CONTROL BLEEDING FROM HEMODIALYSIS PUNCTURE SITE**

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**Introduction and Aims:** Many patients undergoing hemodialysis(HD) have thin and weak skin over the vascular access sites due to repeatedly punctures. Furthermore, patients not only have coagulopathies associated with chronic renal failure, but also use heparin and oral anticoagulants. In case of prolonged bleeding at the vascular access site after HD, a nurse must compress the bleeding site longer than usual and might cause thrombosis. To investigate whether application of a chitosan-based bandage (HemCon Strip, HemCon Medical Technologies, Portland, USA) to stop bleeding from a HD puncture site shortens the time to hemostasis compared to a standard topical hemostatic alginate dressing (KALTOSTAT® Calcium Sodium Alginate Dressing), we conducted a prospective randomized trial on 30 patients undergoing HD. Patients were randomized session by session to receive chitosan-based bandage (CBB) or alginate dressing (AD) as a hemostatic agent.

**Methods:** Of 450 patients with an arteriovenous fistula in the upper extremity, 30 patients (18 males and 12 females) continued to bleed after 30 minutes of compression of the puncture site, and satisfied the eligibility criteria of the study.
Nadia Sarween1, Anna Price1, Sarah Powers1, Clive Allen1, Madelaine Holland2, Richard Corbett1, Nicolo Demicheli2, Francesco Iori2, Lorenza Grechy2, Ravi Khiroya2, David Ellis1, Jeremy Crane1, Mohamad Hamady3

Results: At the beginning of HD, platelet count was 16500 ± 4600/L and activated clotting time during HD was 138.0 ± 17.0 min. Before the experiment, average time to achieve hemostasis was 15-60 min. By using CCB, hemostasis was achieved within 2 min in 37 of 38 sessions, and an additional 1 minute of compression was required in one session. By using AD, hemostasis was achieved in only 31 of 51 sessions. A significant difference was detected between the two methods (Pearson’s chi-square test p<0.01). No adverse effects such as contact dermatitis and infection were observed in either method.

Conclusions: Our study suggests that the chitosan-based bandage is a safe and more effective hemostatic agent than hemostatic alginate dressing to stop severe, prolonged post-HD puncture site bleeding.

Maria Teresa Parisotto1, Volker Schoder1, Peter Kaufmann1, Cristina Miriunis1, Aileen Grassmann1 and Daniele Marcelli1

Introduction and Aims: There is a close link between the availability of a well-functioning vascular access and patient survival on haemodialysis. Consequently, every effort should be made to maintain the functionality of the vascular access for long-term use. However, practices of access cannulation vary from clinic to clinic, mainly for historical reasons. The aim of this study is to investigate the impact of cannulation technique on the survival of the arteriovenous fistula (AVF) and grafts (AVG).

Methods: In April 2009, a cross sectional survey was conducted in 171 dialysis units located in Europe, Middle East and Africa to collect details on vascular access cannulation practices. The results have already been published (Gauly et al, J Vasc Access 2011; 12(4): 358-64). On the basis of this survey, a cohort of patients was selected for follow-up, inclusion being dependent on the availability of corresponding access survival/intervention data in the clinical database. Access survival was analyzed using the Cox regression model (adjusted for within country effects) defining as events the need for first surgical access survival intervention. Patients were censored for transplantation, death, loss of follow-up, or end of the study period (March 31, 2012).

Results were adjusted for age, gender and diabetes mellitus.
Conclusions: Our results showed that the ESRD patients undergoing online-hemodiafiltration. AVF was used by 252 patients (78%), whereas 70 patients using the Kidney Disease Quality of Life-Short Form (KDQOL-SF). According to the type and location of vascular access used. There is, however, a lack of information about the impact of the type of vascular access and about AVF localization on patient’s perception of health-related quality of life (HRQoL). In this cross-sectional study, we aimed to evaluate the patient-reported HRQoL, according to the type and location of vascular access used.

Methods: In this transversal study we enrolled 322 ESRD patients under online-hemodiafiltration. AVF was used by 252 patients (78%), whereas 70 patients (22.8%) had a central venous catheter (CVC). Besides AVF location, data about comorbidities, hemoglobin concentration, dialysis adequacy and inflammatory markers, we performed a patient’s reported health status and quality of life score, by using the Kidney Disease Quality of Life-Short Form (KDQOL-SF).

Results: No differences were found between the two groups of ESRD patients (AVF vs CVC) for hemoglobin concentration, C-reactive protein, dialysis adequacy and in the prevalence of diabetes. However, patients with AVF showed a significant improvement, not only in physical but also mental aspects of HRQoL, namely in energy/fatigue (p = 0.046), quality of social interactions (p = 0.044), physical functioning (p = 0.001), emotional well-being (p = 0.009), role-emotional (p = 0.008) and energy/fatigue (p = 0.014). When comparing patient’s reported health status and quality of life scores by AVF location, we found a significant increase in general health perception in ESRD patients using AVF in the right upper-arm, when compared with those using AVF in the left upper-arm.

Conclusions: Our results showed that the ESRD patients under online-hemodiafiltration using AVF as vascular access had higher HRQoL in several domains when compared to patients with CVC. Additionally, we also found that dialysis patients using AVF in right upper-arm presented lower HRQoL perception in general health.

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**SP498**

**THE DIABETES AFFECTS THE PATIENTS SURVIVAL BUT NOT THE VASCULAR ACCESS PATENCY**

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Introduction and Aims: The prevalence of diabetes mellitus (DM) is very high worldwide. Diabetic nephropathy is a major vascular complication of DM. In many countries diabetic nephropathy has become the most frequent cause of prevalent ESRD patients (pts) undergoing hemodialysis. It is believed that in diabetics the creation of native vascular access (NVA) might be difficult but has proven to offer lower infection rates, fewer procedures and lower mortality risk compared with catheters or grafts.

Methods: We evaluated NVA creation in 232 pts during the period January 2003 to December 2008 with follow-up to 31/12/2012. Pts were divided into 2 groups: 60 diabetic pts (Dpts) (Dpts: 39 M; 21 F; mean age: 66 ± 16 years) and 172 non-diabetic pts (NDpts) (NDpts: 112 M; 60 F; mean age 62 ± 19 years). We compared the type of NVA, NVA survival and pts survival in these groups. NVA survival was calculated using the Kaplan-Meyer analysis and statistical significance using the Chi square test.

Results: Age was significantly higher in Dpts (66 years vs 62; p<0.005). At the end of the follow up 73% of Dpts and 50% of NDpts died (p=0.005); the median survival is 29 and 63 months for Dpts and NDpts, respectively (p<0.0001). No differences in the transplant eligibility were observed. In Dpts we performed 69 NVA: 35 distal, 25 middle arm, 9 upper arm. In NDpts we performed 199 NVA: 112 distal, 67 middle arm, 20 upper arm. No statistical difference between groups in type of NVA. No statistical difference between groups in NVA survival.

Conclusions: Our study revealed that the type of vascular access and location of vascular access is associated with a higher survival benefit than in non diabetic pts, confirming that diabetes is the main determinant of death, not of vascular access outcome.
Methods: Echocardiograms were obtained from 72 patients (40 women and 32 men, mean age: 56.3±30 years) who were then followed for 12 months. AVF calcification score was assessed by means of computed tomographic analysis described previously. Study endpoint was a thrombotic dysfunction of AVF that has been diagnosed angiographically and required percutaneous intervention. Cox multivariate analysis was used to assess the independent prognostic value of echocardiography.

Results: Mean left atrial ejection fraction (LAEF), indexed left atrial volume (LA Volume), conduit and reservoir values were 42.4±11.6%, 42.7±8.6 ml/m², 46±10.4% and 18.1±7.9 cm³ respectively. AVF calcification score showed no correlation with left atrial conduit and reservoir values, except LA Volume (r=0.344, p=0.019) and LAEF (r=-0.305, p=0.05). Left atrial conduit and reservoir values did show no significant difference between patients with AVF dysfunction and patients without AVF. However, patients with AVF dysfunction during 1-year follow-up had both lower LAEF and LA Volume compared to patients with AVF and LA Volume values compared to patients with patent AVFs (46.0±10.5 vs 40.6±12.8 ml/m², r=0.344, p=0.019 and LAEF values below the median value, had decreased AVF survival compared to patients with LAEF greater than median LAEF value of 45.0% (log-rank, P=0.028). In multivariate analysis, LAEF was one of the independent predictors of AVF thrombosis (B=-2.07, P=0.046).

Conclusions: Among the echocardiographic left atrial parameters, LAEF was an independent predictor of AVF dysfunction in maintenance hemodialysis patients in the present work, suggesting novel association among cardiac and vascular diseases.

Introduction and Aims: Decrease in vascular access blood flow (Qa) is a common sign of stenosis, albeit attenuation up to 20–30% can be in the physiological range. However, reduction in blood pressure during hemodialysis (HD) can reduce Qa and differences in needle placement and hemodynamics may cause larger variability between the HD sessions than within the sessions. The aim of our study is to clarify: 1. Is there a clinically relevant change in Qa during HD? 2. Is there any correlation between Qa and blood pressure during treatment? 3. Comparison of the variability of Qa within and between the sessions.

Methods: We investigated 131 HD patients bearing native arteriovenous fistulas (age 60±17 years, 58% male, 40% diabetic, 79% distal fistula, 16% proximal, 6% both due to change during study). 3066 Qa measurements were performed in 1022 HD sessions at the beginning (Qa1), at half time (Qa2), and at the end of treatment (Qa3) with the Fresenius blood temperature monitor. Blood pressure (MAP) was measured simultaneously and Qa corrected for 100 mmHg MAP (Qac) was calculated. Correlation between Qa and MAP, and the variability of Qa calculated by coefficient of variation (CV) within sessions and between sessions was evaluated. 172 investigations of vascular access stenosis using angiography, ultrasonography or both confirmed stenosis in 41% of cases, corresponding to 36% of patients. Steatic and non-stenotic cases and access by the fistula position were also evaluated separately.

Results: Qa1: 111±5.6 ml/min, Qa2: 108±5.79 ml/min, Qa3: 108±5.58 ml/min, Qa2–Qa1 (delta Qa2): -2±3.09 ml/min (p=0.0025), Qa3–Qa1 (delta Qa3): -25±3.14 ml/min (p=0.0113). Qa3–Qa1c (delta Qa3c): 31.4±400 ml/min (p=0.0145). Change in MAP at the end of treatment was -51±12 mmHg (p=0.0001). In cases without stenosis, neither Qa nor Qac changed significantly. In distal fistulas we observed a slight but significant decrease in Qa (delta Qa3c: -31±32 ml/min, p=0.005); Qa did not change significantly. In proximal fistulas there was no significant change in Qa, but Qac increased significantly (delta Qa3c=8±37 ml/min, p=0.01). MAP and Qa changes did not correlate significantly. Within-session pooled CV of Qa was 20.6%, while between-session CV was 31.3% (p=0.001). We suggest correction of Qa for MAP only for distal fistulas, which balances the significant decrease of Qa in the late period of HD. 3. Within-session CV of Qa is significantly lower than between-session CV, but both are within the physiological range.

Introduction and Aims: Strategies to prevent vascular access (VA) thrombosis include mapping, early stenosis diagnosis and preventive treatment. USG (US) by nephrologist may substantially change practice to intervene in all steps. The aim is present the results after creation and consolidation of a Vascular Access Unit based on the US use by nephrologist in a multidisciplinary approach.


Results: 1. VA: n=560 2. Age: 64.8±15.1, 53% M, 47% F, Charlson Index = 7.8 ± 3.1 3. Assisted primary patency: 1, 2 and 3 years: 74, 70 and 67%. Higher patency in humeral AV and males (p<0.05). No differences between resident and staff 4. Thrombosis: 0.01-0.05/VA/year 5. Initial set HD with VA >80% and HD reconstructions without catheter >90% 6. Maturation failure: 20% (12% immediate) 7. Mapping: need angiogram <5%. After mapping, sex and gender differences corrected.

Conclusions: 1. US by nephrologist make the multidisciplinary approach more efficient, so provide the team of an integrated decision in mapping, diagnosis, treatment and prioritization. This may low VA morbidity in high comorbidity patients. 2. It should be part of the armamentarium in nephrology and include their learning in the specialty training.
urea RC values (figure 1). AL pCO2<40mmHg was shown to have the best sensitivity and AL pH<7.25 the best specificity. RC index, i.e. the AL pCO2/pH ratio, was found to have superior test characteristics compared to pH and pCO2 (sensitivity 95% and specificity 88% for values >5.5) making it a powerful diagnostic as well as screening tool.

Conclusions: We propose the regular AL blood gas measurement as a novel method of AVF function surveillance and RC diagnosis. AL pH<7.25, pCO2<40mmHg and RC index >5.5, exerted by rather high pO2 and low K+ by the end of dialysis session, was probably earlier as well, signify an important RC (>20%) and warrant further investigation of AVF patency.

Results: The catheter-related infection rate was 0.40 episode/1000 CVC-days in treatment and 0.9 episode/1000 days in control (p=ns), suggesting that the DCC may reduce the risk of infection, though our pilot study was underpowered to detect significant differences. Table 1

Conclusions: The use of the CVC with the variant double-cuff, although the short observation period and the small size of the sample, showed a lower incidence of infections. In our opinion these preliminary results are satisfactory and therefore encourage us to extensively use the new device.

**A NEW MODEL OF HAEMODIALYSIS LONG-TERM CATHETER WITH DOUBLE CUFF**

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**Introduction and Aims:** The vascular access is the lifeline of chronic haemodialysis patients; one of the most widely used vascular access for maintenance haemodialysis is the central venous catheter (CVC). Haemodialysis via a CVC is associated with a significantly lower catheter survival due to bacteraemia and/or tunnel/exit site infection, increased patient hospitalisation and increased incidence of death. A CVC can be non-tunneled (for a short-term haemodialysis use) or tunneled (also known as cuffed, permanent catheter, for a long-term haemodialysis). Tunneled cuffed catheters are associated with a much lower risk of bacterial colonization, exit site infection and bacteraemia compared with non-tunneled and non-cuffed device. The protective effect of tunnelling and cuffing is postulated to be due to a combination of prevention of bacterial migration along the sinus tract and provision of more effective catheter anchorage and immobilization. All long-term CVC currently used have a single-cuff in the subcutaneous tract. We hypothesized that infection complication could be reduced by the use of a double-cuffed catheter (DCC), with one cuff adjacent at the exit-site aiming to provide a more effective antimicrobial barrier and the other cuff adjacent to the blood vessel aiming to provide a more effective catheter anchorage.

**Methods:** A pilot study was performed at the Haemodialysis Unit of Santa Chiara Hospital in Trento between July 2009 and October 2012. A DCC was inserted in 11 patients (treatment), while a SCC (single cuff catheter) was placed in 38 (control) patients. Patients in the two groups were similar in age and average comorbidity. All CVC were always positioned by the same operator, no used antimicrobial catheter

<table>
<thead>
<tr>
<th>SP494 Table 1.</th>
<th>Treatment CVC double-cuff</th>
<th>Control CVC single-cuff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>72.4 ±18.4</td>
<td>70.9 ±11.9</td>
</tr>
<tr>
<td>n° patients</td>
<td>11</td>
<td>38</td>
</tr>
<tr>
<td>Female sex</td>
<td>8 (72.7%)</td>
<td>16 (42.1%)</td>
</tr>
<tr>
<td>CVC days</td>
<td>5064</td>
<td>17905</td>
</tr>
<tr>
<td>Charlson Comorbidity Index</td>
<td>6.0</td>
<td>6.1</td>
</tr>
<tr>
<td>Catheter Related Infection</td>
<td>0.2 (0.40/1000days)</td>
<td>0.17 (0.90/1000days)</td>
</tr>
<tr>
<td>Exit-site and Tunnel Infection</td>
<td>0.2 (0.40/1000days)</td>
<td>0.11 (0.61/1000days)</td>
</tr>
<tr>
<td>Bacteraemia</td>
<td>0</td>
<td>6 (0.33/1000days)</td>
</tr>
</tbody>
</table>

**Introduction and Aims:** After the earthquake that struck northern of Italy with the consequence of the stock break of supply of the connection of the transonic, we found to accomplish this study. If the use of connection is necessary when measuring vascular accesses with the transonic.

**Methods:** In 62 hemodialysis patients we measure during the same dialysis session fistula blood flow with the HD02 (Transonic® System Inc.,Ithaca, NY) device with specific connection (Transonic Flow QC® set) named “Standard” and without specific connection named “without” with different blood line set only (GAMBRO BLOOD TUBING SYSTEM BL105, FRESENIUS LIFEINE AV-SET BR DT R 4068, FRESENIUS LIFEINE AV-SET ONLINEPLUS BVM 5008 R) all measure was done in duplicate mean value was obtained and in case of discrepancy more than 30% between the two value a third was done. Result were express as mean +/- SEM. Statistical analysis include Normality test (Shapiro–Wilk), Comparison test for non parametric measure (Wilcoxon-Spearman) and Bland and Altman representation of adequacy of two measurement methods.

**Results:** A total of 248 measurement series were performed. Mean fistula blood flow was 869.8 ml/min +/-18.4 [135-3145] and 889.9 ml/min +/-18.7 [135-3565] By Standard and Without respectively . As expected correlation appears good: r : 0.96 (p<0.0001). No significant difference were identified by Wilcoxon test (p=0.0828). Bland and Altman comparison bias between the two methods of measurement "Standard" and "without" was only 20ml/min witch appears not clinically relevant. SD of bias was 131 interval 1.33 to 5.08.

**Conclusions:** These results suggest a role for the DCC in the AVF and call for preventive strategies that target MDA and/or lipids peroxidation to decrease the risk for AVF thrombosis.

**Introduction and Aims:** Dialysis access procedures and complications represent a major cause of morbidity, hospitalization, and cost for chronic dialysis patients. It is not well known whether enhanced oxidative stress contributes to the dysfunction of arteriovenous fistulas (AVFs) in these patients. The aim of our study was to determine the existence of a relationship between symptomatic AVF thrombosis (AVFT) and oxidative stress level analyzed by total antioxidative capacity, malondyaldehyde (MDA) as a lipid peroxidation biomarker and reactive carbonyl groups (RCG) as a marker of oxidative modification of proteins.

**Methods:** One hundred and twenty six patients aged 24-78 years with end-stage renal disease (ESRD) were evaluated prospectively for a period of 36 months. In addition to standard biochemistry, demographic and clinical data were accessed from patients medical records. All fistulas were evaluated clinically as patent at the start of this study. Patients were followed-up for any evidence of AVFT within 36 months. Finally, all factors (diabetes, hypertension, ultrafiltration, age, gender, hypotension during dialysis, fistula site, epoetin usage, lipid paramethers and oxidative stress level) were analyzed in a stepwise regression analysis.

**Results:** The incidence of AVFT was 18% (25 of 142). Multivariable analysis found that older age (>65 years, odds ratio [OR] 3.2, P < 0.001), history of diabetes (OR 2.14, P = 0.06), erythropoietin beta usage (OR 3.7, P < 0.001) and LDL cholesterol (OR 16, P = 0.002) were independently associated with AVFT. In addition, up to 67% of the patients with higher levels of MDA (>9.0μmol/L) had AVFT compared with 28% of those with lower levels (<9.0 μmol/L, P < 0.001). In multivariate analysis, plasma MDA independently nearly tripled the risk for AVFT (hazard ratio 2.69, 95% confidence interval 1.33 to 5.08).

**Conclusions:** We propose the regular AL blood gas measurement as a novel method of AVF function surveillance and RC diagnosis. AL blood pH<7.25, pCO2>40mmHg and RC index >5.5, exerted by rather high pO2 and low K+ by the end of dialysis session, was approximated by projection and do not necessarily corresponds to the actual values that need to verified by future studies.

**DOES SPECIFIC TRANSONIC FLOW QC®SET USEFUL FOR MEASUREMENT OF FISTULA BLOOD FLOW?**

Sissoko Aicha Henriette1, Alenabi Farideh2, Bibaci Daniela3, Takia Zafer2 and Chantrel François3
3Dialyse AUral Mulhouse France, 2Nephrologie Hopital Pasteur Colmar France, 3Nephrologie Centre Hospitalier Mulhouse France

**Introduction and Aims:** Fistula相关ated Infection rate was only 20ml/min witch appears not clinically relevant. SD of bias was 131 interval 1.33 to 5.08.

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Jose Ibeas1, Joaquim Vallespín2, Jose Fortuño3, Jana Merino2, Xavier Vinuesa1, Jordi Branera3, Alexis Mateos3, Valle Jimeno3, Maria Bolos1.

Conclusions: To our knowledge, this is the first study showing no significant difference of measurement fistula blood flow between Transonic® Blood line set only and Blood line set with specific connecting. Further large studies are necessary to answer our question. However for high blood flow values measurement are too variable to conclude the inutility of this connection. 1-2010 Transonic Systems,Inc. Hemodialysis Flow Calibration Check.

Results: 1. Procedures, n=139. PTA=63, Surgery=76 2. Age: 67.2±14.7 years. Gender 67% M and 33% F. No differences in age and sex 3. Time in HD: 42±30 months. No differences between groups 4. Radial: 68%, Humeral: 32%, significant dominance in radial territory for surgery (p=0.005) 5. Patency at 1, 2, 3 and 4 years. PTA: 72, 66, 61 and 61%, Surgery: 80, 77, 77% (Log Rank: 0.289) 6. Complications. PTA 3%: 2 minor vein ruptures (resolved with compression and stent).

Conclusions: 1. Angioplasty is a safe procedure that can prolong the vascular access life 2. Surgery has improved assisted patency, although not significantly 3. It is needed a study with enough sample to establish whether really there is difference and if it is cost effective.

SP498 SURVIVAL OF PTFE GRAFTS VS. TUNNELED CUFFED CATHETERS (TCCs) FOR HEMODIALYSIS

Gabriele Donati1, Anna Scrivo1, Giuseppe Cianciolo1, Gaetano La Manna1, Laura Panicali1, Paola Ruco2, Antonio Marchetti2, Emanuela Giampalma3, Maria Galaverni3, Rita Golfieri3 and Sergio Stefoni1

Introduction and Aims: Vascular access related complications are still one of the most important causes of morbidity in hemodialysis patients. The aim of this study is to compare the survival of PTFE grafts vs TCCs by means of an observational study during a 1-year follow-up period.

Methods: 92 chronic hemodialysis patients were enrolled: 28 (M/F=16/12) with a PTFE graft as vascular access for hemodialysis vs. 64 (M/F=33/31) with a TCC. All the patients underwent antithrombotic or anticoagulant prophylaxis. Mean age 65.2±13.2 (grafts) vs. 73.7±10.9 years (TCC, p<0.01). The vascular access survival was assessed as the difference between the vascular access placement and its removal or substitution.

Results: The number of vascular accesses before graft implant was 1.4±1.0 vs. 2.1±1.3 vascular accesses before the TCC placement (p<0.05). The two groups did not differ as regards gender, LDL, smoking, diabetes, hypertension, ischemic cardiac injury, cerebral and peripheral arteriosclerosis, Charlson score. Patients with TCC were significantly more affected by atrial fibrillation in comparison with patients with grafts (28.1% vs. 7.1%, p=0.05). During a 12 month follow up, 19 cases of PTFE graft loss were observed (67.8%) vs. 10 cases of TCC loss (15.6%, p<0.001). 64.2% of the PTFE grafts was affected by thrombosis, 3.6% by infections; 12.5% of TCCs was affected by infections, 3.1% by thrombosis. The comparison of the survival of the two groups by means of the Kaplan Meier analysis showed a significant difference favoring TCC use.

SP497 JUXTA-ANASTOMOTIC STENOSIS OF NATIVE VASCULAR ACCESS: PROSPECTIVE STUDY OF SURGICAL TREATMENT VERSUS ANGIOPLASTY

Jose Ibeas1, Joaquim Vallespín2, Jose Fortuño2, Jana Merino2, Xavier Vinuesa1, Jordi Branera3, Alexis Mateos3, Valle Jimeno3, Maria Bolos1, Angel Rodríguez-Jornet1, Antonio Gimenez2 and Manuel Garcia1

1Nephrology University Hospital Parc Taulí Sabadell Barcelona Spain, 2Vascular Surgery University Hospital Parc Taulí Sabadell Barcelona Spain, 3Interventional Radiology University Hospital Parc Taulí Sabadell Barcelona Spain

Introduction and Aims: Clinical guidelines suggest surgery as treatment with better outcomes in juxta-anastomotic stenosis in native vascular access, although evidence level is not high. Furthermore, recent studies show angioplasty (PTA) results with high permeability in assisted patency. Few studies comparing both techniques, limited by small sample size and methodologically. The objective of this study is comparing both techniques with a representative sample in a prospective study in a single center.


Results: 1. Procedures, n=139. PTA=63, Surgery=76 2. Age: 67.2±14.7 years. Gender 67% M and 33% F. No differences in age and sex 3. Time in HD: 42±30 months. No differences between groups 4. Radial: 68%, Humeral: 32%, significant dominance in radial territory for surgery (p=0.005) 5. Patency at 1, 2, 3 and 4 years. PTA: 72, 66, 61 and 61%, Surgery: 80, 77, 77% (Log Rank: 0.289) 6. Complications. PTA 3%: 2 minor vein ruptures (resolved with compression and stent).

Conclusions: 2. Surgery has improved assisted patency, although not significantly 3. It is needed a study with enough sample to establish whether really there is difference and if it is cost effective.

SP496
Introduction and Aims: Creation of vascular access for hemodialysis is of utmost importance for effective treatment and remains a challenging task. Modern dialysis population is changing: the number of aged and/or diabetic patients usually burdened with concomitant pathologies is increasing. For a significant number of patients the creation of arteriovenous fistula is either impossible or takes extended time and, as a result, the implantation of central veins catheter (CVC) is required. Some patients undergo multiple implantations of CVC, which is a major risk factor of central venous stenosis development. Objective: To evaluate the immediate outcomes and safety of CVC implantation combined with the percutaneous venous angioplasty in patients with central vein stenosis.

Methods: 119 implantations of tunneled CVC for hemodialysis performed in 2011-2012 were analyzed. All the implantations were performed in a specialized radiological surgery room. All the patients had stage 5 chronic kidney disease (CKD KDIGO) and required maintenance hemodialysis. The majority of patients had a history of arteriovenous fistulae thrombosis, previously implanted CVC and catheter associated infections. In 14 cases the CVC implantation was possible only after performing of the transluminal angioplasty of central vein. In all these cases broad spectrum antibiotics were administered and the prophylaxis of catheter related thrombosis was done with direct anticoagulants. The patients were monitored for 2 weeks on the inpatient basis, and later during their regular dialysis sessions.

Results: In 25 (21.0 %) cases from 119 manipulations, the central vein stenosis was visualized. Due to the impossibility of another vein, available for catheter implantation, in 14 cases (56.0%) from diagnosed with stenosis, the transluminal angioplasty of central vein stenosis was performed. The feasibility of venous dilation was assessed by the absence of acute vein thrombosis and the stable general condition. The dilatation of jugular and brachiocephalic veins was performed in 7 cases (50.0%), of the iliac veins in 4 cases (28.6%), of the yena cava superior or inferior in 3 cases (21.4%). All the patients survived the procedure, no cases of embolism were observed. No episodes of internal bleeding due to possible vascular wall damage were signed. In 4 cases (28.6%) moderate venous insufficiency was observed in the post surgical period, which lessenened with time. The removal of catheter was required in no cases. In all the cases were achieved satisfactory blood flow.

Conclusions: In cases of chronic venous stenosis preventing catheter implantation the dilatation of central veins with useful option to provide access to hemodialysis. The absence of severe complications, moderate intensity of venous insufficiency in the post operative period, could be attributable to the chronic character of vein stenosis. The age of stenosis and its compensation could be assessed by means of scurupulous history taking, physical examination and data from imaging techniques.

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SP501 DETERMINATION OF RELIABILITY OF SOME TESTS IN EVALUATING AV FISTUL FLOW RATE IN HEMODIALYSIS PATIENTS
Yasemin Coşkun Yavuz1, Nimo Dilmaz Seçil2, İbrahim Güneyi and Lütfüallah Altıntepelerı
1Nephrology Hacettepe Erbakan University, Faculty of Medicine Konya Turkey, 2Nephrology Konya Education and Research Hospital Konya Turkey

Introduction and Aims: Vascular access flow is the most accurate method measured by Doppler USG showing AV fistul function in hemodialysis patients. We aimed to compare glucose pump test and Doppler USG imaging technique in evaluating vascular access flow rate and determining reliability of this test with static pressure measurements.

Methods: 93 patients from Konya city center were involved in this study initiating hemodialysis with AV fistulae. Doppler USG and GPT tests were performed on one of their free days to measure fistul flow rate which they didn’t undergo hemodialysis. Also a static pressure measurements were performed to all patients which is another technique to follow up vascular access. The vascular access flow results measured with GPT test and Doppler USG were compared and the relationship of these methods with static pressure measurements was evaluated. Statistical testing was performed with the use of SPSS 13.0 software version. Student’s t-test was used in normal dispersial datas to compare means. In analysing non-dispersial datas we used Mann-Whitney U test. Relation between variables were evaluated with Pearson’s correlation analysis. A p value < 0.05 was considered statistically significant.

Results: The findings of Doppler USG and GPT were compared which are the methods to evaluate access flow rate. Mean access flow rates were not different between these two methods. Both methods were also well correlated (p < 0.001, r = 0.49).

The sensitivity and specificity of Glucose Pump Test was %962 and %953, respectively when the vascular Access flow rate normal range was between 400-1000 ml/min. Static pressure ratios of 0.78 of the patients indicated vascular stenosis. However, the stenosis was not detected with physical examination and Doppler ultrasound imaging. Kt/V was more than 1.2 in %87 of the patients. Furthermore, vascular flow rates which were measured by GPT and Doppler USG were not affected by the patients’ sex, diabetes, Kt/V and aneurysms (p > 0.05). Access flow rates which was measured by Doppler USG and GPT was not correlated with access flow rates’ arterial and venous ratios.

According to the static pressure rate the stenosis findings in patients with vascular accesses were not significantly different (p > 0.05).

Conclusions: In hemodialysis patients, GPT technique was compared with Doppler USG in follow-up of the function of AV fistul which is a more expensive, less operable and more operator dependant test. But no significant relevence was found in static pressure measurements performed by GPT or Doppler USG which are both used in follow-up of vascular access, so it was understand that static pressure measurements can not be used instead of Doppler USG.

SP502 SUSPECTED CATHERTER-RELATED BLOODSTREAM INFECTION – NONTUNNELED VS TUNNELED HEMODIALYSIS CATHETERS
Vesna Gerasimovskia and Biljana Gerasimovska-Kitanovska1
1University Clinic of Nephrology Skopje The former Yugoslav Republic of Macedonia

Introduction and Aims: Complication of central venous catheterization for hemodialysis are catheter thrombosis and catheter-related bloodstream infection (CRBI). In this study we report rates of bacteremia experienced with all types of central venous catheters (CVC). We used femoral and subclavian catheters as non-tunneled CVC (NTCVC) and tunneled CVC (TTCV)- femoral, subclavian and jugular catheters.

Methods: In a prospective study we looked at the outcome of a group of 640 patients (pts) with acute and chronic renal failure treating with hemodialysis vs a 821 central venous catheters during the 3-year period . Catheters were placed by nephrologists in a
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SP503 OUTCOMES OF NATIVE ARTERIOVENOUS FISTULA IN HEMODIALYSIS PATIENTS OVER 65 YEARS OF AGE
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1Department of Nephrology University Medical Center Ljubljana Ljubljana Slovenia

Introduction and Aims: Native arteriovenous fistula (AVF) remains the best vascular access for chronic hemodialysis. The results of the outcome of AVF in the elderly, specifically women and diabetics, are still controversial. The aim of this study was to analyze the outcomes of native AVF creation in elderly patients ≥65 years of age.

Methods: The study was performed retrospectively on prospectively collected data. The study period was between January 1, 2005, and September 1, 2011. The first attempt of AVF creation in elderly patients was recorded. Before the conduit was created, preoperative duplex ultrasound (US) imaging of arteries and veins of both arms and forearms was performed in all patients. AVFs were constructed by interventional nephrologist. The primary outcomes were primary patency (intervention-free interval) and secondary patency (cumulative survival, interval from AVF creation to permanent access abandonment or the end of observation period). Kaplan-Meier survival analysis was used to estimate patency rates, censored for patient’s death with functioning AVF. Multivariate Cox proportional hazard models were used to determine the effect of factors considered relevant to the primary and secondary AVF patency rates (age - stratified at 65-75 years or >75 years, gender, diabetes status).

Results: During the observational period, 214 incident patients with end-stage renal disease, aged 76±6 years (range 65-93 years), 51% >75 years, 58% men, and 41% diabetic were referred for AVF construction. 50% were already treated by chronic hemodialysis. Based on preoperative US, in 75% (159/214) of patients AVF was placed, predominantly on forearm (124/159; 78%). Immediate patency of AVF was achieved in all but 3 patients. Polytetrafluoroethylene grafts were created in 4% (9/214). In 21% (46/214) of patients construction of AVF was not performed (suboptimal vessels or a limited life expectancy of the patient). From 159 patients with AVF placed, 11 patients were in predialysis period, and 4 patients were lost to follow-up. From the remaining 144 patients, primary failure of AVF was observed in 24 patients (17%).

Finally, 120 patients had functional AVF and were included in survival analysis. Median follow-up was 21 months (IQR, 11 to 36 months). Primary patency rates of native AVF at 12, 18 and 24 months were 81%, 78% and 74%, respectively. Diabetes was the only significant predictor of primary patency loss (HR, 1.99; 95% CI, 1.034 to 3.785; p=0.037), and of borderline significance related to secondary patency loss (HR, 1.97; 95% CI, 0.817 to 4.756; p=0.131). Patient gender and age were not associated with AVF patencies.

Conclusions: Our results are in favor of the principle that using preoperative duplex US, AVF placement is possible and worthwhile in the majority of elderly patients. Diabetes was the only independent predictor for reduced primary patency rate, but not for cumulative survival, and no differences were observed in patency rates in relation to patient age and gender.

SP504 VASCULAR ACCESS IN DIAZELIZED PATIENTS OVER 70 YEARS OLD
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Introduction and Aims: The dialysis population has dramatically changed in recent years: the incidence of old patients (pts) increased in the western world, accounting for 20-25% over 75 and 40-44% over 65 years old. Because of their several comorbidities, such as arteriosclerosis and diabetes, the arterovenous fistula on native vessel creation is often difficult to perform. However the AVF is recommended as first access in all patients, because the associated lower mortality rate. The aim of our study is to evaluate the vascular access (VA) in elderly pts.

Methods: We reviewed the VA performed in incident dialyzed pts over 70 years old from January 2007 to December 2011. We compared the cumulative patency rates at 12, 48 and 60 months of distal (DVA), middle arm (MAVA) and upper arm (UAVA) fistula. We evaluated the number and the type of VA, the use of central venous catheters (CVC) and the mortality rate in three different groups: A 70 to 75 yrs old, B 76 to 80 yrs old and C over 80 yrs old.

Results: 88 pts (M 61, F 27) over 70 yrs old were included, A 39 (44%), B 28 (31.8%) and C 21 (23.8%). We performed 103 VA: 2 graft and 101 native VA (NVA), NVA were composed of: 47 (46.5%) DVA, 48 (47.5%) MAVA and 6 (6%) UAVA. Cumulative patency rates were 76%, 64.6% and 52.9% for DVA, 76%, 62.5% and 52.1% for MAVA at 12, 48 and 60 months, respectively (p=ns). The cumulative patency for UAVA was 80% at 12 and 24 months. Primary failure was DVA 10%, MAVA 14%, UAVA 16%. In six pts (6.8%) CVC was the unique access. The type of VA is not different among the three groups: 38.3%, 53%, 55% DAV, 51%, 43%, 43% MAVA, 10.7%, 0% UAVA, respectively. The permanent patency rates were 12.9%, 9%, 7% A, B and C, respectively. The number of temporary CVC per pts was 0.77 in A, 0.78 in B, 0.9 in C during the follow up. A temporary CVC was the first access for 23% in A, 43% in B and 38% in C. 36% in A, 28.5% in B and 28.5% in C never needed central venous catheterization. At the end of the follow up 35.9% in A, 42.8% in B and 33% in C died.

Conclusions: Our study demonstrates that the age could not be considered a limit for the creation of AVF on native vessels and the “fistula first policy” must be recommended for elderly too. In addition, the distal and middle arm AVF shows a similar good outcome. Surprisingly, the mortality rate also is not different among the three groups and the risk of death in very old pts is becoming similar to the general population.

SP505 SP505 ULRAN-BASILIC DIRECT ARTERIOVENOUS FISTULA (UBAVF) AT WRIST FOR HAEMODIALYSIS: REVIEW OF LITERATURE AND OUR EXPERIENCE
Jacopo Scrivano1, Laura Pettorini1, Anna Giuliani1, Giorgio Punzo1, Paolo Menè1 and Nicola Pirozzi1
1Nephrology Unit Sapienza University Rome Italy

Introduction and Aims: Ulran-basilic fistula (UBAVF) is a vascular access (VA) option for haemodialysis (HD). Few reports of outcomes of this type of AVF are available. We analyzed our single center experience and reviewed the relevant literature.

Methods: We retrospectively analyzed prospectively collected data from our single vascular access centre from 2007 to 2012. Patient demographic and comorbidity factors are listed in table 1, whereas in table 2 are data about functional status and VA. Tab.2: Functional status, previous and actual VA (K/D:chronic kidney disease; CVC:central vein catheter) All patients, after preoperative ultrasound exam, were treated by end-to-side UBAVF at the wrist. Preventive haemostasis and operative microscope were routinely used. Follow-up was carried out at 1 day, 1 week, 1 month and 12 months after creation. Functional patency was defined as an angioaccess successfully used for haemodialysis. Early failure was defined as thrombosis or undialyusable VA 1 month after creation. Patency rate were analyzed by Kaplan-Meier test.

Results: Immediate (24h) patency was 94%; early failure rate was 20%. Primary and secondary 1 year patency were 65.4% and 80% respectively. However, a significant drop out occurred; by an intention to treat basis, 53% of patients have a functional UBAVF at 12 months. From the analysis of the indexation publication available, primary and secondary patency rate at 1 year varies from 42% to 78% and 44% to 78.3% respectively. A significant heterogeneity of studies were observed.

Conclusions: UBAVF is a valuable distal autogenous option as haemodialysis angioaccess. In papers with a rigorous protocol of study, the primary and secondary patency rates are clearly worse than those observed in distal radio-cephalic AVF.

SP505 Table. Demographic and comorbidity factors (BMI:body mass index).

<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>10 (66%)</td>
</tr>
<tr>
<td>Age (mean ± SD)</td>
<td>63 ± 13</td>
</tr>
<tr>
<td>Hypertension</td>
<td>15 (100%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>5 (33%)</td>
</tr>
<tr>
<td>Obesity (BMI &gt; 30)</td>
<td>3 (20%)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>10 (66%)</td>
</tr>
</tbody>
</table>

| CKD Table. Demographic and comorbidity factors (BMI:body mass index). |
|-----------------|-----------------|
| Primary CVC | 3 (20%) |
| CVC after AVF thrombosis | 3 (20%) |
| Dysfunctional AVF | 5 (33%) |
| CKD conservative treatment | 4 (27%) |
SP506  THE IMPACT OF PRESENCE OF PERIPHERAL ARTERIAL DISEASE ON OUTCOME AFTER PERCUTANEOUS TRANSLUMINAL ANGIOPLASTY FOR ARTERIOVENOUS FISTULA: A 1-YEAR RETROSPECTIVE ANALYSIS

Mustafa Bakır1, Ayse Türkvatan2, Sibel Mandirouglu3, Baris Altun2, Fahri Mandirouglu1 and Alper Kirganc1
1Nephrology RPM Renal Tedavi Hizmetleri Ankara Turkey, 2Cardiology Türkعطاء Yüksek İhtisas Hastanesi Ankara Turkey, 3Radiology Türkعطاء Yüksek İhtisas Hastanesi Ankara Turkey, *Physical Therapy and Rehabilitation Ankara Fazik Tedavie Hastanesi Ankara Turkey, 4Radiology Konya Numune Hastanesi Konya Turkey

Introduction and Aims: A significant proportion of end stage renal disease patients undergoing percutaneous transluminal angioplasty (PTA) for arteriovenous fistula (AVF) have concomitant peripheral arterial disease (PAD), which plays a crucial role in the selection process of determining an optimal vascular access site. The aim of the present study was to determine the impact of PAD on 1-year AVF patency after percutaneous transluminal angioplasty in a large hemodialysis facility.

Methods: A retrospective analysis was performed for a total of 200 patients (92 females and 108 males, mean age 59±13 years, mean hemodialysis vintage: 56±36 months). Study patients were divided into 2 groups: Group 1 (patients without PAD; n=147) and Group 2 (patients with a previous angiographic diagnosis of PAD; n=53). The clinical and laboratory files were reviewed for the development of AVF dysfunction that required percutaneous intervention.

Results: Compared to Group 1 patients, patients in Group 2 were elder (63±10 vs 55 ±13 years, p=0.02) and had more diabetes (70% vs 25%, p=0.016) and more history of documented coronary artery disease (42% vs 17%, p=0.001), reflecting more frequent and severe comorbidities. The review of clinical files revealed that 57 patients in Group 1 (38.8%) and 37 patients in Group 2 (69.8%) developed angiographically confirmed AVF dysfunction that required PTA in one year time (p<0.001). In the multivariate regression analysis, PAD (HR: 2.14, 95%CI 1.26–4.04, p=0.006) was an independent predictor of 1-year AVF thrombosis after PTA.

Conclusions: Assessment of PAD should play an important role in developing strategy for vascular access placement.

SP507  IS CARPAL TUNNEL SYNDROME RELATED WITH VENOUS HYPERTENSION IN EARLY HEMODIALYSIS PATIENTS?

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Introduction and Aims: Carpal tunnel syndrome, (CTS) is one of the frequent problems of patients who underwent hemodialysis (HD). Although, precise etiology is still unknown, the role of venous hypertension due to arteriovenous fistula (AVF) has not clarified yet. Therefore, we aimed to investigate the role of venous hypertension due to AVF in hemodialysis patients who had CTS.

Methods: We included 12 hemodialysis patients that have undergone HD less than 5 years and newly diagnosed CTS with the same arm of AVF. All patients diagnosed with clinically and confirmed by both nerve conduction studies and electromyography. Open carpal tunnel release surgery performed to all of them. Venous pressure was measured in all patients before and after two week of surgery.

Results: shows comparison of pressures in different localizations before and after operation. There were significant differences before and after surgery with regard to pressures (p <0.05). The reduction in venous pressure (ΔP) was calculated following formula: ΔP = (pressure before the operation)– (pressure after the operation) / (pressure before the operation) x 100. ΔP in all localizations did not correlate with levels of serum B2MG level, high sensitive C-reactive protein, and intact parathyroid hormone, dialysis duration, body mass index, and systemic systolic and diastolic blood pressures (p >0.05). After surgery, all carpal ligament specimens of patients did not stain with Congo red for the presence of amyloid deposits.

Conclusions: Our results revealed that increased venous pressure on the same arm with AVF could be responsible for CTS in hemodialysis patients. Carpal tunnel release surgery is the main treatment of this disease by reducing compression on the nerve.

SP508  SUPERFICIALIZED BRACHIOBASILIC FISTULA FORMED AS A 1-STEP OR AS A SECOND PROCEDURE. WHAT IS THE BEST?

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Introduction and Aims: Brachio basilic fistula is considered in patients if radio cephalic fistula is unavailable. Superficialization is performed on 1 step or second procedure. Controversy exists about recommended procedure. The purpose of our study was to compare patency rates and complications in superficialized brachio basilic fistula formed as a 1-step and 2-steps procedure.

Methods: We performed a retrospective study of the medical histories of 70 patients with brachio basilic AVF performed by a single surgeon.

Results: Mean age was 48 years (age range, 18-80 years) underwent superficialized brachio basilic fistula. Eighteen were diabetics. Forty three had 1 step procedure (GI) and 27 had a second procedure (GII). Patients were aged meanly of 50,6 years GI VS 50,8 years GII. Brachio cephalic fistula was the first fistula in 32,6% GI VS 66,7% GII. Complications such as hematoma, stenosis, thrombosis, aneurysm and infection of the fistula were similar into the 2 groups. The patency rate is not affected by diabetes. Superficialized brachio basilic fistula formed as a 1-step procedure showed a patency and a complication rate similar to the second procedure. Complications are not more frequent than in delayed procedure.

Conclusions: We recommend that the basic vein should be superficialized in 1 step as it can be more quickly used with fewer complications.

SP509  VASCULAR ACCESS STENOSIS: INTIMA MEDIA THICKNESS ULTRASOUND SURVEILLANCE. FROM BASICS TO A RISK PREDICTOR?

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Introduction and Aims: It is not well known intimal hyperplasia (IH) predictive value in vascular access patency and inflammation influence. There is no data of IH surveillance by ultrasound (US) as prognostic factor. Aims: Study: 1) Relationship of inflammation with IH progression, stenosis and catheter antecedent 2) Value of IH surveillance with US, validated with histology.

Methods: Prospective cohorts study. 100 arteriovenous fistulas, 2 years follow up. 1. Variables: Demographic, Clinical, Vascular access (VA), Charlson Index, surgery,
SP510 THE SIGNIFICANCE OF ULTRASOUND VASCULAR MAPPING BEFORE THE CREATION OF ARTERIO-VENOUS FISTULA FOR HEMODIALYSIS

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Introduction and Aims: It was shown in several studies that preoperative ultrasound vascular mapping increases the chance of successful arterio-venous fistula (AVF) creation. Nevertheless, attempts to create AVF without prior ultrasound evaluation are performed. According to the literature following criteria indicates suitable vessels for creation of native AVF: artery internal diameter ≥ 2.0 mm and vein diameter ≥ 2.5 mm. The aim of this study was to evaluate the prevalence of suitable radial artery and cephalic vein to create forearm radiocephalic AVF.

Methods: Vascular ultrasound mapping with Doppler flow assessment was performed in 63 patients (F=23, M=41), aged 23-88 years, scheduled for AVF creation, of whom 23 (41%) were aged ≥ 65 years. Upper limb arteries and veins were examined in 86 limbs (54 left and 32 right). Limbs with dressing or vein cannula were not evaluated. Results: Brachial artery (BA) was visualized in all examined limbs. Mean BA internal diameter (ID) was 3.80±0.5 mm, and BA flow was 135±88 ml/min. Proximal radial artery (PRA) was visualized in 81 (94%) of examined limbs, PRA ID was 2.2±0.4 mm, and PRA flow 42±37 ml/min. PRA ≥ 2.0 mm was found in 60 (70%) of examined limbs. Proximal forearm cephalic vein (CV) was visualized in 68 (79%) of the limbs, and CV diameter of ≥ 2.5 mm was found in 54 (63%) of the limbs. In proximal forearm both ultrasound criteria were met in 49 (57%) of the examined limbs. Among patients aged ≥ 65 years, these criteria were met in 18 of the examined 34 limbs (53%). Radial artery in distal forearm (DRA) was visualized in 74 (86%) of the examined limbs. DRA ID was 1.8±0.4 mm, and DRA flow 28±22 ml/min. DRA ≥ 2.0 mm was found in 29 (34%) of the limbs. Distal forearm cephalic vein (CV) was visualized in 47 (55%) of the limbs, and CV diameter of ≥ 2.5 mm was found in 33 (38%) of the limbs. In distal forearm both ultrasound criteria were met in 18 (21%) of the examined limbs. Among patients aged ≥ 65 years, these criteria were met in 4 of the examined 34 limbs (12%).

Conclusions: Making attempt to create distal forearm radiocephalic fistula without proximal mapping may lead to a high risk of procedure failure, particularly in elderly patients.

SP511 OUTCOMES OF VASCULAR ACCESS CREATION -ARTERIOVENOUS FISTULA PRIOR TO HEMODIALYSIS

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Introduction and Aims: Starting renal replacement therapy with an arteriovenous fistula (AVF) increases patient survival following dialysis initiation. AVF creation should occur at least six months prior to anticipated hemodialysis (HD) initiation to allow for AVF maturation, evaluation and necessary interventions, and in order to avoid catheter use. Therefore, early creation of an AVF is strongly recommended.

Methods: A 2-year single institution experience of the success rate, survival and complications of arteriovenous fistula (AVF) creation before dialysis initiation is reported. Study cohort: all patients (pts) who underwent AVF creation before need for dialysis (n =141, aged average 61 year, male 76 and female 65) divided in three groups (gr) - diabetic (AVF6 = 47), hypertensive pts (AVFH = 49) and others (AVFO=45).

Results: Mean glomerular filtration rate (gGFR) at creation in AVF6 group was higher (15.04 ± 4.5 ml/min vs. 13 ± 3.2 ml/min, p<0.005). Only 17 pts underwent second AVF and 4 pts had a third AVF creation (more frequently in females). During the study period, in 76% (n =110) of all pts a mature fistula was used as their first dialysis access, 16% (n =22) were still without dialysis and 12% (n =18) started HD with central venous catheters. Median time to first cannulation of AVF were: gr AVF6 = 202 ±114 days, gr AVFH= 197±97,5 days and AVFO= 176±114 days. No significant difference was found for median time to first cannulation of AVF in different groups (p >0.29). Significant difference was found in creatinine level when HD was started, hematocrit and albumin level and gGFR when pts started with HD (gGFR AVF6 =11,70 ± 6,05ml/min, gr AVFH= 7,83±3,2 ml/min and AVFO= 8,32±2,2 ml/min (ANOVA p=0,494, p=0,000.). No association of AVF creation with pts characteristics of age and gender. Sixty five pts were elderly >65 years (AVF6 =27 , AVFH=29 and AVFO=9). No significant difference was registered in the survival of AVF in patients with started HD in comparison to those that have not started hemodialysis. Restriction to diabetes mellitus (log-rank 0.16). Greater hematocrit (HR, 1,0495/CL1,01 to 1,09) and albumin level (HR,1,79/CL,3,37 to 2,33) showed an independent association with survival. We did not find the significantly poorer fistula survival in elderly and diabetic pts.

Conclusions: In conclusion, the success rate of early AVF creation is reasonable and can be used. We present early clinical outcome and complications of percutaneous placement of tunneled dialysis catheters. The preferred site for catheter insertion is right internal jugular vein (RIJV), due to its straight route, relatively easy access and lowest number of complications. However, in many dialysis patients, especially with the history of previous catheter use, other access sites need to be used. We present early clinical outcome, access and complications of percutaneous placement of tunneled dialysis catheters.

Methods: Between 01.01.2012 and 31.12.2012 105 cuffed tunneled catheters were placed in 101 patients by the same team of nephrologists. Arterio-Cannon II catheter (with backward tunneling) was used in 93 cases, Bard Hemofirst in 10 cases and Tal Palindrome in 2 cases. Before procedure both IJV were located with ultrasound and the route of the preferred vein was marked on the skin. After insertion both arms of the catheter were tested for patency, flushed with heparinized saline, filled with respective volume of heparin solution (5000 U/ml) and control chest X-ray was performed.

Results: In 69 cases catheter was inserted into RIJV in, in 20 cases into left internal jugular vein (LIJV). Right and left subclavian veins were used in 3 and 2 cases, and right and left femoral veins in 6 and 5 cases, respectively. LIJV was used because of thrombosis, serious narrowing of RIJV or ultrasonic examination, local skin infections, hematomas. LIJV was also used if during insertion on the right side no free passage of guidewire was achieved. Local hematoma and prolonged wound bleeding was the most common complication of insertion procedure, similar on the right and left side (66% vs. 66%). Prior to insertion, blood access, the patient died despite transfusions and vascular surgery intervention. There was no case of pneumothorax. In 1 case thoracic duct was punctured on the left side with aspiration of the chyle. There were no cases of immediate malfunction when the catheter tips were properly positioned. Malposition of the catheter tips occurred only with LIJV insertion. They included malposition into the right innominate vein (2 cases), and into vena azygos (4 cases). In all cases position of catheter tips were immediately corrected under fluoroscopic control by partial withdrawal of the catheter and subsequent insertion.

Conclusions: Bleeding and hematoma formation appears to be the most common and important complications of percutaneous placement of tunneled dialysis catheters. Malposition of the catheter tip into innominate vein or vena azygos was specific and relatively common complication of LIJV access (6 out of 20 insertions). Especially during catheterization of LIJV fluoroscopy should be used to control guidewire and catheter passage and to correct malposition as soon as possible.
SP514 VASCULAR CLAMS USED FOR ACCESS PROCEDURES MAY CAUSE A VASCULAR ACCESS FAILURE ON SOME FUTURE OCCASION

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Introduction and Aims: The best way to establish a vascular access (VA) is by creating an arteriovenous fistula (AVF) in patients undergoing chronic hemodialysis. Although surgeons have strived to gain longer-lived VA using various devices in surgery, VA accidents still occur. The most serious complication of AVF is access dysfunction by late stenosis. Surgical instruments and tools are critically important, because these can affect the results of operations. Vascular clamps are indispensable for occluding arteries and veins during anastomosis, whereas those are likely to cause an injury to vessels to some extent, both to arteries and veins. Unexpectedly, there were few reports concerning this complicated subject. The present work was initiated to estimate the adequacy and safety of vascular clamps.

Methods: Arteries are comprised of a tunica intima, a tunica media and a tunica adventitia. Though veins have a thin wall compared to arteries, these also consist of three layers. The tunica adventitia is partly composed of collagen and elastic fibers. The tunica media has fewer elastic fibers and smooth muscles. The quickly excised carotid tissue was certainly damaged by the clamps. Surprisingly, the measured pressures were not from 330g to 490g; the average being 387g. The results suggest that the clamps applied more than enough pressure to occlude a radial artery, and much more than enough to occlude a cephalic vein. Vascular clamps are usually required on the proximal artery (arterial inlet), the distal artery (arterial outlet), and the proximal vein (venous outlet). So a proper pressure should be required for each. In collaboration with Takasago Medical Industry Co., LTD., Tokyo, we had been planning to produce small vascular clamps available for access procedures, many of which are made of metallic materials. For most of them, the pressure setting is a secret. Clamp pressures were measured on eight currently available clamps of different sizes and shapes; each product was imported from Germany.

Results: The microsections showed discontinuities of the elastic tissue and lack of uniformity of the smooth muscle layers in some places. These findings prove that the tissue was certainly damaged by the clamps. Surprisingly, the measured pressures were to be from 330g to 490g; the average being 387g. The results suggest that the clamps applied more than enough pressure to occlude a radial artery, and much more than enough to occlude a cephalic vein. Vascular clamps are usually required on the proximal artery (arterial inlet), the distal artery (arterial outlet), and the proximal vein (venous outlet). So a proper pressure should be required for each. In collaboration with Takasago Medical Industry Co., LTD., Tokyo, we had been planning to produce small vascular clamps available for access procedures, many of which are made of metallic materials. For most of them, the pressure setting is a secret. Clamp pressures were measured on eight currently available clamps of different sizes and shapes; each product was imported from Germany.

Conclusions: Neither total WBC counts nor WBC subtypes were related with primary AVF failure. Higher RDW and ferritin levels had a prognostic value for development of primary AVF failure. PR: 0.24, RDW (Odds Ratio: 1.436, P: 0.032) and ferritin (Odds Ratio: 1.474, P: 0.003) were independently related with primary AVF failure.

SP515 VASCULAR HETEROGRAFTS IN HEMODIALYSIS: COMPARISON BETWEEN UNIPUNCTURE AND BIPUNCTURE TECHNIQUE

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Introduction and Aims: Survival and quality-of-life of dialysis patients is related with quality and duration of their vascular access. Although the ideal vascular access to the native arteriovenous fistula, there are many patients that need vascular heterografts, because they had exhausted a great part of their vascular accesses.Despite of the high quality of the vascular grafts nowadays, their viability could be related on the number of punctures that received. Our aim was to assess the vascular graft viability and the efficacy of hemodialysis using the unipuncture technique, compared to bipuncture technique.

Methods: We analyzed 28 consecutive patients in chronic dialysis program with functional vascular grafts, in which was performed the unipuncture technique. We also analyzed 30 consecutive patients that received the classical bipuncture technique. The patients who left the dialysis program (exits, transplant) with functional graft and patients who continue dialysis currently using vascular graft were excluded in order to analyze the viability of vascular grafts. We registered the viability of the vascular graft and the adequacy of dialysis in every patient.

Results: The patients age was 75.38±8.2 years in the group that received unipuncture and 72±10 years in the group that received bipuncture. In both groups unipuncture and bipuncture there were 50% women and 50% men. The equilibrated Kt/V was 1.37±0.24 in the unipuncture group and 1.56±0.38 in the bipuncture group, with p=0.06. In both groups the adequacy of dialysis was correct according to current requirements. The equilibrated Kt/V was higher in the bipuncture group, probably related by the fact that most of these patients had received hemodiafiltration online. The viability of the vascular graft in the group receiving unipuncture was 29.4±32.2 months and 18.4±12 months in the bipuncture group, with p=0.18. The total number of vascular accesses (catheters, native arteriovenous fistulas, grafts) previous of the actual graft was 1.9±1.6 in the unipuncture and 2.89±1.5 in the bipuncture group. Viability of vascular grafts was associated with age of patient at the time of graft collocation and with presence of vasculopathy, although without reaching statistical significance (p=0.08, p=0.07).

Conclusions: We observed a tendency to higher viability with 11 months in the group receiving unipuncture compared to bipuncture technique, although not enough to reach statistical significance. Further investigations are needed to confirm this difference. The unipuncture technique was effective and safe for patients, according to current requirements of adequacy of dialysis.

SP516 ASSOCIATION BETWEEN VASCULAR ENDOTHELIAL GROWTH FACTOR AND THROMBOSIS OF NATIVE ARTERIOVENOUS FISTULA IN PATIENTS ON MAINTENANCE HEMODIALYSIS

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Introduction and Aims: Vascular endothelial growth factor (VEGF) induces endothelial cell proliferation, promotes cell migration, and inhibits apoptosis. AlsoVEGF induces angiogenesis as well as permeabilization of blood vessels, and plays a central role in the regulation of vasoclogenesis. Increased VEGF levels is reported in the plasma of patients with peripheral arterial occlusive disease. VEGF can be a useful predictor of AVF thrombosis in ESRD patients on maintenance hemodialysis. Aim of the study was to evaluate the association of serum levels of vascular endothelial growth

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<tr>
<th>CRP (mg/L)</th>
<th>Group I</th>
<th>Group II</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Min. – Max.</td>
<td>3.0 – 66.0</td>
<td>3.0 – 32.0</td>
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</tr>
<tr>
<td>Mean ± SD</td>
<td>19.16 ± 17.02</td>
<td>7.07 ± 6.98</td>
<td>0.002*</td>
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<tr>
<td>Median</td>
<td>13.90</td>
<td>4.15</td>
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<tr>
<th>VEGF (pg/ml)</th>
<th>Group I</th>
<th>Group II</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Min. – Max.</td>
<td>42.0-1300.0</td>
<td>48.0-500.0</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>358.50 ± 348.44</td>
<td>174.20 ± 128.54</td>
<td>0.033*</td>
</tr>
<tr>
<td>Median</td>
<td>195.0</td>
<td>130.0</td>
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P: p value for Mann Whitney test for comparing between the two studied groups

*Statistically significant at p ≤ 0.05.
factor (VEGF) and thrombosis of native arteriovenous fistula in hemodialysis patients.

Methods: This study was carried out on 40 patients divided into 2 groups. Group I contains 20 patients with thrombosed AVF, proved by Doppler ultrasound and group II contains 20 patients with normally functioning AVF for at least 6 months with no previous vascular access thrombosis. All patients were investigated for CBC, BUN, Cr, FBS, fasting lipid profile, liver function tests, C reactive protein (CRP), and VEGF.

Results: There was statistically significant difference between the two groups, according to CRP and VEGF.

Conclusions: VEGF can be a useful predictor of AVF thrombosis in ESRD patients on maintenance hemodialysis.

SP517 THE PREOPERATIVE VASCULAR MAPPING WITH DUPLEX ULTRASONOGRAPHY IN SUCCESSFUL VASCULAR ACCESS CREATION

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Introduction and Aims: Preoperative vascular mapping is used to evaluate the structural and functional quality of the vasculature which is to be used for the creation of a vascular access. This procedure offers the opportunity to choose the most appropriate vessels, thus guiding the vascular surgeon in terms of the type and location of the access. Given the improved survival of peripheral native arteriovenous fistulae (AVF) compared with synthetic grafts, vascular mapping contributes to enhanced creation of radio-cephalic anastomoses (AVFs).

Methods: We retrospectively studied the reliability of preoperative vascular mapping in 44 patients with end-stage renal disease (ESRD) in relation to the creation of a peripheral native AVF. The studies were performed at bedside by a nephrologist, with a portable ultrasound scanner (Sonosite MicroMaxx), one to two days prior to planned surgery. The vascular access was considered successful if it's efficient to support a 4-hour dialysis session, after its first cannulation.

Results: Of the 44 patients studied, in 36 individuals (82%) the sonographic and surgical findings were matched and the AVF that was performed has been indicated by the previous mapping study. A radio-cephalic fistula at the left wrist (non-dominant arm) was created in 16 of these 36 patients (36%) (group 1), while in 20 patients (group 2) the vascular access was created in various other sites according to the sonographic findings. In 8 patients (18%) (group 3) the sonographic findings did not correspond to the findings during surgery. The median values of the diameter of the left radial artery at the wrist (measured by ultrasound) in the three groups of patients were: Group 1: 0.29 cm (IQR 0.22 – 0.30), Group 2: 0.21 cm (IQR 0.20 – 0.24), Group 3: 0.22 cm (IQR 0.18 – 0.24). The values of the cephalic vein diameter at the wrist were in Group 1: 0.30 cm (IQR 0.26 – 0.35), in Group 2: 0.25 cm (IQR 0.22 – 0.36) and in Group 3: 0.29 cm (IQR 0.22 – 0.36) respectively. The radial artery diameter was statistically significantly greater in the Group 1 compared with the other Groups (2 and 3) of patients.

Conclusions: Conclusively, preoperative vascular mapping using Duplex ultrasonography seems to be a reliable method to guide the surgeon to create a suitable and sustainable peripheral native vascular access.

SP518 SINGLE-CENTER EXPERIENCE OF TUNNELED HEMODIALYSIS CATHETER INSERTION WITHOUT FLUOROSCOPY

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Introduction and Aims: The aim of this study was to evaluate the efficacy and safety of TCC insertion without fluoroscopy.

Methods: This study was divided into two phases, that is, temporary non-tunneled catheters (NTC) were inserted between March 2010 and February 2011 (Phase I), and tunneled cuffed catheters (TCC) or NTCs were inserted between March 2011 and February 2012 (Phase II). Catheter survival, nurse satisfaction, and reasons for catheter removal were analyzed.

Results: Two hundred and sixty patients in Phase I and 300 patients in Phase II participated in this study. The success rate of TCC insertion was 98.3%. The catheter survival rate in Phase I was 65.5% at 1 month, and in Phase II was 74.9% at 1 month (P = 0.023). TCC survival was higher than NTC survival (P < 0.001). Furthermore, the removal rate for a catheter-associated problem was lower for TCC than NTC.

Conclusions: TCC insertion without fluoroscopy can be performed safely. TCC insertion without fluoroscopy can provide a reasonable alternative for hemodialysis (HD) catheter placement in patients requiring long-term HD.
ANAEOMA IN CKD 5D

Introdution and Aims: Peginesatide is a once-monthly, peptide-based erythropoiesis-stimulating agent (ESA) approved in the US for treatment of anemia due to chronic kidney disease (CKD) in adult patients (pts) on dialysis. Peginesatide demonstrated noninferiority to epoetin in maintaining hemoglobin (HB) in hemodialysis (HD) pts in two Phase 3 randomized trials (EMERALD 1, 2; Faissbauer et al. NEJM 2013). Time to dose stability with a less frequently administered ESA is an issue of clinical interest. This post-hoc analysis evaluated the time to achieve initial dose stability in pts who converted from stable epoetin to peginesatide, or maintenance of dose stability in pts who remained on epoetin. Methods: Data were pooled from the EMERALD trials assessing safety and efficacy of peginesatide (QW; n=1066) vs epoetin alfa/beta (1-3x weekly; n=542) in HD pts previously on stable epoetin. Dose adjustments were to be made no more than once QW (unless for safety reasons) to maintain Hb 10-12 g/dl (per guidelines in effect at time of trial). Hb was measured QW (or QW during evaluation period [Wk 29-36] and dose postponements). Due to different dosing frequencies, definitions of dose stability were different between treatments: (1) subsequent dose change by <20% of prior dose, with 21-35d between doses (peginesatide) or total dose in subsequent month changed by <20% of prior month’s total dose (epoetin); and (2) at least 1 Hb was within target between doses (peginesatide) or between first dose of consecutive months (epoetin). The evaluable population were pts who received ≥2 peginesatide doses (n=1034) or ≥2 months of epoetin (n=528).

Results: Similar proportions (96.6%) of pts achieved (peginesatide) or maintained (epoetin) dose stability. For peginesatide and epoetin, respectively, dose stability was achieved or maintained after: 1st dose in 61.4% and 54.9%, 2nd dose in 76.7% and 67.4%, and 3rd dose in 84.9% and 77.2% of pts. The most common reason for not achieving peginesatide initial dose stability at 1st dose was a ≥20% decrease in the 2nd dose. Both groups achieved or maintained dose stability at similar rates (in wks; Fig).

Conclusions: After conversion from stable epoetin, >75% of peginesatide pts achieved initial dose stability within 1-2 doses. Compared with pts who remained on epoetin, peginesatide pts did not differ in achievement of dose stability. These post-hoc results may warrant further study.

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SP526

COMPARATIVITY OF I.V. AND S.C. INJECTION OF CONTINUOUS ERYTHROPOIETIN RECEPTOR ACTIVATOR (C.E.R.A.) EFICACY IS CONFIRMED NOT ONLY BY INCREASE OF RED BLOOD CELLS AND RETICULOCYTES BUT ALSO BY ERYTHROBLAST MATURATION KINETICS AND IRON DYNAMICS

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1Product Research Department Chugai Pharmaceutical Co., Ltd. 200 Kajiwara, Kamakura Japan

Introduction and Aims: Continuous Erythropoietin Receptor Activator (C.E.R.A.) differs from epoetin beta by integration of methoxy-polyethylene glycol and is a novel long acting erythropoiesis stimulating agent, proven to maintain hemoglobin levels effectively with once monthly administration. It stimulates erythropoietin progenitor cells in bone marrow, leading to an increase of reticulocyte and hemoglobin levels. Although it is shown that the elimination half-life of intravenous (i.v.) and subcutaneous (s.c.) injection of C.E.R.A. is quite similar, other important pharmacokinetic parameters such as area under the blood concentration-time curve were different. These differences could affect not only proliferation of erythropoietin progenitors but also downstream process such as erythroid maturation kinetics and iron dynamics. In this study, we analyzed erythroid blast maturation kinetics and iron dynamics as well as hematological parameters in mice with i.v. or s.c. treatment of C.E.R.A.

Results: C57BL/6N mice were intravenously or subcutaneously treated with 2, 10 μg/kg of C.E.R.A. or vehicle. Mice were sacrificed at 2, 5, 8, 11, 14 days after C.E.R.A. treatment, and analyzed hematological and iron parameters, as well as the maturation status of bone marrow erythroblast by flow cytometry stained with TER119 and CD71. Results: C.E.R.A. stimulated erythroid progenitor proliferation, were detected by gradual decrease of TER119+CD71hi immature erythroblasts and delayed increase of TER119+CD71lo between i.v. and s.c. treatment with respective dose of C.E.R.A. Conclusions: These results indicate that C.E.R.A. stimulates effective erythropoiesis with marked iron demand and leads to effective iron recruitment for erythroblasts by intensive hemoglobin suppression in both i.v. and s.c. treatment. It is also noteworthy that the response of erythroid maturation kinetics and iron dynamics, which are downstream events of C.E.R.A.-induced erythroid progenitor proliferation, were stimulated equivalently between i.v. and s.c. treatment with respective dose of C.E.R.A. Although some pharmacokinetic parameters are different in i.v. and s.c. treatment, the similarity of the response of erythropoietin maturation kinetics and iron dynamics induced by i.v. or s.c. treatment of C.E.R.A., strongly support the compatibility of the C.E.R.A. efficacy treated from different injection route.

SP527

REPEATED ADMINISTRATION OF CONTINUOUS ERYTHROPOIETIN RECEPTOR ACTIVATOR (C.E.R.A.) REPRODUCES SINGLE ADMINISTRATION IN TERMS OF ACTIVATION OF HEMATOPOIESIS AND IRON MOBILIZATION IN MICE

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Introduction and Aims: Continuous Erythropoietin Receptor Activator (C.E.R.A.) is a novel long-acting erythropoiesis stimulating agent, proven to maintain hemoglobin levels effectively with once monthly administration. In the previous study, we showed that C.E.R.A. maintained stable hemoglobin levels by enhancing iron metabolism through down-regulation and controlling maturation rate of erythroid-lineage cells in mice. Although serum hepcidin levels were significantly suppressed until 8 days after C.E.R.A. injection, significantly higher hepcidin levels were observed at 14 days after C.E.R.A. injection. In this study, we examined the reproducibility of the effects on hepcidin and hepcidin suppression by repeated administration of C.E.R.A.

Methods: Male C57BL/6N (B6) mice were intravenously injected with 10 μg/kg of C.E.R.A. or vehicle on Day -14 and Day 0. Mice were sacrificed and blood and bone marrow cells were collected on 2, 5, 8, 11, and 14 days after second C.E.R.A. administration. Hematological parameters and serum iron concentrations were analyzed, and mouse serum hepcidin levels were measured by liquid chromatography-tandem mass spectrometry method. We also analyzed the maturation status of erythroid-lineage cells in bone marrow by flow cytometry technique, staining TER119 and transferrin receptor (CD71), 7-Amino-Actinomycin D (7-AAD) and annexin V. Correlation analysis was conducted between serum hepcidin levels and hematological parameters and erythroid maturation status.

Results: Mice injected with vehicle on Day -14 and with C.E.R.A. on Day 0 (V-C group) showed significant elevation of hemoglobin and the reduction of serum hepcidin levels. V-C group also showed up-regulation of hepcidin levels on Day 14. In V-C group, significant negative correlations were observed between serum hepcidin levels and percentage of Ter119 +CD71 + immature erythroblasts, as well as reticulocyte number and reticulocyte maturation-related parameters such as IRF, MFR, HFR and LFR. On the other hand, mice injected with C.E.R.A. both on Day -14 and Day 0 (C-C group) kept high hemoglobin levels. We also observed that C-C group showed strong hepcidin suppression until Day 8, indicating that repeated administration of C.E.R.A. counters the elevation of hepcidin occurred around the 14th day after C.E.R.A. administration and enhances iron mobilization.

Conclusions: It is evident that the compatibility of hemoglobin kinetics and iron dynamics induced by i.v. or s.c. treatment of C.E.R.A., strongly support the compatibility of the C.E.R.A. efficacy treated from different injection route.
Nephrology Dialysis Transplantation

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subsequent time periods (Q1 2011 – Q1 2011 – Q2 2011 – Q3 2011 – Q4 2011). Discrimination was assessed by C-statistic and calibration by comparison of observed versus predicted transfusion risk.

Methods: Demographic, biochemical, clinical and transfusion data were abstracted from the DaVita Clinical Data Warehouse. In the training set, predictor variables Q4 2010 were used to predict transfusion risk in Q1 2011. Bivariable associations with outcomes were used to guide specification and prioritize potential predictors. A multivariable logistic model was built by sequentially adding variables and assessing outcomes were used to guide specification and prioritize potential predictors. A multivariable logistic model was built by sequentially adding variables and assessing

Conclusions: TSAT <20 was common (25%) and consistent with markers of ESA-hyporesponsiveness due to absolute iron deficiency and/or inflammation. Compared with TSAT, ferritin was less clearly correlated with Hgb or ESA dose. The observed patterns of IV iron use and broad distribution of TSAT/ferritin combinations suggest heterogeneity of IV iron dosing practices; patterns of IV iron overuse (at high TSAT/ferritin) and underuse (at low TSAT/ferritin) are seen. Follow-up of trends in practice and their effects on clinical outcomes since publication of the KDIGO Anemia Guideline (2012) and European Renal Best Practice commentary (2013) are warranted.

Introduction and Aims: Transfusion is an option of last resort for anemia management, and may adversely impact dialysis patients’ survival, well being, and transplant candidacy. The ability to prospectively predict which patients are at risk for transfusions may facilitate implementation of avoidance strategies. The goal of this study was to develop a prediction algorithm enabling prospective identification of patients at high risk of transfusion.

Results: The training set contained 103,350 patients (mean age 62 years, 45% female, 38% black, 45% diabetic) of whom 1756 had a transfusion in Q1 2011. Thirty-two variables were identified and included in the final model; each variable incrementally improved prediction (C-statistic, 0.73). The model demonstrated excellent calibration over the full 20-fold range of risk observed (Figure). In the 3 validation cohorts, discrimination (C-statistic, Q2 = 0.74, Q3 = 0.71, Q4 = 0.74) and calibration (not shown) were similar.

Conclusions: An algorithm has been developed that uses routinely available patient data and accurately predicts subsequent transfusion risk. Future studies are needed to validate the algorithm externally and to test potential transfusion avoidance strategies that could be used in concert.

Introduction and Aims: Continuous Erythropoietin Receptor Activator (C.E.R.A.), methoxy-polyethylene glycol-modified epoetin-beta, is a novel long-acting erythropoiesis stimulating agent (ESA), proven to maintain hemoglobin levels with once monthly administration. The difference in iron dynamics including hepcidin metabolism and erythropoiesis after C.E.R.A. and epoetin-beta (EPO) treatment were investigated.

Methods: Fifteen hemodialysis (HD) patients receiving 100 µg C.E.R.A. Q4W and 8 HD patients receiving 4500 IU/week EPO, who had been stably maintained hemoglobin levels by each ESA without iron supplementation, were enrolled after written informed consent were obtained. All patients were continued anemia treatment with same ESA before registration. During 25 days observation period, blood samples were obtained prior to every dialysis. Hematological and iron parameters were analyzed including serum hepcidin-20, -22, -25 levels.

Results: Hemoglobin levels were stably maintained in both EPO- and C.E.R.A.-treated groups. Although transferrin saturation (TSAT) declined weekly, no consistent change of other parameters were observed in EPO-treated group. On the contrary, rapid and sustained suppression of hepcidin-25 and gradual increase of reticulocytes, followed by reduction of hepcidin-20 and -22 levels were observed in C.E.R.A.-treated group. In this group, TSAT reduction followed by gradual recovery and gradual reduction of ferritin were also observed. These parameters were recovered toward the end of the observation period.

Conclusions: These results clearly show that iron dynamics after EPO and C.E.R.A. treatment are quite different. EPO treatment induces stable iron mobilization. On the other hand, C.E.R.A. promotes intensive and prolonged proliferation of erythroblasts, triggers rapid increase of iron demand, leads to sustained suppression of hepcidin-25 levels, and result in effective iron incorporation into erythrocytes. Intensive iron consumption results in rapid reduction of TSAT decline and gradual reduction of ferritin, nevertheless sustained hepcidin-25 suppression demonstrates intensive iron mobilization from iron storage to erythropoiesis. Moreover, reduction of hepcidin-20 and -22 levels subsequent to reduction of hepcidin-25 levels indicates that reduction of hepcidin-25 levels after C.E.R.A.-treatment is due to inhibition of production or elimination from blood, but not activation of proteolytic breakdown process of hepcidin-25.
Introduction and Aims: Recent studies have shown that increased resistance to erythropoiesis-stimulating agents was related to cardiovascular an all-cause mortality in patients on hemodialysis. Increased red cell distribution width (RDW), a quantitative measure of anisocytosis was also found to be associated with higher mortality in different patient groups and also in the general population.

Methods: We examined the association between ESA resistance and RDW in a cohort of 1226 chronic dialysis patients (64.2±14.2 years of age, 49% female, all Caucasian, 37% diabetic and 8% on PD) from 10 dialysis centers in Hungary. Demographical and laboratory data were extracted from electronic medical records of the past 5 years. ESA hyporesponsiveness index (EHRI) was calculated from weight adjusted monthly ESA dose and hemoglobin level. Patients in the highest EHRI quartiles were considered to have high EHRI. Multivariate logistic regression models were created to assess the association between RDW and EHRI.

Results: The mean hgb was 116.2±13.9 and 11.8% of patients were anemic (hgb<100g/ l). The median weekly ESA dose was 7500U. EHRI was significantly higher in females (34.6 vs 30.5, p=0.006), patients without diabetes (35.1 vs 28.3, p=0.003). The mean RDW was 15.17±1.47 and 47% of patients had RDW above the normal range (11-15%). EHRI was associated with RDW (rho=0.37, p<0.001), hgb (rho=-0.467, p<0.001), transferrin saturation (rho=-0.237, p=0.001), albumin (rho=-0.231, p=0.001) and CRP (rho=-0.221, p=0.001). In a multivariable model RDW was independently associated with EHRI after adjustment for age, gender, diabetes, dialysis modality, dialysis vintage, albumin, CRP and transferrin saturation. A 1% increment in RDW was associated with a 51% greater likelihood of having high EHRI (odds ratio: 1.51, 95% confidence interval [CI]: 1.34-1.70). Odds ratios in the 2nd, 3rd and 4th quartile of RDW were 1.35 (0.77-2.37), 2.47 (1.45-4.20) and 4.24 (2.49-7.23), respectively, compared to the 1st quartile in the fully adjusted model.

Conclusions: Our data suggests that RDW is a strong and independent predictor of resistance to ESA.

Introduction and Aims: Chronic inflammation and anemia are common and interrelated problems associated with poor clinical outcome in end-stage renal disease (ESRD) patients (pts). We investigated whether Delta-He, a marker of erythropoietic activity, was calculated as the difference between mean Hb contents of reticulocytes (Ret-He) and erythrocytes (RBC-He) respectively, associates with inflammation, ESA response, and mortality in PD pts.

Methods: 82 PD pts were followed for 13 weeks with measurements of Delta-He, erythrocyte indices, and high-sensitivity C-reactive protein (hs-CRP) weekly, and interleukin-6 (IL-6) and iron parameters every fourth week. All-cause mortality was observed during 36 months follow-up. Cox’s proportional hazards ratios (HR) were calculated for mortality and were adjusted for potential confounding factors. The relation between Delta-He and ESA response was analyzed by dividing the pts into tertiles based on their ESA hyporesponsiveness index (EHRI, calculated as weekly ESA dose per kg bodyweight divided by the Hb level). The relationship between inflammatory markers, iron parameters, and Delta-He was evaluated in pts and a group of healthy subjects (n=87).

Results: Delta-He was independently associated with mortality (HR 0.70/pg (0.50-0.97), p<0.05) after adjustment for age, gender, IL-6, nutritional status (subjective global assessment) and Davies comorbid score. Delta-He (p<0.01), Ret-He (p<0.01), IL-6 (p<0.05) and hs-CRP (p<0.05) were significantly different in the tertiles of EHRI. Delta-He was significantly associated with IL-6 (rho = -0.45, p<0.001), hs-CRP (rho = -0.36, p<0.001), Ret-He (rho = 0.63, p<0.001), plasma iron (rho = -0.43, p<0.001), and EHRI (rho = -0.43, p<0.001) in the PD pts. The linear mixed model showed that time, hs-CRP and Davies comorbid score influence significantly the variability of Delta-He. Intraclass correlation analysis suggests that Delta-He variation is high within individual pts. Delta-He was significantly associated to Ret-He in healthy subjects (rho = 0.65, p<0.001).
INTRODUCTION AND METHODS: DOPPS identified 6 modifiable haemodialysis practices associated with increased mortality risk: catheter access (i.e. arteriovenous fistula), Kt/V<1.2, serum PO4>5.5mg/dl, serum albumin<3.5g/dl, interdialytic weight gain (IDWG)>5.7%, and HB<11g/dl. We examined these 6 modifiable risk factors using baseline data of the MONITOR-CKD5 study, a European study examining the multi-level determinants, predictors and clinical outcomes of biosimilar epoetin alfa in haemodialysis patients.

METHODS: Prospective 24-month pharmacoepidemiological study of 1615 CKD5 patients enrolled to date with renal anaemia on biosimilar epoetin alfa treatment in 10 European countries.

RESULTS: Mean age was 64.8±14.8y. Mean time since CKD diagnosis was 3.7±4.9y. Primary CKD5 etiologies were diabetic nephropathy (25.5%), chronic glomerulonephritis (20.2%), and renal vascular disease (15.3%). Table 1 shows the 6 modifiable risk factors for both the MONITOR-CKD5 data and the 2002-03 US DOPPS II sample (* denotes region with superior result). For the 2 risks with higher prevalence in the European MONITOR-CKD5 study, there was significant variability by country ranging from 30.7-57.4% for HB<11g/dl (p=0.0001) and from 18-93% for Kt/V<1.2 (p=0.0001). Patients from Central and Eastern Europe were significantly more likely to have HB<11g/dl than patients from Western Europe (p=0.0032); there was no significant difference between the regions for Kt/V<1.2 (p=0.080).

CONCLUSIONS: Management of some modifiable risk factors in HD in Europe in 2010-12 more often reaches guideline recommendations than in US-DOPPS 2002-03. Yet, despite reduction in target HB in ESA labels and best practice guidelines, country and regional disparities persist in HB achievement as well as Kt/V.
LONG-TERM EFFECTS OF CORRECTION OF ANEMIA WITH RECOMBINANT HUMAN ERYTHROPOIETIN (rEPO) ON BLOOD VOLUME IN CHRONIC HEMODIALYSIS PATIENTS

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Introduction and Aims: To investigate blood volume changes in chronic hemodialysis patients before and after long-term treatment for their anemia with rEPO.

Methods: This study included forty patients undergoing regular hemodialysis (mean age 38 ± 11 years, mean duration of dialysis 5.3 ± 3 years) with severe renal anemia (hematocrit < 0.25). There was no iron deficiency; serum folate acid and vitamin B12 were in normal range. All patients were treated with rEPO intravenously three times in week in adjustable doses. Blood volume were evaluated at three occasions: a) basal - before EPO therapy, b) intermediate - after reaching target hemoglobin (Hb) of 100g/L, and c) late - after 12 ± 2 months of therapy with rEPO. Blood volume was measured with Tc-99m-labeled human serum albumin using dilution technique adjusted and validated in our department.

Results: At the beginning mean Hb was 72 ± 8 g/L, increased to 111 ± 12 g/L at intermediate studies during 3.8 ± 1.6 months and was maintained thereafter. The hematocrit value was 24.4 ± 0.9% at the basal studies, rose to 29.7 ± 1.1% intermediate (p < 0.01), and was further increase to 36.7 ± 1.5%. p < 0.01, at late studies. After correction of anemia, red-cell volume was significantly increased from 12 ± 3 ± 16 ± 3 mL/kg in intermediate studies, p < 0.0001. However, no further significant change between intermediate and late studies (14 ± 4 mL/kg) was found. Consequently, plasma volume was significantly decreased from basal 48 ± 9 to 42 ± 9 mL/kg at intermediate examinations, p < 0.02. and was further decreased to 38 ± 7 mL/kg in late studies, p < 0.001. In contrast, total blood volume remained unchanged at intermediate studies (58 ± 11 vs. 57 ± 10 mL/kg, p = NS), whereas blood volume was significantly reduced to 52 ± 8 mL/kg, p < 0.001, in late investigation.

Conclusions: Significant increase in red-cell volume occurred shortly after correction of anemia with EPO in patients on chronic hemodialysis, followed by decrease in plasma volume. However, total blood volume only decrease after a long-term treatment of anemia in chronic hemodialysis patients.

CHANGING FROM DARBEPOETIN TO EPOETIN ZETA – WHAT IS THE CONVERSION FACTOR IN HEMODIALYSIS PATIENTS?

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Introduction and Aims: With the rise of bio similar erythropoiesis-stimulating agents (ESA’s) the choice of treatment for renal anemia has increased as well as the need for converting from one ESA to another. Especially, the conversion factor between darbepeotin and erythropoietin is still unclear and has attracted little attention (1).

Methods: 79 hospital-based HD patients at the Department of Nephrology at Skåne University Hospital, Malmö and Lund, who could be followed for six months after changing from darbepeotin to epoetin zeta, were included (observation period 1). Initially, the patients were given darbepeotin once a week intravenously (iv) and were switched to epoetin zeta once a week iv. The majority of the patients were on regular intravenous iron (Venoferr). This schedule was left unchanged leaving the transferrin saturation and ferritin levels stable. The initial epoetin zeta dose was calculated according to the conversion factor previously reported, when switching from epoetin beta (Darb) to darbepeotin, 257:1 (2). After an observation period of 6 months the patient required an epoetin zeta dose exceeding 5000 U per week were converted from once to twice a week iv (observation period 2). This subgroup of patients was also followed for 6 months. The conversion factor was calculated as the mean of each patient’s individual conversion factor.

Results: Results before and six months after switch of ESA (mean values ± SD). During the first observation period (6 months) the switch was from darbepeotin to epoetin zeta once weekly iv to epoetin zeta (epo zeta) once weekly iv. During the second observation period (6 months) the switch was from once to twice weekly to epoetin zeta iv for patients with a dose > 5000 U/week.

Conclusions: In this clinical follow-up a conversion factor of 1.296 was required to maintain a stable hematocrit when changing from darbepeotin iv to epoetin zeta once weekly iv. This is higher than we reported earlier for a switch from epoetin beta to darbepeotin (2). One reason for the higher conversion factor in the present study could be different routes of administration. In the present study the switch was from iv darbepeotin to iv epoetin zeta, whereas the switch from epoetin beta to darbepeotin was from subcutaneous to iv administration. Moreover, we found a significant gain in hematocrit level when giving epoetin zeta twice instead of once per week at an equivalent dose. Ref 1. KDQCI-UK 2006 Update on hemoglobin target 2. Sterner G, Priutz KG. Conversion from epoetin beta to darbepeotin: what is the equivalent dose? Nephrol Dial Transplant 2008; 23(1): 301.
**SP540** REDUCTION IN ERYTHROPOIESIS-STIMULATING AGENT REQUIREMENTS AFTER INTRAVENOUS FERRIC CARBOXYMALTOSE IN ND-CKD PATIENTS PREVIOUSLY ON ORAL IRON THERAPY

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**Introduction and Aims:** The anemia management of CKD continues to have several controversial components: optimal Hb levels, ESA doses, potential adverse outcomes and costs. The aim of this pilot study was to determine if a possible reduction in erythropoiesis-stimulating agent (ESA) requirements would occur after switching from oral to intravenous iron as ferric carboxymaltose (FCM) administration (single dose of 1000mg) in patients with ND-CKD.

**Methods:** Patients’ ESA requirements during a 5-month period on oral iron were compared to those during a 5-month period after switching to FCM. The goal of both treatment regimens was to maintain Hb values according to international recommendations. Key inclusion criteria: ND-CKD (CrCl ≤ 60 mL/min), Hb between 11-12 g/dL, serum ferritin < 100 ng/mL, or TSAT < 20%, being treated with ESA and oral iron during the last 6 months according to regular (monthly) institution protocol. A pre-specified algorithm was followed for the ESA dosing during the iv iron regimen period.

**Results:** Twenty-five patients were included (mean age 70.6 ± 12.4, 13 males, 12 females). Primary end-point and lab values see Table. Two patients were hospitalized in the oral iron regimen period (respiratory tract infection) respectively once in the iv iron regimen period.

**Conclusions:** Among ND-CKD patients previously on oral iron therapy, switching to intravenous FCM (single dose of 1000mg iron) was associated with a significant and substantial reduction (81.2 ± 9.2%) in ESA administration and an improvement in the oral iron regimen period.

**SP541** ERYTHROPOIESIS STIMULATING AGENTS IN PD PATIENTS - GENDER DEPENDANT DIFFERENCES

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**Introduction and Aims:** In the general population, haemoglobin (Hb) concentration is higher in men than in women, the average difference being as high as 2-3 g/dL between genders. However, in both target Hb levels in dialysis patients set constant regardless of the patient’s sex. The aim of this study was to evaluate the differences in Hb concentration between genders in patients undergoing peritoneal dialysis (PD) and to assess the usage of erythropoiesis stimulating agents (ESA) in these subjects taking gender into account.

**Methods:** The study was performed on the basis of the national PD registry, in 2205 prevalent PD patients. For comparisons, the weekly dose of ESA in patients not taking erythropoietin-β was converted into erythropoietin-β units.

**Results:** The study included 1050 women and 1155 men. There were no significant differences between genders regarding age and co-morbidities. The percentage of women on ESA was significantly higher than men (68.1 vs 60.7%; p<0.001). Similarly, the average weekly dose of ESA was higher in women than in men (2435 vs 2119 IU).
level in control and responder groups. In the non-responder group, negative significant correlation was found between hepcidin and erythropoietin (EPO) as EPO down regulates the production of hepcidin by the liver. Conclusions: Hepcidin may become an important biomarker of iron status in CKD, especially because current markers appear suboptimal.

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**SP544**

### IS HEMOGLOBIN CHANGE DURING HEMODIALYSIS SIGNIFICANT?

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**Introduction and Aims:** Anemia is one of the most common signs of CKD, including HD patients and is mainly caused by relative erythropoietin deficiency. The recommended only partial anemia correction is based on higher mortality associated with higher Hb concentration, particularly with Hb above 130 g/L. The target Hb is the concentration just before the first or the middle week HD, with presumably maximal body fluid overload at that time. The aim of the study was to determine whether HD itself renders Hb concentration above the safety range by the fluid overload removal.

**Methods:** Study in 30 patients (21 F, 29 M) treated by HD 3 times weekly for at least 3 months, with stable Hb concentrations, ranging from 100 to 130 g/L during the last 3 months. Excluded were those with global heart failure, nephrotic syndrome, decompensated liver failure or total protein plasma concentration less than 60 g/L or albumin below 30 g/L. Each patient underwent Hb concentration measurement 3 times (the 1st just before HD, in upright position - Hb1, the 2nd just before HD, after 30 minutes in supine position, lying on back - Hb2, the 3rd just before the end of HD, supine - Hb3) and volume of the fluid removal (ultrafiltration) determination as the difference between body weight at the beginning (W1) and at the end of the HD.

**Results:** The patient’s age at the time of the study was 68±11.4 years. They were treated by HD for the previous 80±68 months. Mean Hb1 was 116.7±9.2 g/L, Hb2 107.5±10.3 g/L and Hb3 125.2±11.7 g/L. Mean Hb2 was higher than Hb1 for 10.2±7.7 g/L or 8.9±6.9%, whereas for 17.6±8.5 g/L or 16.7±8.5% from Hb2. The differences between Hb concentration before and at the end of HD were significant (T0 vs T12: 13.9:±6.0, T12 vs Hb1: 5.9:±0.01). Significantly lower hepcidin levels were measured in the study group, while an increase has been detected in the control group. A drop of albumin was detectable in the study group; the levels stabilized after about 2 weeks at the lower level. The intra- and interindividual HDs' RRs of Hb and Hb FLCS had been high in the study group compared to controls (80 ± 7% and 72 ± 9% vs. 47 ± 9% and 12 ± 8% (P <0.005).

**Conclusions:** The data of this pilot study suggests that high cut-off dialysis allows a significant better removal of large uremic toxins (3 FLCS) and improves ESA responsiveness (indicated by a rise in Hb levels and a fall in hepcidin). Larger studies with strict control of ESA dose adjustment are needed to confirm if regular treatment with high permeability membranes leads to an improvement in anemia of chronic inflammation in HD patients.

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**SP545**

### IMPROVEMENT OF ESA RESPONSIVENESS IN HEMODIALYSIS PATIENTS TREATED BY HIGH CUT-OFF HEMODIALYSIS - PILOT STUDY (CIEPO-PILOT)

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**Introduction and Aims:** Chronic inflammation in hemodialysis patients is caused by multiple inflammatory stimuli and linked to clinical signs and symptoms and cardiovascular mortality. Inflamed dialysis patients also show an impaired response to erythropoiesis-stimulating agents (ESA). Aim of this pilot study was to investigate if HD treatment with a membrane having a high molecular permeability in a broad molecular weight range improves ESA responsiveness (ESA resistance index, ERI) and attenuates the chronic inflammatory state.

**Methods:** 24 ESRD patients (6 women, 65 ± 16 years, 70 ± 11 kg) on 3x per week chronic high-flux HD or HDF (for ≥3 months, with stable Hb concentrations, ranging from 100 to 130 g/L during the study period) are shown.* p<0.05 vs T0; ° p<0.05 vs T12

**Results:** A drop of albumin was detectable in the study group; the levels stabilized after about 2 weeks at the lower level. The intra- and interindividual HDs’ RRs of Hb and Hb FLCS had been high in the study group compared to controls (80 ± 7% and 72 ± 9% vs. 47 ± 9% and 12 ± 8% (P <0.005).

**Conclusions:** The data of this pilot study suggests that high cut-off dialysis allows a significant better removal of large uremic toxins (3 FLCS) and improves ESA responsiveness (indicated by a rise in Hb levels and a fall in hepcidin). Larger studies with strict control of ESA dose adjustment are needed to confirm if regular treatment with high permeability membranes leads to an improvement in anemia of chronic inflammation in HD patients.
EFFECTS OF IRON PARAMETERS ON PLATELET COUNTS IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Targeting to normal hemoglobin levels using erythropoiesis-stimulating agents (ESAs) is associated with risk of death or cardiovascular events in chronic kidney disease (CKD) patients. Platelet reactivity plays a central role in the genesis of thrombosis and thromboembolic events, especially in atherosclerotic cardiovascular disease and the leading cause of death in these patients. Further, it has been postulated that increased mortality risk is caused by thrombocytosis as a result of functional iron deficiency induced by ESAs treatment, “platelet link hypothesis [E. Streja et. al., AJKD 2008]”. However, whether platelet counts (Plt) within the normal range could be affected by iron reactivity, inflammatory markers such as C-reactive protein (CRP), serum ferritin (Fer), malnutrition and ESAs dose has not been elucidated. Therefore we investigated whether decreased iron reactivity were associated with increased Plt in hemodialysis (HD) patients.

Methods: We examined 154 maintenance HD outpatients from 2002 to 2010, prospectively. Relationships between Plt and iron parameters such as transferrin saturation (TSAT%), serum iron levels and Fer were tested by mixed effect model with adjusting time, age and gender. In 80 out of 154 patients, we also examined which variables were independent correlates of Plt with additional adjustment variables, serum albumin (Alb), CRP, a weekly ESAs dose and a monthly i.v. iron dose within 4-year duration.

Results: In univariate regression analyses, TSAT%, serum iron levels and Hb(10.3) were significantly negatively correlated with Plt (p<.001), while Fer was not (p=.53). TSAT and serum iron levels had flexion point near 21% and 49 ng/mL. In multivariate model, the estimated slopes for TSAT was significantly associated with Plt (n=154, p<.001). For TSAT and CRP, the estimated slopes were significantly associated with Plt after adjustment for Alb, CRP, ESAs dose and iron dose (n=80, p=.0062 and p<.0001). In the analysis for trends and variability of TSAT was significantly negatively associated with that of Plt (n=154, p<.0001 for both). For trends and variability of Fer, the nonlinear effect was detected and it was significantly positively associated with that of Plt only below 50 (n=154, p=.0028). Trends and variability of TSAT and Fer were associated with that of Plt significantly after adjustment for Alb, CRP, ESAs dose and iron dose (n=80, p=.0004 and p=.01).

Conclusions: We demonstrated that Plt was negatively correlated with TSAT and positively correlated with Fer after adjustment for Hb, Alb, CRP, ESAs dose and iron dose. These observations suggest that decreased functional iron levels (TSAT) and increased iron storage regardless of ESAs may directly induce thrombocytosis, thereby being involved in the progression of cardiovascular disease in HD patients.
PATHOPHYSIOLOGY AND CLINICAL STUDIES IN CKD 5D

SP548 CORRELATES OF INTRADIALYTIC CHANGE IN SERUM SODIUM: THE ROLES OF PRE-DIALYSIS DIALYSATE-TO-SERUM SODIUM GRADIENT AND TREATMENT TIME

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Introduction and Aims: In hemodialysis (HD) patients, sodium concentrations in the dialysate (DNa+) and serum (SNa+) and the resulting sodium gradient (GNa+) affect SNa+ changes during HD. A rise of SNa+ post-dialysis may increase osmolality and trigger post-dialytic thirst. GNa+ is a potentially modifiable determinant of post-HD SNa+ (Hecking, Am J Nephrol 2011). Here we expand current knowledge by investigating the influence of treatment time on post-HD SNa+ in three datasets encompassing dialysis patients undergoing HD with distinctly different treatment times.

Methods: In this observational study we investigated patients undergoing conventional, short daily and long nocturnal HD. The association between pre-HD GNa+ and the post-HD minus pre-HD SNa+ difference (PPSD) was assessed by simple linear regression. To account for multiple measurements per patient, a linear mixed model (LMM) was developed with random intercepts and slopes with PPSD as the dependent variable, and pre-HD GNa+ and treatment time as fixed effects.

Results: We studied 188 HD patients with the following treatment characteristics: a) conventional HD (n=65; average treatment time: 152 minutes); b) short daily HD (n=25; average treatment time: 126 minutes) and c) long nocturnal hemodialysis (n=98, treatment average time: 422 minutes). Pre-HD GNa+ significantly predicted PPSD in all three patient groups (Figure 1 for correlation coefficients), and in the entire pooled dataset (R2=0.44). LMM analysis corroborated GNa+ as a predictor of PPSD (estimated slope 0.55 mEq/L; intercept -1.05 mEq/L; both P<0.001). Treatment time was not associated with PPSD (estimated slope -0.001 mEq/L per minute; P=0.5).

Conclusions: While PPSD is predictable based on pre-HD GNa+, it is not correlated with treatment time. This may be due to the dominant initial effect (reflected by the magnitude of the Estimate in comparison to the Estimate of treatment time in the model) of GNa+ in the first one or two hours of HD, which dissipates later in the treatment. Formal intradialytic studies of sodium kinetics should provide further insights into the dynamics of SNa+ change during HD.

SP549 ADEQUATE SODIUM PROFILING EFFECTS GOOD QUALITY OF DIALYSIS AND SODIUM & FLUID BALANCE

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Introduction and Aims: We developed a dialysis maneuver of sodium profiling in order to avoid Intra-Dialytic Hypotension (IDH) in the group of prone patients.

Methods: The neutral step down sodium profile (time-averaged mean of dialysate conductivity 142.25) was compared to conventional dialysis (conductivity 140) in terms of dialysis quality (Kt/V), Interdialytic Weight Gain (IDWG) and diffuses sodium gain (ANa), as pre-to-post dialysis change. Positive sodium balance was considered when ANa>0. The parameters were measured in the 4 weeks period of treatment maintenance.

Results: 86 patients were included in the study and sodium-profiling pattern was applied at 45(52%) of them. Controls were dialyzed by same dialyzer membranes and surfaces as IDH prone patients. There was no significant difference in the diffuse sodium gain in both groups (p=0.328). Positive sodium balance occurred in same number of patients (8[20%] vs 13[29%], p=0.330). Also, the IDWG, episodes of Intra-Dialytic discomfort, dialysis time and required UF to achieve dry weight did not differ (p=0.376, p=0.182, p=0.364, p=0.698, p=0.143).

Conclusions: We found the neutral sodium balance profile to be a good choice, which ensures dialysis quality without sodium gain-related complications.

SP550 IODINATED CONTRAST MEDIA CAN INDUCE LONG-LASTING OXIDATIVE STRESS IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Due to their comorbidities, dialysis patients have many chances to undergo radiologic procedures using iodinated contrast media. We aimed to assess time sequenced blood oxidative stress level after contrast exposure in hemodialysis (HD) patients compared to those in the non-dialysis population.

Methods: We included 21 anuric HD patients (HD-CAG group) and 23 persons with normal renal function (non-HD-CAG group) scheduled for coronary angiography (CAG) and assessed 4 oxidative stress markers (AOPP, advanced oxidation protein products; catalase; 8-OHdG, 8-hydroxydeoxyguanosine; and MDA, malondialdehyde) before and after CAG, and subsequently up to 28 days. As controls, we chose 23 healthy volunteers who visited the health promotion center for general health

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examination and 22 anuric HD patients who did not perform CAG.

Results: In the non-HD-CAG group, only AOPP increased immediately after CAG and returned to baseline within one day. However, in the HD-CAG group, all four oxidative stress markers were significantly increased starting one day after CAG, and remained elevated longer than those in the non-HD-CAG group. Especially, AOPP level remained elevated for a month after contrast exposure. Table 4. Baseline oxidative stress markers in the study subjects.* Values are mean ± SD. † p<0.05 vs. non-HD-CAG group; HD, hemodialysis; CAG, coronary angiography; AOPP, advanced oxidation protein products; 8-OHdG, 8-hydroxydeoxyguanosine; MDA, malondialdehyde.

Figure 1. Changes in the oxidative stress markers after CAG, *p<0.05 vs. baseline; †p<0.05 vs. non-HD-CAG group; 5, p<0.05 vs. HD-control AOPP, advanced oxidation protein products; 8-OHdG, 8-hydroxydeoxyguanosine; MDA, malondialdehyde.

Conclusions: Our study showed that iodinated contrast media induces severe and prolonged oxidative stress in HD patients.

SP551 SPLANCHNIC ISCHEMIA IS UNLIKELY TO OCCUR WITH MODERATE ULTRAFILTRATION DURING HEMODIALYSIS

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Introduction and Aims: To study whether the magnitude of ultrafiltration-induced changes in splanchnic perfusion in a group of stable hemodialysis (HD) patients was likely to explain splanchnic ischemia.

Methods: During a midweek HD session splanchnic blood flow was measured four times in hourly intervals using indocyanin-green (ICG) clearance and on-line hematocrit monitoring by the CritLine device. (Fresenius Medical Care, Utah, USA)

Mean arterial pressure (MAP) and heart rate were recorded, and splanchnic vascular resistance given in peripheral resistance units (PRU, mmHg.s/mL) was estimated from MAP and splanchnic blood flow.

Results: Seven (4 female) stable chronic HD patients were studied twice, the mean ultrafiltration volume was 1.8 ± 0.7 L. ICG plasma clearance significantly decreased from 0.76 ± 0.35 L/min at dialysis start to 0.63 ± 0.28 L/min (p = 0.01) at the end of treatment. Splanchnic blood flow significantly dropped from 1.16 ± 0.51 L/min to 0.99 ± 0.43 L/min (p = 0.03) corresponding to an average decrease of 14%. MAP and heart rate did not change significantly during the study period. Splanchnic resistance marginally increased from 5.9 ± 2.5 PRU at HD start to 6.7 ± 3.3 PRU (p = 0.25) at dialysis end.

Conclusions: Splanchnic vasoconstriction is an important mechanism to provide hemodynamic stability in hypovolemic states, but prolonged vasoconstriction is thought to lead to regional ischemia and ultrafiltration-induced gut stunning in HD patients. We observed that moderate ultrafiltration only caused a modest decrease in splanchnic blood flow without changes in splanchnic vascular resistance. Therefore, we think that moderate ultrafiltration is unlikely to induce ischemia-mediated changes in the splanchnic region during HD.

SP552 ACE INHIBITOR THERAPY CAN INFLUENCE THE EFFECT OF ACE I/D POLYMORPHISM ON SURVIVAL IN CKD-5D PATIENTS

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Introduction and Aims: The vast majority of clinical observation proved that one of ACE gene polymorphism D/D genotype could be a risk factor for mortality in CKD (chronic kidney disease) patients, however, the mechanism of action has not been answered yet because of conflicting result of morbidity research site. Our hypothesis was that DD genotype is a survival factor as well as its effect could be influenced by ACE inhibitor (ACEi) therapy in dialysed CKD (CKD-5D) patients.

Methods: Among 716 CKD-5D patients 373 subject were treated by ACEi therapy and they were follow up to 20 years long. The ACE I/D polymorphism was detected by PCR method. Genotype distribution of patients was the following: 141 pts with II, 305 pts with ID and 270 pts with DD genotype. The survival time was analyzed in two age groups divided them at age 65 years old. We performed Kaplan-Meyer analysis and the survival time was compared by log rank test.

Results: In patients on ACEi therapy there were not differences in survival time among groups divided by genotypes and age. Without ACEi therapy among patients age < 65 years the median survival time (month) was the following: II genotype (n=45): 107,3 (IR: 58,1-179,5); ID genotype (n=119): 100,5 (IR: 52,9-181,8); DD genotype (n=96): 75,8 (IR: 51,2-123,6) (II vs ID p<NS; ID vs DD p<0.05; DD vs ID p=0.05). Without ACEi therapy among patients age > 65 years the median survival time (month) was the following: II genotype (n=24): 73,1 (IR: 36,1-108,1); ID genotype (n=47): 48,2 (IR: 33,3-80,0); DD genotype (n=42): 50,6 (IR: 34,2-89,2) (II vs ID p=0.05; ID vs DD p<NS).

Conclusions: ACEi therapy can influence the effect of DD genotype on survival time. Without ACEi therapy the survival time is significantly shorter in CKD-5D and age below 65 years patients with DD genotype than with II genotype. Without ACEi therapy the survival time is significantly shorter in CKD-5D patients with DD genotype than with ACEi therapy. Further ACE I/D polymorphism research is needed and during this work ACEi therapy should be taken account. This study was supported by Hungarian Scientific Research Fund OTKA3927.
VASCULAR EFFECTS OF FGF23 IN HAEMODIALYSIS PATIENTS

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Introduction and Aims: FGF-23 levels rise progressively in renal failure. FGF-23 associated vascular toxicity is currently investigated. We investigated the associations of iFGF-23 levels with arterial stiffness and wall thickness in chronic haemodialysis (HD) patients.

Methods: In 81 stable chronic HD patients (52 male, mean age 59.9±15.7y) we measured serum levels of c-terminal FGF-23 (iFGF-23) and intact FGF-23 (iFGF-23) by ELISA, common carotid intima-media thickness (cIMT) by ultrasound, and carotid to femoral pulse wave velocity (PWV) with transdermal applanation tonometry (SphygmCor®, AtCor® Medical). At inclusion patients were older than 18 years, free of active infection, malignancy or liver disease and without a history of steroids. Associations in this setting.

Results: Levels of iFGF-23 (mean log10±SD 2.61±0.41) and cFGF-23 (mean log10±SD 3.51±0.52) correlated strongly with each other (p=0.00, r=0.798), with phosphorus levels (p<0.000 and p=0.003 respectively) and iPTH levels (p<0.001, both). Higher than the mean levels of iFGF-23 but not cFGF-23 were associated with higher cIMT (p=0.03, 95% CI= -0.15 to -0.01), This association was independent of age, gender, and levels of CRP, phosphorus and iPTH (p=0.037, standard beta=0.176). In a subgroup of 59 patients without coronary heart disease (CHD) a PWV<9m/s vs ≥9m/s was associated only with higher iFGF-23 levels (p=0.01, 95% CI= -0.6 to -0.9).

Conclusions: Study limitations include a cross-sectional design, precluding proof of causality, and sample size, affecting statistical power. Nevertheless higher iFGF-23 levels were associated with higher cIMT as already described. Our results hint also to a novel association of iFGF-23 with higher PWV in HD patients without CHD, implying potential association with early vascular toxicity. Although considered equally representative with levels of the intact molecule, FGF-23 fragments tend to accumulate in HD. Therefore iFGF-23 might prove more sensitive in revealing potential associations in this setting.

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<td>CON</td>
<td>24.7±9.0</td>
<td>1.3±0.51</td>
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<tr>
<td>BHD-C</td>
<td>65.5±22.3**</td>
<td>2.48±0.93**</td>
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<tr>
<td>BHD-Tc</td>
<td>35.9±10.8*</td>
<td>1.53±0.52</td>
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<td>HDF</td>
<td>61.9±29.7**</td>
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*p<0.05 vs CON  °p <0.05 vs BHD-Tc

WEIGHT BASED DOSING OF VANCOMYCIN IN HIGH FLUX HAEMODIALYSIS IMPROVES TIME SPENT BELOW TROUGH THERAPEUTIC LEVELS

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Introduction and Aims: Infections cause approximately 10-15% of all deaths in people receiving haemodialysis in Australia. Sepsis as a result of Staphylococcus infection is common in Haemodialysis (HDx) patients. Vancomycin is the antibiotic of choice for MRSA in HDx, but must achieve adequate therapeutic concentrations to be effective. High Flux Hdx influences drug dosing as a result of the >30% clearance of Vancomycin during administration. Vancomycin dosing schedules in High Flux Hdx vary between units. We aimed to compare serum therapeutic Vancomycin levels pre and post weight based dosing implementation in a single centre, Western Health, Victoria, Australia.
Methods: The % time of Vancomycin levels <20 mcg/ml in patients receiving more than a single dose of Vancomycin were compared prospectively i.e. (Pre-WBD) and post (Post-WBD). Vancomycin dosing was as follows: On high flux Hdx: 30mg/kg loading/25mg/kg IV maintenance when level <25 mcg/ml; Off high flux Hdx 25mg/kg loading dose/20mg/kg IV maintenance when level <20 mcg/ml. This was compared to previous ceiling dosing of 1.5g IV when levels were <20 mcg/ml. The % time included the period between the 1st and last dose, and if levels were above or below <15 mcg/ml, the time between this period was split evenly between the target and off target groups. Pre-WBD and Post-WBD groups were compared, results are reported as mean ± standard deviation and groups were compared using student t-tests, p<0.05 was considered significant.

Results: 15 Pre-WBD and 33 Post WBD patients were compared aged 70 ± 16 and 61 ±19 years (p=0.11), with 60% and 52% *(p=0.50) male subjects respectively. There was an average of 4.2± 2.3 and 3.7± 2.6 doses events (p= 0.49) in each group. 25±4.17.3 vs. 9.1± 14.4 % (p<0.001) of time was spent below the therapeutic target <15 in each group.

Conclusions: Weight based dosing delivers better therapeutic levels during the treatment course for MRSA in patients on high flux Hdx, by ensuring less time below trough therapeutic concentrations <15 mcg/ml.

SP556 IS THERE AN ASSOCIATION BETWEEN Copeptin and NT-proBNP in Hemodialysis Patients?
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Introduction and Aims: Copeptin, precursor to vasopressin, is associated with body fluid volume and heart dysfunction. Therefore, this study was intended to investigate the level of copeptin and the relationships with fluid and heart dysfunction markers in patients with hemodialysis.

Methods: This study included forty-one patients with hemodialysis. At the time of their visit for hemodialysis treatment, laboratory data including NT-proBNP levels were collected and excessive body fluid (OH, overhydration, liter) was measured by bioimpedance spectrumometry (BIS). In addition, E/Ea ratios were obtained by echocardiography for assessing left ventricular dysfunction (LVD).

Results: The mean concentration of pre-dialysis copeptin was 224.67±241.91 pg/ml. Pre-dialysis copeptin had positive correlation with pre-dialysis OH (r=0.314, P=0.046), but not with NT-proBNP (r=0.163, P=0.308) and E/Ea ratios (r=0.023, P=0.888). Body fluid markers other than copeptin, such as NT-proBNP and pre-dialysis OH, E/Ea ratio, all showed significant correlation with each other. Based on previous reports, non-LVD and LVD groups were defined by a cut off value of NT-proBNP 5300 [pg/ml] (specificity 0.8, sensitivity 0.93). When comparing the non-LVD group with the LVD group (non-LVD vs. LVD), the results showed significant differences in pre-dialysis copeptin (141.33±209.20 vs. 259.9±255.7 pg/ml, P=0.014), NT-proBNP (2294.70±1233.53 vs. 22826.85±11739.56 pg/ml, P=0.000), pre-dialysis OH (1.75±1.03 vs. 3.15±1.90 liters, P=0.023), E/Ea ratio (4.33±1.30 vs. 6.00±2.27, P=0.002), KIV (3.12±0.13 vs. 1.47±0.25, P=0.014). In addition, the ROC curve for discriminating LVD from non-LVD showed that the AUC of pre-dialysis copeptin was 0.737 (P=0.023), and the cut-off value was 125.48 pg/ml (specificity 0.8, sensitivity 0.7).

Conclusions: The level of pre-dialysis copeptins was elevated in patients with hemodialysis. In addition, copeptin was correlated with pre-dialysis volume status. However, copeptin did not show a significant relationships with NT-proBNP, E/Ea ratio. Finally, the patients with LVD showed higher level of pre-dialysis copeptins than the patients without LVD.
also no statistically significant differences in survival between the cirticotic and non-cirticotic patients. When we analyzed the subgroups according to dialysis modalities, HBV carriers and patients with liver cirrhosis were not statistically significantly associated with mortality among patients undergoing HD and PD, respectively.

**Conclusions:** HBV and liver cirrhosis do not influence mortality in patients with ESRD. Regardless of dialysis modalities, the effect of HBV and liver cirrhosis on mortality was not different.

**Introduction and Aims:** Many studies reported that LTD improves mortality of hemodialysis patients. Although routine laboratory data of LTD patients were not monitored, any other specific data were not enough reported. The purpose of this study was to measure serum IL-6, TNF-α, FGF-23 including routine laboratory data in order to reveal the efficacy of LTD.

**Methods:** Subjects were 206 hemodialysis patients, who accepted the consent of our study in documents. They were well-controlled out-patients in our clinics and divided in two groups, whose hemodialysis product, HDF was higher or lower than 54 (ex. 6 hours/session and 3 times weekly). HDP is an index of dialysis adequacy and calculated to reveal the efficacy of LTD.

**Results:** Serum phosphorus level fell significantly (P<0.001), together with a significant increase of serum calcium (P<0.001). There was more decrease of serum β2-MG and IL-6 in LTD patients compared to those in SD patients. Furthermore, serum levels of TNF-α were significantly lower in LTD patients compared to those in SD patients.

**Conclusions:** LTD might bring better outcome to hemodialysis patients.
In healthy population due to their positive balance of magnesium in kidney. There are several studies which reported that serum magnesium level was correlated with endothelial function positively. Recently it has been reported the patients with higher serum magnesium level revealed the less endothelial dysfunction in CKD patients. Thus, the following study was carried out in an effort to redefine the relationship between serum magnesium level and endothelial dysfunction to those on hemodialysis (HD) with the end-stage renal disease (ESRD).

Methods: This is a cross-sectional study. The enrolled 27 ESRD receiving HD patients were subjected to the measurement with iontophoresis, and FMD (flow mediated vasodilation), IMT (intima-media thickness), which represented endothelial function assessment from February 2011 to September 2012. And also the average serum magnesium level in patients was measured for the last three months including examination month. The Pearson’s correlation coefficient analysis was performed to define the association magnesium and endothelial function.

Results: From univariate analysis, higher serum magnesium level was associated with better endothelium-dependent vasodilation (EDV) of FMD in ESRD undergoing hemodialysis (r=0.516, p=0.007). When participants were divided into two groups according to median value of magnesium level (3.466 mg/dl), there are significant difference in EDV of FMD (less than 3.466 mg/dl: 8.26±3.13% vs. more than 3.466 mg/dl: 8.65±3.33%, p=0.008). Smoking, sex, age, chronicity including diabetes mellitus, previous cerebrovascular accident history showed no significant correlation between the serum magnesium level and EDV.

Conclusions: This study showed that higher serum magnesium level may associate with better endothelium function even in ESRD patients. Furthermore, it is required a prospective study of larger population to identify the relationship between magnesium and endothelial function and establish optimal reference range of serum magnesium level instead of strict restriction of magnesium in HD patients.

**Introduction and Aims:** Atherosclerotic vascular complications, related with endothelial dysfunctions are the most important reason of mortality in chronic renal failure (CRD). There are various studies about the factors affecting endothelial functions in CRD. Recent researches showed that endothelial progenitor cells (EPCs) have an important role to maintain the vascular integrity and circulating endothelial cells (CECs) are good markers to assess endothelial dysfunction. In this study we aimed to examine the potential relationship between erythropoietin; which is frequently used to examine the seasonal variation in end-stage renal disease patients. Therefore, we investigated the seasonality of vitamin D and the prevalence of vitamin D deficiency in haemodialysis (HD) patients.

**Methods:** In a prospective observation study, we evaluated 239 patients on HD. Serum 25-hydroxyvitamin D (25-OHD) levels were measured at the end of spring (June), summer (September), autumn (December), and winter (March). Vitamin D deficiency was defined as a 25-OHD level < 15 ng/ml.

**Results:** 25-OHD levels at the end of spring, summer, autumn, and winter were 11.9 ± 4.9, 12.8 ± 5.8, 8.9 ± 4.1, 9.1 ± 3.9 ng/mL, respectively (p < 0.001). There were 192 (80%), 169 (71%), 224 (94%), and 225 (94%) patients with vitamin D deficiency at the end of spring, summer, autumn, and winter, respectively. Excluding patients taking vitamin D analogues (n=117), the 25-OHD level at the end of spring, summer, autumn, and winter was 12.2 ± 5.3, 13.6 ± 6.0, 9.4 ± 4.7, 9.5 ± 4.1 ng/mL, respectively (p < 0.001). Multiple linear regression showed that female, diabetes, and a history of medications with a vitamin D analogue during the study period were negative correlated with 25-OHD levels.

**Conclusions:** Vitamin D deficiency is very common, and there is marked seasonal variation in the vitamin D levels in HD patients. Patients who are female, diabetics, and have a history of vitamin D analogue medication should be monitored for vitamin nutrition carefully and vitamin D supplementation should be considered.

**Introduction and Aims:** Hypotension is one of the most common and serious complications during hemodialysis (HD) treatment. The purpose of this study is to examine the correlation between blood pressure (BP) and the sounds of internal shunt. And to evaluate whether continuous measurement of sounds of shunt would be useful for early detection of fall in BP of patients during HD.

**Methods:** 26 stable patients (19 male, 7 female) treated in our institute were surveyed. 6 had diabetes and the mean age was 67.8±11.9. The mean treatment time was 3.7 hours (for 2-3days per week) and the length of HD therapy was 7-56.8 years. During HD therapy, we obtained the data of sounds of internal shunt by using electronic stethoscope (Elckio, Asahikasei) equipped with the return line of HD. We estimated BP by analyzing the amplitude of sounds of shunt and calculated the correlation between estimated BP (ERB) and systolic BP taken every 15 minutes. Then we evaluated a usefulness of this method by calculating the accuracy of early diagnosis of BP falls. The rate of EB falls was surveyed which could correctly diagnose BP drops. BP falls were defined with systolic BP reduction over 20% compared with BP at the time of 30 minutes after starting of HD.

**Results:** The mean correlation factor between ERB and actual BP was 0.78 (p<0.001) and the accuracy of diagnosis of BP falls was 90% (26:29).

**Conclusions:** We showed the correlation between BP and ERB from the sounds of shunt. This method would be helpful for early detecting changes of circulation dynamics of HD patients.
immunosuppression. This clinical entity associates with high prevalence of mortality and morbidity.

Methods: We describe several cases of patients receiving hemodialysis who were diagnosed with spondylodiscitis in a period of three years. Blood cultures were positive in five cases and the causative microorganism was staphylococcus aureus. Three patients suffered from diabetes type II and they all were on hemodialysis using a central venous catheter. The manifestations of the infection were fever (not too high) and acute back pain (not successfully controlled with plain pain killers). Furthermore they were all found with positive inflammatory markers like high white blood cell, CRP and ESR.

Results: The diagnosis of spondylodiscitis was based on MRI and blood cultures. Biopsies of the lesion were performed on five patients and pyogenic infection was found. All patients were treated by intravenous antibiotics which was a combination of daptomycin, ciprofloxacin and rifabutin. After a two-month period the inflammatory markers were found negative and the patients' clinical status was significantly improved.

Conclusions: Spondylodiscitis in hemodialysis patients especially in those with central venous catheter is a serious condition and should be suspected when fever and acute or chronic vertebral pain are evident. Aggressive antibiotic therapy should be used at least for two months or until the inflammatory markers are found negative.
Nephrology Dialysis Transplantation

SP572 | COGNITIVE FUNCTIONS AMONG ELDERLY HEMODIALYSIS PATIENTS

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Introduction and Aims: As the hemodialysis patients are getting older, it is important to realize special issues related to aging. Moreover, the number of people who have kidney disease is increasing more rapidly in geriatric population than other age groups. Memory complaints in elderly patients are common problems. Both memory complaints and chronic kidney failure may have negative effects on daily living activity of elderly patients. The aim of this study was to evaluate the cognitive function and activity of daily living of elderly hemodialysis patients.

Methods: Patients older than 65 years who were on hemodialysis for more than 3 months and gave informed consent were included in the study. The patients were dialysed for four hours thrice a week. The study was approved by the local ethics committee of BUV (no: 9/13). All patients were evaluated according to the comprehensive geriatric assessment methods used by MARTHEL Index (B1), instrumental activity of daily living (IADL), mini mental stage examination (MMSE), and geriatric depression scale (GDS) tests by the same investigators (AC, EA) during the midweek hemodialysis session in the dialysis units. Statistical analyses were performed using IBM SPSS software version 19.0. Continuous variables were described by the use of statistical characteristics (means and standard deviations). Discrete variables were described as counts and percentages.

Results: 121 (53 F, 68 M, mean age=73.1 ± 6.11 years) patients were included in the study. The mean duration of HD was 6.14±4.11 (range: 1-18 years). Hemodialysis fistula were present among 89% of the patients. The others (11%) had catheters for dialysis access. According to the comprehensive geriatric assessment, results are presented in the table. 25 (21 F, 34 M, mean age: 72.36±3.6 years) patients did not have depression when GDS results were analysed. 28 (13 F, 15 M, mean age: 73.4±5.3 years) patients had mild depression scores. Moderate depression scores were detected in 31 (15 F, 16 M, mean age: 73.2±5.8) patients. Only seven (5.7%) patients had severe depression score and they were on HD for a mean of 61.95 years which was not statistically different then the duration of HD of the other patients. 61 (21 F, 40 M, mean age:71.5±5.5 years) patients had upper than 24 in MMSE test. The duration HD was not different among the patients with different MMSE scores. According to ADL scores, 62 (61.2%) patients had lower than 95% in B-ADL and 90 (74.4%) patients had lower than 15/17 in I-ADL. The HD duration was not different among the patients with different ADL scores, either.

Conclusions: Our results demonstrated that HD negatively affected mood, cognitive functions, and activity of daily living performance of elderly patients with chronic kidney failure. Therefore, these problems should be kept in mind under the HD therapy for elderly patients.

SP573 | EFFECT OF HEMODIALYSIS ON COGNITIVE FUNCTION IN END STAGE RENAL DISEASE PATIENT

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Introduction and Aims: Uremia is associated with impairment of different cognitive functions in patients with end stage renal disease (ESRD). However the pathogenesis of this cognitive dysfunction is still unknown. In this study, Symbol Digit Modalities Test (SDMT) and Complex Reaction Time Test (CRT), a battery of computer generated psychological tests were used to assess changes in cognitive function due to haemodialysis (HD) treatment.

Methods: We measured cognitive function in 41 ESRD patients maintained on HD, one hour before and one hour after they underwent HD. To evaluate whether removal of uremic toxins during HD session is associated with change in cognitive functions selected population of 41 (13 females, 28 males) adult patients on maintenance (4.07 ± 2.98 years) HD (aged 60.83 ± 11.14 years) were investigated. Assessment of cognitive function was performed by SDMT and CRT tests to measure simple visual discrimination of signal location, short-term memory, simple convergent visual orientation and convergent thinking test. Results of CRD-series tests were given as total time of test solving (TT) and minimum time of test solving (MT). Higher CRD-series tests scores (TT and MT measured in seconds) indicate poorer cognitive performance. Also, SDMT was used to measure oculomotor abilities and hand-eye coordination. Higher SDMT score indicated better cognitive performance.

Results: The results demonstrated a significantly better cognitive performance in MT of solving simple convergent visual orientation test (1.40 ± 0.44 vs. 1.26 ± 0.41, p = 0.004), TT of solving convergent thinking test (222.05 ± 77.27 vs. 210.33 ± 68.10, p = 0.034) and SDMT test score (29.59 ± 11.24 vs. 32.07 ± 13.07, p = 0.002) after HD treatment.

Conclusions: Removal of uremic toxins by HD leads to an improvement in cognitive processing. Further research, with larger number of participants in a prospective research model, should continue to examine which cognitive domains are particularly related to uraemia in ESRD population.

SP576 | ATORVASTATIN (ATO) TREATMENT IS ASSOCIATED WITH A NON-SPECIFIC INCREASE IN MONOCYTE CD36 EXPRESSION IN HEMODIALYSIS (HD) PATIENTS

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Introduction and Aims: ATO may influence CD36 directly or by improvement of serum lipid profile. To elucidate this problem, we examined monocyte CD36 expression during therapeutic lifestyle change (TLC) or ATO treatment in HD patients.

Methods: HD patients (n=49), dyslipidemic according to KDOQI (2003) and not taking lipid lowering drugs, were enrolled into the prospective study started from 4 week education in TLC (low-fat diet and physical activity). In 34 persons, still dyslipidemic after 21 weeks from TLC implementation, ATO was added for 14 weeks. After 4 weeks, an initial ATO dose (10 mg/d) was increased to 20 mg/d in still dyslipidemic patients. Only patients who underwent entire interventions (TLC n=42, ATO n=32) were analyzed. Efficacy of interventions was evaluated by improvement of serum lipid profile. Individuals, age and gender matched to enrolled HD patients, which declared full health, but showing dyslipidemia according to criteria of HD patients, served as controls (n=37).

Results: Improvement in serum lipid profile in HD patients were shown after 14 weeks from the start of both interventions. TLC-induced serum LDL-Ch decrease (141±56 vs 116±27 mg/dL, HDL-Ch 64±16.4 mg/dL, triacylglycerols (TG) 136±71 mg/dL, CD36 MFI 2,054 ±1,413. In both interventions, the initial HDL-Ch was lower (p<0.001 for TLC and p<0.004), TT of solving convergent thinking test (222.05 ± 77.27 vs. 210.33 ± 68.10, p = 0.034) and SDMT test score (29.59 ± 11.24 vs. 32.07 ± 13.07, p = 0.002) after HD treatment.

Conclusions: Removal of uremic toxins by HD leads to an improvement in cognitive processing. Further research, with larger number of participants in a prospective research model, should continue to examine which cognitive domains are particularly related to uraemia in ESRD population.
Toward personalized haemodialysis by low molecular weight amino-containing compounds: future perspective of patient metabolic fingerprint

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Introduction and Aims: Patients on regular haemodialysis (HD) treatment generally tend to develop a state of carnitine deficiency due to reduced renal synthesis, poor dietary intake, and elevated intradialytic loss. This alteration may contribute to several abnormalities such as muscle pain, cardiomypathy, cramps, and dyslipidemia. The aim of our study was to apply targeted metabolic fingerprint in order to evaluate the metabolic status of HD patients.

Methods: Plasma levels of all carnitine esters (short – medium – and long chain) and of several aminocarboxylic acids were quantified in a Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) multiplex experimental setup in 28 uraemic patients (13 non diabetics and 15 diabetics) and in 10 age-matched healthy controls. Samples were taken before and after the first HD treatment of the week. Multiplexed data were collected in LC-MRM (Multiple Reaction Monitoring) and analyzed by unsupervised multivariate analysis.

Results: In diabetic uraemic patients, we observed lower values of propionylcarnitine than in other groups, while acylcarnitine concentration was higher in uraemics when compared to healthy controls. The HD session induced a decline in free, short-chain, medium-chain and dicarboxylic acylcarnitines, whereas the long chain acylcarnitines remained unaffected. Plasma levels of amino acid proline, ornithine, citrulline and serine were significantly elevated in uraemic patients before dialysis compared to controls. For most tested plasma amino acids, a significant reduction after haemodialysis session was found.

Conclusions: Our study is the first that investigated on possible modifications of the system of carnitine in diabetic patients on haemodialysis not only in relation to the condition of deficiency but also compared to lipid and glucose homeostasis alterations typical of diabetes. Our results indicate that abnormalities in plasma carnitine profile are common in HD patients, regardless of the diabetic state. Patient metabolic fingerprint may be a convenient and useful tool to drive supplementation therapies targeted to normalize the altered plasma carnitine composition by a personalized approach, to the potential benefit of the patient.

Eicosapentaenoic acid (EPA) is an independent predictor of all-cause mortality in hemodialysis patients

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Introduction and Aims: Cardiovascular (CV) disease is a major cause of death in hemodialysis (HD) patients, and oxidative stress increases in HD patients, resulting in acceleration of atherosclerosis. In HD patients, oxidative stress is elevated by various factors, such as a dialyzer membrane, a dialysis circuit, dialsate, etc. Eicosapentaenoic acid (EPA) is known as an agent against hyperlipidemia. Further, it has been shown to have antioxidative effect in several studies. Therefore, in the present study, we examine whether EPA treatment may improve all-cause mortality in HD patients.

Methods: We enrolled 176 chronic HD patients at Tokyo Women Medical University Hospital, Tokyo, Japan and Tsuruta Clinic, Tokyo, Japan, during 2008–2011. The primary end-point is all-cause death. Hazard ratios (HRs) for the all-cause mortality were analyzed using a multivariate Cox proportional hazards regression.

Results: We enrolled 176 chronic HD patients at Tokyo Women Medical University Hospital, Tokyo, Japan and Tsuruta Clinic, Tokyo, Japan, during 2008–2011. The primary end-point is all-cause death. Hazard ratios (HRs) for the all-cause mortality were analyzed using a multivariate Cox proportional hazards regression.

Conclusions: EPA treatment may improve all-cause death in HD patients.
EPIDEMIOLOGY CKD 5D - A

SP580 PERIODONTAL DISEASE AND ALL CAUSE AND CARDIOVASCULAR MORTALITY IN HEMODIALYSIS PATIENTS: A PROSPECTIVE MULTINATIONAL COHORT STUDY

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Introduction and Aims: In the general population, periodontal disease is associated with increased cardiovascular mortality. We have evaluated the association between periodontitis and all-cause and cardiovascular mortality in adults on hemodialysis. Methods: ORAL-D is an ongoing multinational prospective cohort study of consecutive adults receiving hemodialysis in 75 outpatient clinics selected randomly from a collaborative dialysis network in Italy, Hungary, Poland, Argentina, Portugal, France and Spain. A dental surgeon evaluated presence of periodontitis with standard methods, defined as a Community Periodontal Index (CPI) score ≥3 during a standardized oral examination. We assessed survival at 12 months using centralized mortality data. We conducted analysis with Cox regression controlling for age, gender, previous cardiovascular event, income status, clinical performance measures, dialysis prescription and performance indicators and depressive symptoms. Results: 3672 dentate hemodialysis patients in the participating clinics received a complete evaluation for periodontitis and completed follow up. Median follow up was 19.9 (17.0 to 28.0) months. 1516 patients (42%) had periodontitis and 339 (10%) died during follow up. Periodontitis had uncertain associations with risks of all-cause (HR 0.86 [95% CI 0.68-1.10]) or cardiovascular (HR 0.85 [95% CI 0.63-1.15]) mortality. Conclusions: Contrary to data in the general population, periodontitis has uncertain associations with all-cause or cardiovascular mortality in patients on hemodialysis. ORALD will be completed by end of 2013.

SP581 THIRST AND ORAL SYMPTOMS IN PEOPLE ON HEMODIALYSIS: A MULTINATIONAL PROSPECTIVE COHORT STUDY (ORAL-D)

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Introduction and Aims: Thirst and xerostomia, the subjective complaint of dry mouth, may be increased in people on hemodialysis due to reduced salivary and lacrimal secretion, intravascular volume changes, fluid-restriction, endocrine hormone abnormalities, and medication use. Existing data for the prevalence of thirst and xerostomia are limited. We evaluated the prevalence of thirst and oral symptoms in adults on hemodialysis. Methods: ORAL-D is a multinational cohort study of oral diseases in consecutive adults on hemodialysis in 75 outpatient clinics selected randomly from a collaborative dialysis network in Europe and South America. We administered xerostomia and thirst inventories based upon validated methodology. We analyzed prevalence data using descriptive analyses. Results: 4720 hemodialysis patients in the participating clinics completed a self-administered questionnaire on oral symptoms. 1773 (38%) patients reported occasional use of candies for dry mouth sensation, 1095 (34%) had difficulties swallowing and 2437 (53%) needed to sip to aid swallowing. 2112 (45%) reported waking up during the night to drink, 1700 (36%) reported dry mouth sensation and 2309 (50%) had dry lips. The mean xerostomia inventory score was 21.14 (SD 5.56). Thirst was a reported problem for 2895 (62%) patients; 3585 (78%) were thirsty during the day and 2377 (47%) during the night. Overall, 1169 (26%) patients reported that thirst influenced their social life. Conclusions: Oral symptoms are highly prevalent in hemodialysis, with marked interference with daily life. Additional study of the predictors of thirst and xerostomia are now needed.

SP582 ECO-FRIENDLY DIALYSIS WITH THE SYSTEMIC DESIGN METHODOLOGY: AN ECO-FRIENDLY DIALYSIS MAY START FOR "THE GRAVE"

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Introduction and Aims: Dialysis produces about 600,000 tons of plastic wastes per year. The Systemic Design is one of the most innovative method to analyse the environmental impact of hardware and products, producing from “Cradle-to-grave”. In medicine, attention to the environmental impact is still limited. Methods: The pathway of the dialysis disposables was followed since their arrival to the hospital, and potential interventions were identified by a small working group made of nephrologists, trainees, students and nurses, starting from the analysis of the wastes (the grave). Results: Each dialysis session produced 1.5-2 kg of plastic wastes (cost of disposal: 2.2-3 Euros per session, about 10% of the cost of the dialysis supplies); the cost for packaging discharge is not included. 1. External packaging: large amount of boxes (non-recycled cardboard), wrapped in plastic. Suggestion: non-disposable plastic coverage, reusable, for delivery. Cardboard boxes should be reused and reusable; the reuse of the same cardboard boxes for dialysis supplies should be considered. 2. Each box contains at least 2 A4 pages of “instructions”. Suggestion: use of recycled, non acid paper and ink; supply a reference site for instructions. 3. Packaging. There are two main philosophies of packaging: each element individually and “pre-assembled” packaging, in which a plastic “guide” helps mounting the dialysis machine. The latter are conceptually based upon the principle that time is more costly than wastes. Suggestion: consider compact packaging of single elements. 4. Dialysis companies supply pre-assembled “kits” for start and end of the dialysis sessions, which (preparation) could be at least partly substituted with recycled/recyclable or reusable materials. 5. For disposables contaminated by blood, consider optimal geometry of waste bins: even where wastes are disposed by weight, the volume is crucial in determining transportation fees from hospitals to incinerators. 6. Reuse of dialysis filters for a limited time should be weighted against risks of infection, of loss of efficiency and of contamination by disinfectants. Conclusions: The Systemic Design method may be a useful tool for defining single steps of “production” of a dialysis session, suggesting potential strategies. The approach “cradle to cradle” may be a starting point for a critical analysis, opening to further, more innovative steps, such as the “output-input” approach, learning from nature how to create and renovate “systems”.

SP583 IMPACT OF POTENTIAL CONFOUNDERS ON COMPARISONS BETWEEN UNITED STATES FOR-PROFIT AND NONPROFIT DIALYSIS PROVIDERS

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Introduction and Aims: In its ongoing surveillance of clinical outcomes for dialysis patients by provider type as described in the Annual Dialysis Report (ADR 2012), the United States Renal Data System (USRDS) adjusts estimates for age, gender, race, primary diagnosis, and vintage. Previous literature has shown that both predialysis care and having a fistula at the time of dialysis initiation, both of which are outside the control of dialysis provider organizations, have a beneficial impact on mortality and hospitalization rates. The purpose of this study was to assess the degree to which these factors differed across provider types, which if present, could substantively confound external validity estimates. Methods: Because data on initial vascular access time and length of predialysis care are recorded on CMS form 2728, and the data on Medicare patients are aggregated to the facility level in Dialysis Facility Reports (DFR), we used DFR to evaluate the effect of type of facility ownership on both fistula placement and predialysis care in patients starting dialysis in for-profit compared to nonprofit dialysis facilities. Using United States federal claims data and the Dialysis Facility Reports (DFRs) from 2011 (reflecting ownership status in 2010), we determined the length of time that predialysis care was received before starting dialysis and the percentage of incident patients who started dialysis with an arteriovenous fistula (AVF) in place.
Results: In nonprofit facilities, 30% of patients who initiated dialysis did so after receiving greater than 12 months of predialysis care, compared to only 25% of patients who started dialysis at for-profit facilities. In nonprofit facilities, 19.6% of patients initiated dialysis with an AVF in place, compared to only 17.1% of those who entered dialysis in for-profit facilities.

Conclusions: Previous comparisons of outcomes between nonprofit and for-profit providers, including those in the most recent USRDS ADR, have not adjusted for predialysis care and vascular access placement. Since predialysis care and vascular access placement are important determinants of clinical outcomes in patients who start dialysis, our finding that patients who start dialysis at nonprofit facilities are more likely to have had prolonged predialysis care and initiate dialysis with an AVF in place than do those at for-profit facilities calls into question the reliability of previous reports comparing patient mortality by type of provider ownership. In the most recent USRDS ADR, the leading nonprofit provider (Dialysis Clinic, Inc; ie, DCI) and a for-profit provider (DaVita) showed standardized mortality ratios that were statistically equivalent. Further exploration of the impact of length of predialysis care and vascular access placement may provide greater insight into provider-level quality of care comparisons.

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Introduction and Aims: There are regional differences in the survival of incident dialysis patients, but few studies have investigated the reasons. Therefore we evaluated which regional clinical factors might affect survival of incident dialysis patients with use of Japanese Renal Data Registry data for entire dialysis population in Japan.

Methods: We investigated 37 clinical factors from the database from 3,958 institutions of 47 prefectures in 2005. Univariate survival analyses were performed by Kaplan-Meier analysis and log-rank test. The observation period was 1 year after starting chronic dialysis. The factors which can potentially have effects on survival were also tested by Cox's proportional hazards model which patients live in are divided into 2 categories for each clinical factor: preference with either upper or lower values. The variable for the categorization was dichotomized and was subjected to the Cox’s model for each patient as well as age and primary diagnoses.

Results: The age-adjusted 1-year survival rate was 0.832±0.027. A total of 11 factors were significantly correlated with 1-year survival according to the Kaplan-Meier analysis and log-rank test. Deaths occurred 15.0% in 24 upper survival prefectures and 18.7% in 23 lower survival prefectures (P=0.001, unadjusted HR of death in lower survival prefectures: 1.26, 95% CI: 1.17-1.40). 10 factors (protein catabolic rate (males: P=0.0003, age, genders, and presence of diabetes adjusted HR: 0.88, 95% CI: 0.82-0.94), creatinine production rate (males: P=0.0001, 0.88, 0.81-0.94), Kt/V (males: P=0.001, 0.86, 0.78-0.91), dialysis time (males: P=0.0001, 0.87, 0.79-0.92), fluid removal (males: P=0.0024, 0.91, 0.84-0.96), Japan Ministry of Welfare clinical score at initiation of dialysis (males: P=0.0001, 1.13, 1.06-1.19), nighttime centers/total dialysis centers ratios (males: P=0.0001, 0.88, 0.81-0.93), number of full-time dialysis nurses (males: P=0.0427, 0.94, 0.87-1.00), number of full-time dialysis diabetics (males: P=0.0084, 0.92, 0.85-0.98), and blood urea nitrogen (male: 0.015, 1.01-1.13, females: P=0.0032, 1.13, 1.04-1.20), respectively) were significant by the Cox’s model.

Conclusions: Various institutional factors in addition to the clinical factors were closely related to the survival of incident dialysis patients, and regional differences in the survival may be explained, at least partly, by these factors.

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EMERGING FACE OF END-STAGE RENAL DISEASE REQUIRING REPLACEMENT THERAPY IN TURKEY BETWEEN 2000-2011

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Introduction and Aims: The incidence and prevalence of renal replacement therapy (RRT) for patients with end-stage renal disease (ESRD) have been increasing gradually in the world during the past decades. Here we report the emerging face and updated number of kidney dialysis and transplant patients each year in Turkey.

Methods: Since 1990 the Turkish Society of Nephrology has been carrying out the national renal registry with its own resources. The registry has collected nationwide facilities.

Results: The number of centres increased from 2000 to 2011 on a national scale (333 centres to 1009 centres). The incidence and prevalence of RRT patients were increased over last 12 years (an increase of 14-15%, especially between years 2000-2007) as shown the following figure. The numbers of prevalent hemodialysis patients and peritoneal dialysis patients increased approximately 4 fold, 3 fold respectively. Numbers of kidney transplantaion performed each year also increased from 523 to 2955 (>5-fold increase). In 2011, the point prevalence of RRT was 829 pmp and 524 pmp in prevalent and prevalent cases increased, respectively. ONCE INFECTION AFTER PNEUMOCOCCAL PNEUMONIAE INCREASES SUBSEQUENT RISK OF END-STAGE RENAL DISEASE IN ADULT PATIENTS

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Introduction and Aims: The aim of our study is to find out the relation between Pneumococcal pneumonia (PP) and its subsequent risk for end stage renal disease (ESRD).

Methods: From the cohort including 23.5 million people in 1998-2010, 18,302 cases diagnosed to have PP infection upon admission were selected. For comparison, 73,208 individuals without PP matched with age and sex were selected as controls. Both study cohorts were followed until a new diagnosis of end-stage renal disease (ESRD), being censored, death or the end of follow-up on December, 31 2010. The demographic characteristics, incidence and hazard ratios of developing ESRD between two cohorts were compared.

Results: The PP cohort was more prevalent in comorbidity than the non-PP cohort including hypertension (32.6% vs. 16.3%), diabetes (20.0% vs. 8.10%), and hyperlipidemia (6.70% vs. 3.24%). The IRR of ESRD in the PP cohort was 2.8 times (95% CI, 2.70-2.95) higher than that in the non-PP cohort (42.8 vs. 15.0 per 10,000 person-years). Generally, the incidence rate of ESRD increased with age in both cohorts. However, the PP cohort less than 35 years of age had a much greater IRR of 10.7 (95% CI = 8.81-13.0). After adjusted for stratified age, sex, and comorbidities, the HR of the PP cohort was 2.03 (95% CI, 1.75-2.34, p<0.001). The risks of developing ESRD were also greater for patients with diabetes (HRs=2.52, 95% CI=4.71-6.48). The ESRD cumulative incidence curve showed that the PP cohort had a significantly higher risk for ESRD than the non-PP cohort (log rank test p<0.001).

Conclusions: Pneumococcal pneumonia is independent risk factor of renal function progression in adult patients, and the pathophysiologic mechanism could be multifactorial. The concurrence of Pneumococcal pneumonia and comorbid disease would aggravate the risk of ESRD in elderly population. Long-term follow up of renal function is recommended in adult patients despite only one episode of Pneumococcal pneumonia.
ORAL HYGIENE HABITS IN PEOPLE ON HEMODIALYSIS: A MULTINATIONAL PROSPECTIVE COHORT STUDY (ORAL-D)

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Introduction and Aims: Data describing oral hygiene habits in people with end stage kidney disease on hemodialysis as sparse. We prospectively surveyed global oral hygiene habits in a large outpatient hemodialysis population.

Methods: ORAL-D is an ongoing multinational prospective cohort study of oral diseases in people on hemodialysis. We consecutively enrolled adults on hemodialysis in 75 outpatient clinics selected randomly from a collaborative dialysis network in Europe and South America. We assessed oral hygiene habits using standard self-administered patient questionnaires. We summarized data using descriptive statistics.

Results: 4720 hemodialysis patients in the participating clinics from Italy, Hungary, Poland, Argentina, Portugal, France and Spain responded to the questionnaire. Of these, 2388 (52%) did not remember when they had last visited a dentist or reported that they did not have a regular dental practitioner, 1264 (27%) reported their first dental visit at 30 years or older, 533 (12%) never brushed their teeth, 1722 (37%) used mouthwash and only 327 (7%) used dental floss. 1510 (33%) participants changed their toothbrush as needed, and only 1492 (35%) spent more than 2 minutes on daily oral hygiene cares.

Conclusions: Using validated instruments to evaluate oral hygiene, nearly half of adults on hemodialysis do not regularly visit a dental practitioner and many have poor oral hygiene habits. Additional study of the effectiveness of dental intervention and education on dental and clinical outcomes may be warranted.

CLINICAL ANALYSIS OF THE LARGEST NUMBER OF PREGNANT WOMEN IN HD & THEIR CHILDREN IN ARGENTINA

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Introduction and Aims: Although uncommon, pregnancy (P) occurs in women with end stage renal disease (ESRD) even in those undergoing dialysis (HD). The objective of this study was to report the experience in a multidisciplinary team for pregnant women suffering from (ESRD) patients (Ps) in a Public Hospital. Clinical outcome during pregnancy, long term follow up, as well as, perinatal and childhood outcomes are described.

Methods: Transversal study, including 37 non diabetic ESRD patients, that required HD and their offspring’s outcome.

Results: 39 P (3 twin, and 1 triple) in 37 ESRD pts, age (mean ± SEM) 30 ± 1.0 were followed up. 26/37 pts were already undergoing HD at the time of gestation while 11 entered HD because of P between 10 ± 6.7 weeks. 22 Hypertensive Ps. received amloidipine with or without α methyl dopa/ labetalol. 7/22 worsened needing more than 2 drugs to control HTN. Polyhydramnios was found in 16 Pts. Preterm delivery was present in 100% of our population. Babies born to mothers on HD were premature, gestational age at delivery (27 caesarean sections and 12 vaginal deliveries) was 30.9 ± 0.7 wks. Major causes of prematurity included maternal HTN polyhydramnios and premature rupture of membranes. Fetal weight at delivery was 1404 ± 108 g. 22 newborns ‘weight less than 1500 g’. 13/22 survived. 4 displayed serious complications due to prematurity, low birth weight and small gestational age. Fetal demise was high, (especially for the multiple pregnancies, surviving only half of the twin) during the perinatal period. Four fetal deaths were associated with respiratory distress, two with congenital anomalies and finally two died from severe necrotizing enterocolitis. Of those who survive, Infants under 1500 g were followed at a High Neonatal Risk Office. 4 had retinopathy and underwent laser therapy, 2 autitive disorders, 3 developmental delay disorders with dyslexia, 1 had arrhythmia, 1 underwent traumatological surgery because of congenital deformities and 1 had long medical problems. Children whose mothers underwent intensified HD had better weight and no one reported adverse school outcome. The older daughter is now 19 years old, and has been mother of a healthy baby last year.

Conclusions: Pts. with children conceived to get benefits of early and intense dialysis, EPO (doses were double increased) and advances in dialysis, obstetrics and neonatal care have improved the outcomes. It remains difficult to advise this women to conceive during HD.

IMPACT OF SUBCLINICAL HYPOTHYROIDISM ON CARDIOVASCULAR OUTCOMES IN PATIENTS WITH CHRONIC KIDNEY DISEASE STARTING DIALYSIS TREATMENT

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Introduction and Aims: Subclinical hypothyroidism (SCH) is highly prevalent in patients with chronic kidney disease (CKD). Although SCH is thought to be associated with increased risk for atherosclerosis, the data on cardiovascular outcomes were conflicting in general population. Furthermore, little is known about the effect of SCH on cardiovascular outcomes in CKD patients. To explore this question, we conducted retrospective cohort study to evaluate the prognostic effect of SCH diagnosis at dialysis initiation on cardiovascular outcomes in CKD patients on dialysis treatment.

Methods: We retrospectively analyzed the inception cohort data set in which 487 consecutive patients started dialysis between 2001 and 2009 at Rinku General Medical Center and were prospectively followed until December 2010. Patients with 1) abnormal free T4, 2) malignancy, 3) hormone replacement therapy were excluded for analysis. Thus, a sample of 412 patients was included in the final analysis. Blood samples were routinely collected in the morning on fasting subjects within 2 week before the first dialysis session. SCH was defined as a serum thyroid-stimulating hormone (TSH) concentration above the upper limit (3.73μU/ml) of the reference range and the serum free thyroxine within the reference range (0.82-1.67μg/dl). Ankle-brachial pressure index (ABI), intima-media complex thickness (IMT), left ventricular mass index (LVMI), and ejection fraction (EF) were measured as initial and compared between the two groups with and without SCH. Cox proportional hazards models were used to identify the association between SCH and cardiovascular mortality on dialysis treatment.

Results: Prevalence of SCH was 26% (N=105). Patients with SCH had higher prevalence of diabetes (54% vs 33%; P=0.000) and lower serum albumin level (median; 3.7 vs 4.0 g/dl, P=0.003). There was no statistical difference in ABI (N=199, P=0.71), IMT (N=199, P=0.90), LVMI (N=354, P=0.90) and EF (N=354, P=0.71) between the two groups. Cox proportional hazards models revealed that SCH was not associated with cardiovascular mortality but significantly associated with 5-year all-cause mortality (HR 1.036, 95%CI 1.001-1.073, P=0.042) when adjusted for age, gender, diabetes and cardiovascular history.

Conclusions: Our results suggest that SCH is associated with all-cause mortality but not with cardiovascular outcomes in CKD patients starting dialysis treatment.

SEASONAL VARIATIONS IN CLINICAL AND LABORATORY PARAMETERS – A GLOBAL PERSPECTIVE

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Introduction and Aims: We aim to understand whether clinical parameters follow seasonal patterns in a world-wide dialysis population.

Methods: The MONitoring Dialysis Outcomes (MONDO) databases from RRI, FMC Europe (17 countries), FMC AP (9 countries), and FMC LA (5 countries) were queried to identify HD patients who had HD tx for ≥1 year [Unyait, Blood Purification 2013]. Seasons were defined based on treatment date: season 1: Dec-Feb; season 2: Mar-May; season 3: Jun-Aug; season 4: Sep-Nov. Arg of pre-dialysis systolic blood pressure (preSBP), C-reactive protein (CRP), and interdialytic weight gain (IDWG) were computed per patient per season between Jan 1, 2000 and Sep 30, 2012. Patients were stratified into one of four groups based on clinic location: northern/southern hemisphere and temperate/tropical climate (using Tropic of Cancer/Capricorn). Linear mixed models were constructed to determine whether seasons played a role in those four groups.

Results: N=87,399 patients (FMC AP 14,871; FMC Europe 45,282; FMC LA 19,275; RRI 7,521). In northern & south hemispheres, as well as tropical and temperate climates preSBP appeared significantly different between seasons. In northern hemisphere, highest preSBP was in season 1. The observations were reversed for southern hemisphere. Seasonal differences were observed in both temperate and tropical climates. IDWG was highest in season 1 in northern hemisphere and season 3 in southern. There were no significant differences in CRP in the tropical climates. In temperate climates, CRP appeared highest in season 1 in northern hemisphere and in season 3 in southern. Figure 1. Relative effect of seasons. Coefficients are significant compared to season 1, unless otherwise indicated with NS.
**SP597**

**RELATIONSHIP BETWEEN SERUM SODIUM Variability AND HOSPITAL ADMISSION IN HEMODIALYSIS PATIENTS**

Joselyn Reyes-Bahamonde1,2, Jochen Raimann1, Len A. Usvyat1, Stephan Thijssen1, Frank Van der Sande1, Jeroen Kooman1, Nathan Levin1

Introduction and Aims: Recent reports in prevalent hemodialysis (HD) patients indicated that pre-HD serum sodium (SNa+) concentrations are stable over time ("SNa+ setpoint"; Keen, Int J Art Organs 2007). Pre HD SNa+ concentration has been linked to outcomes in HD patients (Waiker, Am J Med 2011) and an increased pre-HD SNa+ variability over time has shown to be related to increased morbidity and mortality (Raimann, ERA-EDTA 2012). We investigate the relation between SNa+ variability and hospitalization in incident HD patients.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Hazard Ratio</th>
<th>95% Confidence Interval</th>
<th>P-value</th>
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<td>0.98</td>
<td>0.97-0.98</td>
<td>&lt;.0001</td>
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<td>Sex</td>
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<tr>
<td>Female</td>
<td>0.74</td>
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<td>7-12</td>
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<td>0.63-0.92</td>
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<td>126.65</td>
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<tr>
<td>None</td>
<td>1.28</td>
<td>1.00-1.65</td>
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**Methods:** This longitudinal cohort study included HD patients between 1/2001 and 7/2008 in US clinics of the Renal Research Institute. Patients with at least three SNa+ measurements in the first 3 months on HD were included and stratified by average SNa+: (1) <137, (2) 137-141, (3) >141 mEq/L and by SNa+ variability: Coefficient of variation (CV) (1) <10%, (2) 10 to 20% and (3) >20%. Patients were followed-up for 18 months. Kaplan Meier analysis was used to estimate time to first hospitalization, stratified by SNa+ concentration and CV. Cox regression was used to compute hazard ratios (HR) of hospitalization in months 13 to 18 adjusted for gender, race, age, vascular access, comorbidities, systolic blood pressure and eGFR.

**Results:** We studied 4451 HD patients (age 61±15.21, 56% male, 56% diabetic, 43% Blacks). Time to first hospitalization was significantly shorter in patients with SNa+<137 and CV<20% (log rank P=0.001) and SNa+ 137-141, CV<20% (log rank P=0.02) see figure 1. Multivariable Cox Regression indicated that patients in the SNa+<137, CV<20% group were at higher risk of early hospitalization (HR 1.4; P=0.011). There appears a non-significant trend towards higher HR associated with higher CV see table 1.

**Conclusions:** Both SNa+ level and stability are associated with hospitalization in incident HD patients. Our study indicates a relation of SNa+<137 mEq/L and high SNa+ variability with a shorter time to first hospitalization. Factors causing higher SNa+ variability remain to be elucidated.

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**SP598**

**IMPLEMENTING AN ANTICOAGULATION PROTOCOL DESIGN - A SAFE AND EFFECTIVE MANAGEMENT OF ANTICOAGULATION THERAPY**

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Introduction and Aims: Literature has emphasized that administration of anticoagulation in dialysis promotes minimal filter clotting and post dialysis bleeding, and improves patient quality of life through prolongation of the vascular access.

**Methods:** This study evaluated the protocol plan designed to deliver both High and Low Molecular Weight Heparins (LMWH, LMWH) as bolus and cath-dwell and develop a relationship between filter clotting, post dialysis bleeding (PDB), blood flow...
Nephrology Dialysis Transplantation

SP699  PERITONEAL DIALYSIS USAGE (PD): WHAT IS A REALISTIC GOAL IN EUROPE?

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1EPOE Health Outcomes Baxter Healthcare Corporation Braine l’Alleud Brabant Wallon Belgium, 2EPOE Medical Affairs Baxter Healthcare Corporation Zurich Switzerland

Introduction and Aims: Studies have shown that 70-78% of patients do not have contraindications to PD.1,2 When offered the choice, 40-50% of patients will choose home,1-3 hence, 28-39% of incident patients will be on PD (vs today’s 19%).

Aims: This study aimed to estimate the potential PD usage considering today’s age distribution of ESRD patients in countries reporting full data to the ERA-EDTA registry.

Methods: The age distribution of ESRD patients were extracted from the 2010 ERA-EDTA registry report. The maximum PD rate in each age group (incident patients) was used to estimate the potential PD usage considering today’s age distribution of ESRD patients overall and per country.

Results: The highest PD usage per age group was seen in Finland (45% in 20-44 years old), Denmark (40% in 45-64 years old), and Sweden (38% in 65-74 years old and 27% in 75+ years old). The average potential PD usage considering today’s age distribution of ESRD patients was 36±1.2%. While Sweden and Denmark could still increase their PD usage by 24.4%, large increases (20-28%) appear possible in Italy, Spain, France, Belgium, Austria, Greece and Romania. The UK (16%), the Netherlands (13%) and other countries (11-13%) lie in between.

Conclusions: This analysis shows that a 36% rate of incident patients commencing PD is achievable considering today’s age distribution of ESRD patients (assuming that the highest reported usage per age group is the maximal achievable). Provided the health status of patients is similar across this basket of 14 countries, there is scope for significant increases in use of PD across Europe. 1. Mendelssohn DC et al. NDT 2009; 24:555; 561-2, 2. Jager KI et al. AKD 2004; 43: 891-899 3. Goovaert T et al. NDT 2005; 20: 1842-1847 4. 2010 ERA-EDTA registry report.

SP800  RENAL REPLACEMENT THERAPY IN HUNGARY 1991–2011

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16th Dialysis Center BBraun Avitum Hungary Szombathely Hungary, 2Hungarian Society of Nephrology Budapest Hungary, 3BBraun Avitum Hungary Budapest Hungary, 4Freshen Medical Care Hungary Budapest Hungary, 5Diaverum Hungary Budapest Hungary, 61st Pediatrics Clinic Semmelweis Medical University Budapest Hungary

Introduction and Aims: A significant improvement has been from 1991 in Hungarian dialysis program because of privatization. The private sphere covers more than 90% of dialysis facilities in Hungary at present. The authors show national data and development in renal replacement therapy (RRT) between 1991 and 2011.

Methods: The year by year questionnaire-based data were collected by Hungarian Dialysis Registry Committee.

Results: Five dialysis centers for pediatric and 39 for adult patients were active in 1991 in Hungary and the number of adult centers have increased to 57 by the end of 2011. First day incidence (per million population-pmp) of new dialyzed patients was 7.2 in 1991 (included 27 for acute kidney injury [AKI] and 45 for end stage renal disease

[ESRD]) and 488 pmp (247 for AKI and 241 for ESRD) in 2011. The number of prevalent dialyzed patients (pmp, at the end of the year) was 139 in 1991, and it has continuously increased to 625 until 2011. The peritoneal dialysis (PD) penetration rate (patients on PD / total number of dialyzed patients at the end of the year) was 12.8 % in 1991 (50-50% of intermittent peritoneal dialysis [IPD] and CAPD, but it decreased to 7.1 % by the end of 2000. From this year the PD (CAPD and APD) penetration rate has been growing: it was 14.2% at the end of 2011. There were delivered 5404 renal transplantation from 1991 to the end of 2011 (the number moved between 250-300 txs/ year). The patient’s number on renal transplantation waiting list was 741 in 1991 and only 871 in 2011. At the end of 1991, 420 patients lived with functioning kidney graft. This number has risen to 2780 until the end of 2011. The prevalence of Hungarian ESRD patients on RRT was 172 pmp in 1991, and 903 pmp in 2011.

Conclusions: There was a significant improvement regarding the RRT’s in Hungary based on the development of clinical nephrology, dialysis therapy and renal transplantation by last two decades. The annual increase in the first day incidence of dialysis treatment was higher in acute cases than ESRD patients in (2011) – but the latter one (241 pmp) was also high, (in contrast with the EDTA average: 125 pmp / 2010). The increase in prevalent patients on maintenance dialysis was much smaller in last few years, than previously. The Hungarian peritoneal dialysis program showed a great increase in last ten years. Unfortunately, the renal transplant activity and the volume of patients on waiting list were not able to grow in the last decade.

SP601  HBV STATUS IN DIALYSIS PATIENTS: A MULTICENTER COHORT STUDY FROM SICILY

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1CRT SICILIA Palermo Italy, 2Università Degli Studi Di Palermo Palermo Italy

Introduction and Aims: The prevalence reported in the literature of HBsAg positive patients on chronic dialysis in the industrialized countries is 1% for USA, 11.2% for Japan and 6.6% for Italy. In 1983 the introduction of the obligatory vaccination determined a reduction of the incidence of HBsAg positive patients to 0.9/100.000 citizens in the general population in 2010. This study reports epidemiologic data concerning HBsAg positivity in Sicilian patients on chronic dialysis.

Methods: The data of prevalent patients on chronic dialysis of the Sicilian Registry of Nephrology, Dialysis and Transplantation were analyzed in 2011. Three indicators have been used: 1) the percentage of HBsAg positive patients (N=59) / prevalent patients (N=4174); 2) vaccination coverage: number of vaccinated patients (N=1110) / total dialysis population (N=4174); 3) rate of seroconversion: no responders (N=467) / total vaccinated patients (N=1110).

Results: The prevalence of HBsAg positive patients on chronic dialysis is low (1.4%); none patients under 35 years old is positive; there are not demographic, clinic and laboratory differences between the two groups of HBsAg positive and HBsAg negative patients. Moreover, HBsAg positive patients have the same probability of being registered on waiting list for kidney transplantation compared with HBsAg negative patients. Vaccinated patients are 37.6% (N=1110) of dialysis patients, they have a high instruction level compared with the ones that are not vaccinated (15% vs 12%); 13% of vaccinated patients is registered on waiting list for kidney transplantation vs 7% of non-vaccinated patients. 81% of vaccinated patients have FAV vs 75% of non-vaccinated patients; the dialytic age is less than 1 year in the 8% of vaccinated patients vs 14% of non-vaccinated patients. No responder patients to the vaccination were reported. 36.7% of new patients and 18.2% of lower datum compared to the one reported in the literature (50%); they are older (68.6 vs 65.5 years old), have a lesser dialytic age (59 vs 81 months), a lesser probability to be non-vaccinated patients (N=1110).

Conclusions: In Sicily, the HBV diffusion is not a significant problem anymore. It is important to submit the dialytic population on screening. It is also important to vaccinate patients on dialysis even if seroconversion is limited to 2/3 of vaccinated patients.

SP802  DIALYTIC TREATMENT DOES NOT INCREASE THE RISK FOR INFECTIVE DEATH IN PATIENTS WITH MYELOMA-RELATED END STAGE KIDNEY DISEASE

Francesco Rainone1, Lino Merlino1, James P. Ritchie2, Magda Marcatti1 and Philip A. Kaira3
1Nephrology and Dialysis Unit San Raffaele Scientific Institute Milan Italy, 2Vascular Research Department Salford Royal NHS Foundation Trust Manchester United Kingdom

Introduction and Aims: Multiple myeloma (MM) is an incurable malignancy that often leads to end stage kidney disease (ESKD), and consequently dialysis. The aim of this study was to evaluate whether dialytic treatment increased the risk for death in myeloma-related patients with ESKD.

Methods: We studied the causes of death in 170 patients with a novel diagnosis of MM and kidney impairment.
Abstracts

Results: 65 patients (38%) presented with ESKD, defined as an estimated glomerular filtration rate (eGFR) of less than 15 mL/min. This was the cohort analyzed for the aim of the study. Median age at presentation was 67.0 (43-86) years, males were 53.8% of the cohort, median eGFR was 7.0 (1-14) mL/min. During a median follow-up time of 2.8 years (IQR 0.9-6.2), 47 patients (72.3%) died and 43 (66.2%) were treated with dialysis, either in the form of hemodialysis (70.4%) or peritoneal dialysis (29.6%). 80% of the patients who required renal replacement therapy (RRT), needed it within 7 days from presentation. The untreated uremic patients (33.8%) were deemed to be too frail to undergo any kind of RRT, and received a conservative management for ESKD. Both cohorts had the same hematologic treatment for MM, except for 3 patients who only received palliative care. The most common causes of death in the two groups were: infections (89.2%), uremia (76.4%, only in the conservatively managed group), bleeding (1.6%), myocardial infarction (1.6%). Patients with ESKD, who were treated with RRT did not have a higher risk for overall death than the untreated (39.5% vs. 21.1%, p= 0.245). We also found that the RRT treated cohort did not have a higher risk for infective death than the untreated (93.8% vs. 86.7%, p= 0.417).

Conclusions: Our study highlights that MM is highly associated with ESKD at diagnosis. MM-related ESKD often requires RRT within few days from its development. Patients should promptly receive RRT if needed, as they may benefit from this therapy with a good quality of life. RRT does not represent a cause for increased overall or infective death.

SP603 EFFECTIVENESS OF MULTIDISCIPLINARY PRE-DIALYSIS EDUCATION AND TEAM CARE ON PATIENTS LIFESTYLES AND CLINICAL OUTCOMES

Omer Toprak2
1Nephrology Balikesir State Hospital Balikesir Turkey, 2Nephrology Balikesir University School of Medicine Balikesir Turkey

Introduction and Aims: Multidisciplinary predialysis education (MPE) programs may improve the medical care of patients and have significantly impact of clinical and quality of life outcomes. The aim of the study was to assess the influence of multidisciplinary predialysis education on lifestyles and clinical outcomes in chronic kidney disease (CKD) patients.

Methods: A total of 4350 chronic kidney disease patients with an estimated glomerular filtration rate between 15 to 60 mL/min/1.73 m² and with an age of 18 to 105 years were included to the study in a period of July 2007 to January 2012. Patients were followed-up for 12 months according to lifestyle and clinical parameters. Also patients were evaluated to control of the hypertension, proteinuria levels, total number of anti-hypertensive medications, and the use of total drugs per day. All patients and their families received at least 5 times interactive pre-dialysis education seminars by a pre-dialysis education team which include 1 nephrologist, 3 physicians, 2 hemodialysis and 1 peritoneal dialysis nurses, 3 dietitians, 1 social work expert, and 1 psychologist. An appropriate diet list was prepared for all patients and an optimal medical care was given based on the NKF/DQOI guidelines.

Results: The percent of smoking cigarettes, excessive salt and alcohol intake, bread consumption, use of non-steroidal anti-inflammatory drugs, use of nephrotoxic antibiotics, use of iodinated contrast agents without prophylactic medications, and the rate of not to consult and collaborate with their physician before taking any medicine decreased significantly (p<0.05). Duration of exercise (p<0.05) and water intake per day increased (p<0.05). The control of hypertension increased, number of antihypertensive drugs taken per day, number of total drugs taken per day, and proteinuria decreased significantly (p<0.05).

Conclusions: Our study suggest that an efficient MPE may play a significant role in control of hypertension and proteinuria in CKD patients. Also MPE reduces the need for antihypertensive medications and helps to make positive lifestyle changes in CKD patients.

SP604 AWARENESS OF CKD IN AN GPS ITALIAN GROUP BEFORE AND AFTER AN EDUCATIONAL INTERVENTION

Giuseppe Quintaliani1, Daniela Ranocchia2, Fabrizio Germinì2, Alfredo Notargiacomo2 and Maria Loreta Ariete3
1Clinical Governance Italian Society of Nephrology Rome Italy, 2Nephrology and Dialysis Dpt Hospital Perugia Italy, 3Local Health Units Perugia Italy, 4GP Perugia Italy

Introduction and Aims: The burden of chronic kidney disease (CKD) is high, (in Italy of 3-5 DOQI is about 6%) and is associated with considerable morbidity and mortality especially in its later stages. If RRT is started, the costs are substantial and forecasted to rise even more in future. The best approach to the under-diagnosis of CKD is to ensure that all health care professionals, both generalists and specialists, understand the importance of the early diagnosis of CKD. Although general screening is not recommended, physicians should be aware that older patients, diabetics, and hypertension pts, or CV disease should be systematically screened for the presence of CKD. This study investigate the under-diagnosis of CKD in primary care following an educational intervention.

Methods: A total of 73 GPs and involved the heads of the administrative-managerial local health units. The inclusion criteria was all diabetics and hypertensive patients over 18 age referred to GPs offices within the previous year. The study consisted of two phases: The first consisted in a snapshot picture of the real situation of the investigation of kidney function (KF) by primary care. The second investigated the screening of CKD after an educational intervention. At the end of the first phase the GPs enrolled, participated to the first training session and discussion of the problem. Subsequently, the GPs extracted from their computerized databases a smaller dataset referred to patients with diabetes and hypertension. From this smaller dataset, 15572 pts, was assessed the % of requested Creatinine, eGFR estimate by MDRD, and the reported ICD9 code. In the second phase we illustrated results related to the first phase, and we underlined that CKD is potential public health problem and the importance of an early assessment of KF. After six months we extracted a dataset of data of patients referred to primary care in this space of time.

Results: We have selected 15572 patients of which 6163 (40%) have had a creatinine assessment. Of which 979 were in class 3-5 DOQI; (16%) only 271 patients were correctly attributed to the related ICD9 code (27%). After the educational intervention we had 9376 pts referred in six months to primary care office and 5473 creatinine prescribed 58%. This corresponds to a relative increase of +45% and an absolute increase of +18% compared to the baseline. In the first phase the patients in DOQI class 3-5 were about 15 % (quite the same of the second phase) while the attribution of ICD9 code were up to 35% from 27% at baseline.

Conclusions: The awareness of the importance of a correct diagnosis of IRC is poor and not widespread. The adoption of appropriate behavioural measures for GPs induced by their personal involvement are able to improve an important approach to a problem that for its prevalence may, if not regulated properly, lead to serious health problems and financial burden.

SP605 ORAL DISEASE IN PEOPLE WITH CHRONIC KIDNEY DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS OF COHORT STUDIES

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1University of Otago Christchurch New Zealand, 2Diaverum Medical Scientific Office Lund Sweden, 3Mario Negri Sud Consortium S.Maria Imbaro Italy, 4University of Sydney Sydney Australia

Introduction and Aims: Oral disease includes a wide spectrum of clinical abnormalities affecting the mouth including mucosa, teeth, periodontal tissue and salivary function. While observational data for oral and dental diseases are available in people with chronic kidney disease (CKD), existing published information has not yet been systematically evaluated. We aimed to summarize the overall prevalence of oral diseases in people with CKD and explore associations between oral disease and mortality in this clinical setting.

Methods: We conducted a systematic review and meta-analysis of observational studies reporting prevalence or clinical outcomes of oral disease in people with CKD. English-language studies were identified from systematic searching, MEDLINE through April 2010. Multiple reviewers extracted details on participant characteristics, tools used to measure oral disease, details of statistical analyses including adjustments for
THE ASSOCIATION BETWEEN SOCIAL SUPPORT AND PSYCHOSOCIAL FACTORS UPON MORTALITY AND QUALITY OF LIFE

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Introduction and Aims: Treating End Stage Renal Disease (ESRD) by hemodialysis (HD) creates changes to relationship patterns, social life, activities of daily living and the ability to attain a satisfactory Quality of Life (QoL). There is an absence of information available in the literature on the impact of these changes in the renal population.

Objective: This study investigated the influence of social support and other psychosocial factors upon mortality, adherence to medical care recommendations, and physical QoL amongst hemodialysis patients.

Methods: 272 HD patients were examined using the QoL questionnaire to determine self-reported inclinations. Logistics regression through Weighted K was used to analyze data.

Results: 53.5% of patients reported health had interfered with their social activities demonstrating a strong association with risk towards All-Cause (p<1.33) and Cause-Specific Mortality including cardiac diseases (p=1.28). These patients had a greater risk of withdrawing (p=1.67) from treatment, non-adherence to Phosphorus (p=1.06) greater than 7.5 mg/dL, and increased risk towards an albumin of less than 3.5 g/dL (p<1.23). Patients reporting dissatisfied with family support (12.0%) were at highest risk to non-adherence to intra-dialytic weight gain (p=1.27), shortening the dialysis session (p=1.21) and increased risk of Potassium level greater than 6 mEq/L (p<1.14). However, patients reporting dissatisfied with staff support (14.1%) revealed a higher risk of decreased physical QoL (p<0.76).

Conclusions: This study demonstrated that QoL was not only affected by medications and other laboratory work-ups but also with additional psychosocial factors. The study led to the development of programs empowering patients and families to participate in their treatment plans. The program includes various counselling approaches directed to patient, families, and health team.

OCTOGENARIANS PATIENTS WHO STARTED HEMODIALYSIS: MORBIDITY AND MORTALITY FACTORS

Juan Carlos Herrero-Borrón1, Carmen Mon1, Milagros Ortiz1, Julie Hinoistroza1, Gabriela Cobo1, Carmen Gallar1, Olmpria Ortega1, Isabel Rodríguez Villareal1, Araniza Olef1, Cristina Dígoa1 and Ana Vig1
1Nephrology Hospital Severo Ochoa Leganes Madrid Spain

Introduction and Aims: Improve in diagnosis and treatment of end-stage kidney disease, has allowed that patients older 80 years started renal replacement therapy (RRT). Nevertheless, this kind of patients has many comorbidity factors conditioning their outcomes and increasing their mortality.

Methods: We reviewed 388 patients who started hemodialysis (HD) in our hospital from January-2004 to October 2012, analyses 33 patients (12%) older than 80 years.

Results: At commencement HD, median age 88 years (interquartile range (IQR) 80-89), 58% female. Cause of renal disease: 33% nephroangiosclerosis, 12% diabetic nephropathy, 64% were followed in nephrology consults, median 13 months (IQR 3-95), and 84% treatment with furosamide furosemide pressure (BP) control. The median Charlson Comorbidity Index were 8 (IQR 7-16), 55% of patients with one, 33% with 2 and 12% more than 3 comorbidity. Mainly were 48.5% patients with diabetes, 21% with cancer and 18% with coronary heart disease. Majority (73%) started with 2 and 12% more than 3 comorbidities. Mainly were 48.5% patients with diabetes, 21% with cancer and 18% with coronary heart disease. Majority (73%) started with 2 and 12% more than 3 comorbidities. Median follow up of 69 months (IQR 3-109), the older patients had a median of 2.5 admission and 39 days of hospitalization per patient, basically for cardiovascular problems, infection disease and problems with vascular access (thrombosis, catheter infection or dysfunction). In echocardiogram, 67% had dystolic dysfunction and 24% pulmonary hypertension. At end of follow-up, 25 patients (76%) died, 1 was transplanted, 2 were lost to follow-up and 5 (15%) continue in HD. Main cause of death: 32% for decline of general status and therapy cessation, 20% for cardiovascular, 20% for infection. In total, 42.5% withdrawal HD. Survival using Kaplan-Meier analysis at 6, 12 and 24 months, were 87, 66 and 28% respectively.

Conclusions: In our octogenarians patients can be included in RRT, reducing a survival more than 50% with appropriate control of BP and dialysis parameters. The mortality was determined by multiple comorbidity factors. The main cause of death was decline of general status and withdrawal HD.
Conclusions: The brainstorming meeting highlighted that flexibility and good integration between physicians, nurses, healthcare professionals and patients seems to be the key for the organization of an ideal dialysis center.

Introduction and Aims: Despite its availability, Palliative Care is underutilized in the care of terminally ill ESRD patients. In this study we tried to address some additional aspects of this issue, especially the process of making decisions.

Methods: We observed the impact of the traditional family relationships, feeling of guilt and being a burden on the family, as factors of final decision. In the 3 years period between 2009-2012, 232 patients were dialyzed in our center. As eligible patients for PC were considered those who had a very poor prognosis, those with a terminal illness from non-renal causes, significant co-morbidities and whose medical condition would interfere with the technical process of dialysis because the patient was unable to cooperate.

Results: 27 (12%) patients aged from 41 to 88 years, were eligible for PC. Not to be dialyzed and treated anymore was decision made by 1 patient and by 4 families for patients unable to decide. The rest of patients decided to continue dialyzing. In 96 % of decision making the patient left the family to decide. Three patients felt as burden for the family. Families consisted of 1-7 members (mean 3.7) and all of them demonstrated feeling of guilt as the main reason for not considering Palliative Care. Different religion did not affect decision. 33% of families were well educated and with good socio-economic status. The mean survival time of the group, which continued dialyzing, was 86±52 days, and 50% of that time was spent in hospital. In 75% of patients fatula was created.

Conclusions: Negative attitude towards discontinuing dialysis relies on deep family relations and reflects traditional non-western society.

Introduction and Aims: Renal services have been available in Malta since 1982. This study represents the first attempt to assess the epidemiology of renal failure in Malta and the associated burden of co-morbidities. The aim was to stage patients with renal failure in a single nephrology clinic in Malta, to detect the frequency of their co-morbidities, and to determine their haemoglobin status.

Method: All prevalent patients attending a single Nephrology clinic in Malta over a period of 12 months (September 2007 till September 2008), were included in this observational study. Demographic and biochemical parameters were obtained from the clinic database. The estimated glomerular filtration rate was determined using the 4-variable Modification of Diet in Renal Disease formula. Staging of renal failure was according to Kidney Disease Outcome Quality Initiative (KDOQI) guidelines. The common co-morbidities studied were diabetes mellitus, hypertension, cardiovascular disease, and malignancy.

Results: The incidence number of patients studied was n=333, 33.3% female, 100% Caucasian, 47.7% >70 years. In the categories of renal failure, 45.5% were in Stage 3, 25.6% in Stage 4, and 19.0% in Stage 5. The frequency of patients in the different categories included 73.3% chronic kidney disease, 9.3% haemodialysis (HD), 9.3% peritoneal dialysis (PD), and 8.1% renal transplants (TR). The frequency of renal replacement therapy (RRT) was (34.8%) for both PD and HD, and 30.3% for TR. 46.8% (n=156) had diabetes, 75.7% (n=252) hypertension, 36.0% (n=120) ischaemic heart disease, 23.5% (n=78) congestive cardiac failure, 9.6% (n=32) peripheral vascular disease, 4.8% (n=16) cerebrovascular disease, 4.8% (n=16) malignancy. Overall, 73.8% of patients had a haemoglobin level above 11.0 g/dl.

Conclusions: The prevalence rates of most co-morbidities coincide with those of other countries in Europe and USA. However, the prevalence rate of diabetes mellitus is higher than in most countries, and that of diabetes in the renal replacement therapy group is even higher. The use of peritoneal dialysis in the dialysis population in Malta is high at 50%.

Introduction and Aims: Sleep apnea syndrome (SAS) is a condition characterized by repeated episodes of apnea and hypopnea during sleep that lead to hypoxemia, hypercapnia, sleep disturbance and activation of the sympathetic nervous system. In patients undergoing hemodialysis (HD), the prevalence of SAS is four times higher than in the general population. The aim of the present study was to examine sleep parameters of HD patients that suffer from SAS.

Methods: 37 HD patients (23 men), suffering from SAS, participated in the study. The mean age was 57.4±12.3 years, the median duration on HD was 21.5 months (range: 3-218) and the mean Body Mass Index (BMI) was 26.8±5.6 kg/m². The night between two consecutive midweek HD sessions, the patients underwent an overnight polysomnography study with a “SOMNOscreenTM” device (SOMNOmedics & Co GmbH, Germany).

Results: Mean Apnea–Hypopnea Index (AHI) was 30±23.5 events/hour. Eleven patients suffered from mild SAS (≤5≤10≤15) with a mean AHI of 8.8±2.8 events/hour, twelve patients from moderate SAS (15≤15≤30) with a mean AHI of 21.3±2.7 events/hour and fourteen patients from severe SAS (AHI>30) with a mean AHI of 54.1±21 events/hour. AHI correlated significantly with patients’ BMI (r=0.422, p<0.05), but not with age and duration on HD. No statistically significant differences on AHI were observed between men and women. Of all apnea episodes recorded, 73.8% were obstructive, 14.5% mixed and 11.7% central.

Conclusions: The results of the present study indicate that, SAS in HD patients correlates both with the BMI but not with their time on HD, neither with their age, in contrast to what has been reported from the general population, where SAS correlates both with BMI and age. Moreover, the patients’ sex does not correlate with SAS and its severity.

Finally, in our HD patients with SAS the recorded apnea episodes were predominantly obstructive, as recorded in the general population. This research has been co-financed by the European Union (European Social Fund – ESF) and Greek national funds through the Operational Program “Education and Lifelong Learning” of the National Strategic Reference Framework (NSRF) – Research Funding Program: Heracleitus II. Investing in knowledge society through the European Social Fund.
Introduction and Aims: Advance Care Planning (ACP) is a process of communication between patients, families, doctors and nurses, for the purpose of clarifying treatment preferences at end-of-life. Stopping dialysis is an option to be explored and if there is any situation in which they would want to stop dialysis because they considered it could no longer provide any benefit to their health.

Methods: Prospective qualitative study carried out on selected ESRD patients. An ACP facilitated with no prior relationship to the participants performed two semi-structured interviews with each patient, including their relatives if they preferred. We used an inductive analysis to create an account of hope in the context of ACP that consisted of identifying and coding the transcribed text into themes that were synthesised to develop a cohesive conceptual description.

Results: From May to November 2012 fourteen ESRD patients (9 male and 5 female) were interviewed: seven patients on haemodialysis and seven on peritoneal dialysis, with an average age of 66 years. Two different interviews were performed with each patient, mean duration 31 and 35 minutes, respectively. They very much trust the doctors and nurses who care for them. Their hope is to receive a transplant that allows them to recover an independent life. There is no information about the plan of care if a transplant is not a real option or if dialysis treatment can’t reach the target of maintaining a good quality of life. Patients would like to participate in decisions concerning their care and end-of-life. They want to keep on with dialysis treatment while their quality of life continues to be acceptable for them; that means being in a good mental frame of mind that allows them to recognize family and friends, being able to talk and understand others and, being independent in terms of walking or eating unaided. When they can’t do these kind of things, patients would prefer to withdraw dialysis. Respecting end-of-life care, dying without pain and to be cared for at home-if it does not lead to a substantial burden for caregivers- are the most important points for them. Patients think that doctors don’t speak to them about end-of-life because they are focused on other aspects of care.

Conclusions: Patients with ESRD may benefit from ACP process because it allows them to share their opinions with doctors, nurses and relatives. Although there are great opportunities to talk with ESRD patients about end-of-life care -time spent in hospital, trust in doctors and nurses and patients’ wishes to talk about it-, this is often not done. Some living conditions with severe cognitive impairment are unacceptable to ESRD patients: in these cases they would prefer to withdraw dialysis. Then they wish to receive care in order to relieve suffering or pain, at home if possible. ACP training for nephrology staff is currently inadequate. Grant: KRONIKGUNE.
responses to the five dimensions allows obtaining an index that express the degree HQQOL.

**Results:** Measuring HQQOL shows the worst index in diabetic patients (P = 0.000), especially in the dimensions mobility (p = 0.000), personal care (p = 0.003), and daily activity (p = 0.002). No differences in rates of pain/discomfort and anxiety/depression were observed. Patients over 65 years had worst ratings in the dimensions mobility (p = 0.004), personal care (p = 0.000), daily activity (p = 0.000), and pain/discomfort (p = 0.045), showing no differences in valuation of anxiety depression. Women showed a worse quality of life (p = 0.002) in each dimension analyzed. Obesity and longer time on dialysis did not differ regarding HQQOL.

**Conclusions:** The EuroQol-5D questionnaire gave usful information quickly and easily in the assessment of the quality of life in patients on hemodialysis. In our study, DM, elderly and female are the variables that condition worse perception of quality of life.

**Alterations of the opportunistic pathogens carriage in hemodialysis patients: a single-center study**

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**Introduction and Aims:** Colonization with Gram-positive cocci is a recognized risk factor for subsequent bacterial infections in hemodialysis (HD) patients. With coagulase-negative staphylococcus, Staphylococcus (S) aureus is one of the most common causes of serious bacterial infections in HD patients. The aim was to study features of the opportunistic pathogens carriage in HD patients with subsequent evaluation of their infectious morbidity.

**Methods:** This study was an observational, prospective, epidemiological tracking, performed in 1.5 years by microbiological and clinical examination. The study included 79 patients with the end stage renal failure (ESRD) on HD from dialysis single-center of Ukraine. 44 (55.7%) patients were men, age from 23 to 77, average 48.4 ± 4.63 years and the most common cause of ESRD was glomerulonephritis (47 patients, 59.5%). Arteriovenous fistulas (AVF) were used as vascular access in 100% of the patients. Central venous catheter (CVC) at dialysis initiation was used in 32 patients. The microbiological investigations was carried by sending swabs from the nose, pharynx and skin around the AVF out in conventional culture media.

**Results:** The most common isolated microorganisms were Gram-positive cocci (80.2%, p < 0.01). Fungi were isolated from 17.7 % positive cultures. Microbiological results are shown in Table. Cultures obtained in dialysis patients.The 26 (68.4±7.5%) methicillin-resistant S. aureus (MRSA) strains were identified in 23 patients. Vancomycin-resistant VRS S. aureus and S. haemolyticus carriers were 28 (35.4%) and 27 (34.2%) patients, respectively. Pharyngeal colonization of vancomycin-resistant enterococci (VRE) was found in 8 (10.13%) patients. During the observation 14 bacterial infections episodes among patients were detected (12 pneumonia, 2 endocarditis, 1 osteomyelitis). Also, we analyzed risk factors for colonization MRSA/ VRS and bacterial infections in HD patients (age, gender, reason for ESRD, type of vascular access in dialysis initiation, comorbidities). Patients with a history of CVC using (n = 32) showed a higher rate carriers MRSA / VRS (87.5% vs. 36.2%, p < 0.01) and cases of bacterial complication (25% vs. 8.3%, p < 0.05) than without it (n = 47). This result was one only positive conclusion in the study.

**Conclusions:** The study demonstrated real vascular access and the relevance of MRSA / VRS screening in HD patients and should alert the physicians that carriage is associated with poor clinical prognosis despite a lack of overt clinical signs of infection.
performed the assay of dopamine, serotonin, adrenaline, at time T0 (clearance ≥ 15ml/min), the T1 (clearance ≤ 10 ml / min) and T2 (after 1 week of treatment replacement / to 1 week after the decision to continue conservative therapy) T3 (after 1 month of starting treatment replacement / to 1 month from the choice of continuing conservative therapy). The data were evaluated by statistical analysis.

Results: The correlation of data bio-humoral and score the test CGA showed the presence of anxiety depression in 40% of the study population. In patients on dialysis outside the body has shown a lower percentage of psycho-physical rehabilitation and social attitudes cyclothetic correlated with higher levels of adrenaline and noradrenaline. Patients treated conservatively and DP have levels of serotonin, dopamine and norepinephrine comparable to healthy controls.

Conclusions: Conservative therapy and home dialysis (PD) represent a better approach to the ESRD population, due to the lower socio-psychological and an early program of physical and social rehabilitation compared to extracorporeal dialysis. The correlation between psychological data and biohumoral allows to highlight a better clinical approach to improve the quality of life of these patients.
TRANSLATION: BASIC SCIENCE

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Introduction and Aims: Mesenchymal stem cells (MSCs) are known to exert regenerative and immunomodulatory effects by releasing paracrine mediators including extracellular vesicles (EVs), small particles involved in cell-to-cell communication through transfer of proteins and genetic information. The aim of this study was to evaluate the protective role of MSC-derived EVs in the mechanisms of T-cell mediated rejection (TCMR) in kidney transplantation.

Methods: MSCs were isolated from bone marrow and EVs were characterized for size, protein and RNA content. The biological effects of EVs were studied in cells isolated from peripheral blood of kidney transplant recipients co-cultured with B cells purified by the spleen of matched deceased donors or on human kidney-derived tubular epithelial cells cultured in an inflammatory microenvironment typical of TCMR.

Results: MSC-derived EVs sized 60-150 nm and expressed on their surface molecules of the integrin family essential for their internalization within target cells. EVs carried different microRNAs and mRNAs including the immunoregulatory FoxP3, Tim-1 and thymosin-β1-similarly to cells from which they originated. EVs were internalized in activated T cells isolated from kidney transplant recipients inhibiting their proliferation induced by phytohemagglutinin + ionomycin or by co-culture with matched-donor B cells used as antigen presenting cells. Of interest, EVs horizontally transferred to T cells FoxP3 mRNA, inducing a Tregs phenotype. In addition, EVs can be internalized in human tubular epithelial cells inhibiting functional alterations and apoptosis induced by inflammatory cytokines, Fas-Ligand, perforin and granzymes. In particular, EVs preserved the expression of different solute carriers down-regulated by apoptosis induced by inflammatory cytokines, Fas-Ligand, perforin and granzymes. The protective effects are mediated by the horizontal transfer of specific RNAs from EVs to target cells.

Conclusions: MSC-derived EVs may have a protective role in TCMR by inhibition of T cell proliferation, by differentiation toward a T regulatory phenotype and by reduction of apoptosis and preservation of functional integrity of tubular cells. These protective effects are mediated by the horizontal transfer of specific RNAs from EVs to target cells.

EFFECT OF CT-1 BLOCKADE WITH ANTI-CT-1 ANTIBODY ON THE SEVERITY OF ACUTE RENAL FAILURE INDUCED BY UNILATERAL RENAL ISCHEMIA

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Introduction and Aims: Ischemia/reperfusion (I/R) injury is a major cause of acute kidney injury and an important determinant of long-term kidney dysfunction. I/R injury is now recognized as a highly complex cascade of events that includes interactions between vascular endothelium, interstitial compartments, circulating cells, and extracellular biochemical entities, in which inflammation is known to be a key mediator. Cardiotrophin-1 (CT-1) is a member of the interleukin 6 (IL-6) family of cytokines, which protects cardiac myocytes and liver from ischemic insults. It has been reported that increased endogenous CT-1 production can act as a protective factor against ischemia. The purpose of this study is to investigate the effect of endogenous CT-1 on the severity of acute renal injury induced in a mouse model of unilateral renal ischemia by blocking CT-1 actions with anti-CT-1 antibodies.

Methods: Male, C57BL/6 mice were randomized into eight groups (n = 6–8) Control groups: mice underwent 30 minutes unilateral renal ischemia with or without 48-reperfusion after uninephrectomy; Control IgG-treated groups: mice underwent 30 minutes unilateral renal ischemia and received goat preimmunized IgG (50 µg/kg) i.v. with or without 48-reperfusion after uninephrectomy; Anti-CT-1 antibody-treated groups: mice underwent 30 minutes unilateral renal ischemia and received anti-CT-1 antibody (50 µg/kg) i.v. with 48-reperfusion after uninephrectomy; Sham groups: mice underwent the same anesthesia and surgical procedures except for ischemia. After reperfusion mice were sacrificed and blood samples were collected directly from the heart for determination of serum urea, creatinine, and TNF-α levels. Left kidney was excised; one piece homogenized for the analysis of different parameters (lipid peroxidation, myeloperoxidase and CT-1) and other piece was fixed in formalin for histological examination (H&E, CT-1 and ED-1 positive cells).

Results: All parameters of renal dysfunction, injury and inflammation measured were elevated in I/R groups as compared with sham groups. Anti-CT-1-treated groups had higher levels of all the studied markers as compared with those of control I/R groups. Control-IgG groups showed non-significant changes in the levels of all the parameters previously mentioned as compared with those in Control groups.

Conclusions: Anti-CT-1 antibody administration exacerbated the severity of ischemic kidney injury in mice, possibly as a result of CT-1 blockade. These data reinforce the role of endogenous CT-1 in protecting the kidney from I/R damage.
THE REGULATION OF THE NITRIC OXIDE SYSTEM CAN MODULATE THE KLOTHO EXPRESSION IN KIDNEY VIA TWIST-2 AND E-CADHERIN

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Introduction and Aims: The klotho was originally identified as an anti-aging protein but was subsequently discovered to have a multitude of biologic actions. Animal experiments clearly showed a transient renal klotho deficiency in acute kidney injury – reperfusion injury. The renal klotho levels were decreased in animals treated with L-NAME, suggesting that decreased nitric oxide (NO) bioavailability may result to the down-regulation of klotho gene expression, but the inter-relationship between these two proteins is still obscure. We investigated the relationship existed between the NO pathway and the klotho expression in kidney, and studied the possible pathway as basic helix-loop-helix transcription factors (TWIST)-1, 2, E-cadherin.

Methods: The 10 weeks Sprague-Dawley rats (N=24, 200g, male) were divided four groups. We supplied low salt diet to the control group (N=6), L-NAME 1 mg/mL in drinking water to the L-NAME group (N=6), and udenafil 5 mg/kg to the Udenafil group (N=6), L-NAME and udenafil to the L-NAME and Udenafil group (N=6) for 4 weeks. After the collection of blood and urine on day 28, the both kidneys were sectioned surgically. The serum creatinine, urine nitrate/nitrite, cGMP by ELISA, and tissues were investigated by immunohistochemical stain, and RT-PCR for klotho, TWIST-1, 2, E-cadherin.

Results: The serum creatinine and urine nitrate/nitrite level did not show the statistical difference between groups. The urine-cGMP level showed 2.59±0.88, 1.79±0.99, 1.20±0.52, 0.69±0.59 pmol/well (p=0.0087). The klotho mRNA expression showed 0.98±0.01, 0.30±0.11, 0.68±0.15, 0.54±0.26 (p=0.0017). The TWIST-2 mRNA expression showed 1.39±0.63, 1.39±0.144, 1.24±0.125 (p=0.0368). The E-cadherin mRNA expression showed 0.64±0.52, 1.57±0.97, 1.24±1.27, 13.82±3.04 (p=0.0029). The blocking of NO system decreased the klotho expression via the TWIST-2 increase. The induction of NO system increased the klotho expression via E-cadherin increase.

Conclusions: The regulation of the nitric oxide system can modulate the klotho expression in kidney via TWIST-2 and E-cadherin.

NEUTROPHIL ELASTASE INHIBITOR IS A POTENT THERAPEUTIC AGENT FOR CONTROL OF RENAL ISCHEMIA-REPERFUSION INJURY IN RENAL TRANSPLANTATION

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Introduction and Aims: Renal ischemia-reperfusion (I/R) injury is a major cause of transplanted renal dysfunction. Activated neutrophils are reported to be closely involved in I/R injury after renal transplantation. Neutrophil elastase, a protease released from activated neutrophil, damages tubular endothelial cells. We investigated the beneficial effect of neutrophil elastase inhibitor (ONO-5046.Na) on renal I/R injury in rats.

Methods: The study was done using 10 male Lewis rats (270-320g) that received intravenously administered ONO-5046.Na (36mg/kg; before ischemia and after reperfusion) (group A) and control rats (group B) in 90-min renal warm I/R injury. Neutrophil elastase expression was analyzed using immunohistochemical staining, and the degree of renal dysfunction was evaluated using HE staining and blood biochemistry.

Results: Neutrophil elastase was detected in tubular endothelial cells. The necrotic area extended and encompassed nearly all of ischemic kidney within 12 hr after reperfusion. The necrotic area and the grade of neutrophil elastase staining were more significantly reduced in group A than in group B. Significant differences of blood urea nitrogen and serum creatinine levels were observed. Survival rates over a 14-day period were examined. No rats survived more than over 4-day period in group B. However, 2 (20%) of 10 rats in survived over 14-day period in group A.

Conclusions: ONO-5046.Na inhibits neutrophil elastase and reduces acute tubular necrosis. Thus it is a potent therapeutic agent for control of renal I/R injury in renal transplantation.

PCR-BASED DETECTION FOR MICROCHIMERISM AND GRAFT OUTCOME IN KIDNEY TRANSPLANT RECIPIENTS

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Introduction and Aims: Microchimerism (MC) is the presence of a small amount of foreign cells or DNA within a person’s circulation or tissues. It has been identified in recipients of solid-organ transplants where it seems to be critical for the development and maintenance of immunological tolerance. Nevertheless, natural and/or iatrogenic MC can be acquired prior to transplantation, deriving from pregnancy and/or blood transfusion. Aim of the present study was to analyse the possible influence of donor MC after kidney transplantation for possible tolerance mechanism purposes.

Methods: This study included 12 female renal transplant recipients (RTR), mean age 47±8.5 years, undergoing their first cadaveric kidney transplantation. All patients were on prophylactic immunosuppressive therapy based on triple drug association (cyclosporine, steroids and Mycophenolate mofetil). They were prospectively studied by using a quantitative real time PCR method (qPCR) for male MC detection in plasma DNA based on the detection of the DYS14 gene sequence on the
Y-chromosome. The presence of Y-related DNA sequence can be considered as a cell-death marker released from necrotic or apoptotic cells in the transplanted organ or donor-derived haematopoetic cells in the recipient’s blood or other organs. Persistence of donor DNA in recipient plasma samples was assessed at 15 days and 12 months after transplantation. A pre-transplant blood sample was collected from each patient to serve as an individual negative control.

Results: Mean serum creatinine levels were 1.36±0.35 mg/dl and mean GFR was 74±15.5 ml/min after one year follow up period of the 12 female RTR. No acute rejection episode was documented. - Median mismatches were 3 - No Y-related DNA was detected in pre-transplant samples. - Mean DNA quantity after 15 days resulted 0.80±0.69 ng/ml plasma corresponding to 121.8±104.8 genome equivalents/ml plasma. - A 5-fold decrease was recorded in median plasma Y-related DNA amount after 12 months from the transplant, resulting 0.15±0.26 ng/ml plasma (23.1±40.0 genome equivalents/ml plasma).

It is worth to note that most of the patients under study (80%) had levels of donor DNA below 10 genome equivalents/ml plasma after one year from the intervention.

Conclusions: Donor-specific DNA sequences are present in the plasma of all patients after 15 days from kidney transplant. A marked decrease in plasma DNA donor concentration was recorded after one year from transplantation. None of the patients experienced acute rejection. Association with clinical and immunological variables remains to be elucidated for those patients experiencing acute rejection.
kynurenine (Kyn); enzyme activity can be estimated as Kyn/Trp ratio. T-cell activation is affected by Trp deprivation and accumulation of Kyn. Activating IDO during immune response counterbalances mechanisms of negative feedback loop of IFN-γ and down-regulates overwhelming immune activation. IDO activation has been reported to be increased during acute rejection and downregulated in vitro by the immunosuppressants used for transplantation (steroids, cyclosporin, tacrolimus, simvastatin and mycophenolate).

Methods: Aim of our study was to investigate IDO activity (Kyn/Trp) in 46 samples of peripheral blood mononuclear cells (PBMC) of 16 children with kidney transplant followed in outpatient clinic and of 11 adults (30 samples at 0, 15 and 30 days after kidney transplantation). IDO activity was assessed in sera as Kyn/Trp ratio, simultaneously determined using an isocratic RP HPLC method with UV detection. Real time PRC (Taqman) was used to measure mRNA of TLR2, TLR3, TLR4, TLR9 and regulation-associated genes of Treg including forkhead box P3 (Foxp3), Th17-related factors (IL-17), retinooid orphan nuclear receptor (RORC), and TGFB-1 which modulates the differentiation of Th17. Values were normalized using Abelson housekeeping gene mRNA and expressed as fold changes.

Results: In transplanted patients IDO was significantly activated in comparison to healthy controls (HC) (Kyn 3.97±1.14 vs 2.05±0.33 in HC, p<0.0001; Trp 38.24±13.49 vs 54.02±7.32 in HC, p<0.0001; Kyn/Trp: 11.72±5.84 vs 3.83±0.67 in HC, p<0.0001), TLR innate immunity pathway was also activated (TLR2 mRNA 4.5±6.1 vs 1.4±0.8 in HC, p<0.0001). The results of our study suggest that, adiponectin levels are elevated in patients with acute humoral rejection and/or high dose immunoglobulin and plasmapheresis. Bortezomib offers theoretical benefit in antibody mediated rejection by targeting B cells. We looked at the efficacy of combining Bortezomib with low dose immunoglobulin and plasmapheresis in acute antibody mediated renal rejection.

Methods: Patients who developed acute humoral mediated rejection in our centre between October 2010 and September 2012 received a combination of 2mg of Bortezomib given intravenously on days 1,4,8 and 11 and alternate day plasmapheresis and /or high dose immunoglobulin. Bortezomib offers theoretical benefit in antibody mediated rejection by targeting B cells. We looked at the efficacy of combining Bortezomib with low dose immunoglobulin and plasmapheresis in acute antibody mediated renal rejection.

Methods: Patients who developed acute humoral mediated rejection in our centre between October 2010 and September 2012 received a combination of 2mg of Bortezomib given intravenously on days 1,4,8 and 11 and alternate day plasmapheresis and /or high dose immunoglobulin. Bortezomib offers theoretical benefit in antibody mediated rejection by targeting B cells. We looked at the efficacy of combining Bortezomib with low dose immunoglobulin and plasmapheresis in acute antibody mediated renal rejection.

Results: Of 64 live related renal transplantations done between October 2010 and September 2012 in our centre, acute antibody mediated rejections were noted in five (7.8%) with a mean age of 28.6±8.2 years. Mother was the donor in 4 and father in one. The native kidney disease was chronic glomerulonephritis in three and reflux nephropathy and chronic tubulointerstitial disease in one each. All received a combination of 2mg of Bortezomib given intravenously on days 1,4,8 and 11 and alternate day plasmapheresis with post plasmapheresis low dose immunoglobulin(100mg/kg) till serum creatinine reached 20-30% of baseline. They were monitored for any adverse effects.

Results: Of 64 live related renal transplantations done between October 2010 and September 2012 in our centre, acute antibody mediated rejections were noted in five (7.8%) with a mean age of 28.6±8.2 years. Mother was the donor in 4 and father in one. The native kidney disease was chronic glomerulonephritis in three and reflux nephropathy and chronic tubulointerstitial disease in one each. All received a combination of 2mg of Bortezomib given intravenously on days 1,4,8 and 11 and alternate day plasmapheresis with post plasmapheresis low dose immunoglobulin(100mg/kg). The peak serum creatinine was 4.86+3.2 mg/dL. All five patients responded with the nadir serum creatinine being 1.52±1.2mg/dL. No significant adverse effects were noted.

Conclusions: Addition of bortezomib may be a cheaper and effective alternative to high dose immunoglobulin in the management of acute antibody mediated renal rejection.
TRANSLATION: CLINICAL STUDIES - A

SP636

ENDOTHELIAL DYSFUNCTION IN RENAL TRANSPLANT RECIPIENTS: ROLE OF VITAMIN D AND FIBROBLAST GROWTH FACTOR-23

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Introduction and Aims: Endothelial dysfunction can be detected at early stages of chronic kidney disease (CKD). Although endothelial functions improve after successful renal transplantation, renal transplant recipients have still worse endothelial functions compared to healthy subjects. Recent trials showed that vitamin D deficiency and high fibroblast growth factor-23 (FGF-23) levels may have a role on endothelial dysfunction in CKD patients besides their well-known effects on calcium and phosphorus metabolism. Aim of this study is to investigate the association between endothelial functions, vitamin D and FGF-23 levels in renal transplant recipients.

Methods: One hundred-nine renal transplant recipients (71 male, 38 female) underwent brachial and radial arterial pressure wave analysis (SphygmoCor, AtCor Medical). Serum vitamin D, 25(OH)D, FGF-23 and PWV were measured at the first visit after transplantation. Patients were divided into two groups based on endothelial functions. Vitamin D and FGF-23 levels were compared between patients with normal and abnormal endothelial functions. Correlations between amount of FMD, vitamin D level and FGF-23 were also investigated.

Results: Mean ages of the patients was 40.4±11.5 years, mean duration after transplantation date was 74.7±69.5 months. Endothelial functions were abnormal in 79 patients (72.5%). Prevalence of vitamin D deficiency (<15 mcg/L) was 65.1%. Patients with normal endothelial functions and endothelial dysfunction had similar demographic, clinical characteristics and laboratory values. vitamin D levels were significantly lower in patients with endothelial dysfunction compared to patients with normal endothelial functions (12.6±6.6 mcg/L vs 17.3±10.0 mcg/L respectively, p<0.02). FGF-23 levels were not different between two groups. Vitamin D levels had a significant positive correlation with amount of FMD (r=0.218 and p=0.02). Conclusions: Vitamin D deficiency is one of the causes of endothelial dysfunction in renal transplant recipients. Further studies are needed to clarify whether FGF-23 is a marker or a potential initiation for endothelial dysfunction and the effect of vitamin D replacement on endothelial functions in these patients.

SP639

ARTERIAL STIFFNESS AND CHANGES IN QTc INTERVAL IN RENAL TRANSPLANTATION PATIENTS

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Introduction and Aims: Arterial stiffness plays an important role in cardiovascular diseases and is an independent predictor for cardiovascular mortality. The QTc interval has been reported to be increased and to be associated with high-risk ventricular arrhythmias and sudden cardiac death. As arterial stiffness improves survival, cardiovascular morbidity and mortality still remain as a significant problem compared with nonrenal populations. The aim of this study is to evaluate the association between the QTc interval changes and arterial stiffness in kidney transplant recipients.

Methods: One hundred kidney transplant recipients from our renal transplant outpatient clinic were enrolled into the study. All patients were evaluated for their standard clinical (age, gender, duration of hemodialysis, post-transplant time), biochemical parameters. Anthropometric and body composition analyses were performed for all patients. Body compositions were analyzed by the Body Composition Analyzer (Tanita BC-420MA). PWV was determined from pressure tracing over carotid and femoral arteries using the SphygmoCor system. Pre- and post-recovery electrocardiographic (ECG) evaluations were performed. Each QT interval was corrected for the patient’s heart rate using Bazett’s formula. A QTc interval greater than 440 ms was considered abnormally prolonged.

Results: After renal transplantation maxQTc intervals (456.7 ms to 414 ms) and QTdc (545 ms to 34 ms) of all patients were significantly decreased. In post transplantation period, patients with high QTc intervals had significantly higher PWV (p=0.09) and higher serum CRP levels (p=0.01) than patients with QTc<440 ms. Patients with PWV≥7 m/s had significantly higher maxQTc interval decline than patients with PWV<7 m/s (p=0.05, r=−0.26).

Conclusions: High QTc interval after renal transplantation could be a predictor of arterial stiffness in renal transplant recipients. Electrocardiographic evaluation is seen to be a cheap and reliable way to detect arterial stiffness.

SP638

ARTERIAL STIFFNESS AND METABOLIC SYNDROME INDICES IN RENAL TRANSPLANTATION PATIENTS

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Introduction and Aims: Although renal transplantation improves survival, cardiovascular morbidity and mortality still remain as a significant problem compared with nonrenal populations. In end stage renal disease metabolic cardiovascular risk factors such as hypertension, hyperuricemia, obesity and diabetes mellitus have been confirmed to be positively correlated with arterial stiffness. Arterial stiffness is an important characteristic of the arterial wall and can be assessed noninvasively by the measurement of carotid-femoral pulse wave velocity (PWV). The aim of this study is to evaluate the risk factors for arterial stiffness in kidney transplant recipients.

Methods: One hundred and forty nine kidney transplant recipients from our renal transplant outpatient clinic were enrolled into the study. All patients were evaluated for their standard clinical (age, gender, duration of hemodialysis, post-transplant time), biochemical parameters. Anthropometric and body composition analyses were performed for all patients. Body compositions were analyzed by the Body Composition Analyzer (Tanita BC-420MA). PWV was determined from pressure tracing over carotid and femoral arteries using the SphygmoCor system. Results: Patients were divided into two groups according to PWV levels. The frequency of patients with PWV ≥7 m/s was higher in patients with new onset diabetes (55.9%), hyperuricemia (uric acid level >7 mg/dL) (p=0.029, 0.05). Higher carotid-femoral PWV was significantly related with systolic (p=0.003) and diastolic blood pressure (p=0.002), uric acid (p=0.0001) and fasting glucose (p=0.02) levels. According to body composition analyses, muscle mass, visceral fat ratio and body weight were significantly higher in patients with PWV ≥7 m/s (p<0.005). In patients with high PWV, sagittal abdominal diameters and waist circumferences were significantly higher than patients with PWV < 7 m/s. When criteria for metabolic syndrome (ATP-III) were assessed there was a significant increase in pulse wave velocity in patients with 0-1; 2-3; and 4-5 criteria (p<0.01).

Conclusions: In post transplantation period, metabolic syndrome indices as high blood pressure, hyperuricemia, hyperglycemia and increased waist and hip circumferences are closely related with arterial stiffness. For cardiovascular risk reduction after renal transplantation; blood pressure, serum glucose and uric acid levels should be under strict control.

SP640

VITAMIN D SUPPLEMENTATION CAN SAFELY AND EFFICIENTLY BE ACHIEVED BY MONTHLY ORAL BOLUS CHOLECALCIFEROL IN VITAMIN D DEFICIENT RENAL TRANSPLANT PATIENTS

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Introduction and Aims: Vitamin D insufficiency (> 25 < 50 nmol/L) and deficiency (< 25 nmol/L) are common in stable ambulant renal transplant patients (RTx). This has been associated with adverse skeletal, renal, cardiovascular and cancer outcomes in this population, but a formal repletion RCT with hard end-points has never been completed. We undertook vitamin D repletion using oral Dekristol™ cholecalciferol in a group of long-term renal transplant survivors, all of whom had demonstrated sustained vitamin D deficiency, to assess both efficacy and safety of this intervention.

Methods: Out of 360 long-term (> 8 years surviving) RTx patients we found 57 subjects with sustained very low (< 25 nmol/L) serum vitamin D concentrations, and either or both of raised PTH or otherwise unexplained proximal myopathy and bone pain. We prescribed all of these patients 40,000 IU Dekristol™ cholecalciferol for 6 months (total dose 240,000 IU) and then interrogated the biochemical changes in plasma vitamin D, PTH, alkaline phosphatase, calcium, phosphate and creatinine (eGFR) concentrations over the course of the repletion period. Paired t-tests.

Results: Three patients did not complete the course of vitamin D repletion (two died from unrelated causes, and one developed cancer necessitating major surgery). This left 54 completed (per protocol) repletion courses to examine for efficacy and safety outcomes. Mean age 54 +/- 17 years. Mean time post-transplantation 14.4 +/- 3.5 years. Mean eGFR (at start) 58+/-9 mls/min.
Conclusions: All 54 patients completed their repletion course. In all cases plasma vitamin D concentrations rose to > 25 nmol/L and in 80% to > 50 nmol/L. Two patients experienced a > 20% rise in plasma creatinine (biopsy proven rejection in both cases). The remaining patients had a very modest change in plasma creatinine (proportional to the rise seen in plasma calcium, also modest). Only 5 patients experienced a plasma calcium concentration of > 2.60 mmol/L and in no case was it necessary to discontinue vitamin D treatment. The fall in plasma PTH concentration was significant and potentially valuable. The fall in plasma alkaline phosphatase values just missed significance. Monthly bolus oral cholecalciferol seems a safe and effective means by which to render RTX patients vitamin D replete.

<table>
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<th>Vitamin D (nmol/L)</th>
<th>PTH (pg/mL)</th>
<th>Alk Phos (IU/L)</th>
<th>Calcium (mmol/L)</th>
<th>Phosphate (mmol/L)</th>
<th>Creatinine (umol/L)</th>
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<td>138(115)</td>
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<td>2.40(0.12)</td>
<td>1.0(0.2)</td>
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<tr>
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<td>106(65)</td>
<td>66(31)</td>
<td>2.42(0.14)</td>
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LONG TERM OUTCOMES OF HIGHLY SENSITIZED KIDNEY TRANSPLANT RECIPIENTS

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Introduction and Aims: To follow the clinical outcomes of 45 highly sensitized patients who had undergone a desensitization protocol prior to kidney transplantation, and report the incidence of complications, allograft survival, and Patient survival.

Methods: We conducted a retrospective review of 45 kidney transplant recipients transplanted between 9/2002 and 10/2011, who had a positive T or B cell complement dependent cytotoxic (CDC) crossmatch assay. B cell CDC crossmatches were confirmed with a solid-phase assay to determine presence of class II anti-HLA antibodies.

Results: All subjects completed a desensitization protocol of plasmapheresis, intravenous immunoglobulin, +/- rituximab to render a negative T cell crossmatch or a negative or weak titer B cell crossmatch 24 hours prior to transplantation. Post-transplant all recipients received antibacterial and antiviral prophylaxis; allograft biopsies were performed when clinically indicated. The mean and median follow-up was 5 years. Thirty-three subjects (73%) suffered acute rejection of the allograft, 30 (67%) occurred in the first year post-transplant, and 27 (60%) occurred in the first year post-transplant. There was 1 case of hyperacute rejection necessitating.

Conclusion: BK viremia occurred in 7 patients (15.5%), leading to graft loss in 6 (71.4%).

GENDER PHARMACOKINETICS ANALYSIS OF TACROLIMUS IN KIDNEY TRANSPLANT PATIENTS

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Introduction and Aims: Monitoring of tacrolimus blood concentrations is of utmost importance in the management of renal transplant patients because of its the narrow therapeutic range and highly variable pharmacokinetics. Adverse effects depend on concentration and total body exposure of tacrolimus. As accurate tacrolimus blood concentration monitoring is necessary in the early post-transplant days, there is a need to find a new predictable method for routine clinical use. The aim of this study was to detect systemic exposure to tacrolimus after first oral dose and in steady state in a group of men and women, using AUC0-12 as a predictor of tacrolimus exposure. The secondary objective was to find the best sampling time to predict the exposure of tacrolimus in kidney transplant patients.

Methods: Our study was conducted on 24 kidney transplant recipients (14 men/10 women) on quaternary immunosuppressive therapy. All patients were treated with methylprednisolone (0.5 g/d, i.v.) and mycophenolate mofetil (1.5 g/d, p.o) for 3 days and basiliximab (20 mg) on the first and the fourth day. The first tacrolimus oral dose (0.05 mg/kg) was given on day 5 post-transplant. After reaching steady, the state regimen stabilized and the dosing was conducted in a accordance with level of tacrolimus. Blood concentrations were measured by microcircular enzyme immunoassay method. Twelve-hour AUC (AUC0-12) for each patient was calculated from a plot of tacrolimus concentration versus time from 0 to 12 hour after the first dose in steady state using the linear trapezoidal rule. As the lithium tetraperiod rule. As the post-transplant sampling time point of concentrations and 12 hours after the administration AUC (AUC0-12) were evaluated by Pearson correlation coefficients. AUC0-12 showed remarkable interindividual variations after the first oral T dose. There is statistical gender difference after first oral dose (p<0.01), but this difference is lost in the steady state. The most important time point influencing AUC0-12 was the concentration of tacrolimus measured 4 hours after administration (C4), whereas in steady state the most important time point were concentrations (C2) in women recipients C2 seems to be indicator of total body exposure to tacrolimus after first oral dose and this is also confirmed in a steady state. The three-point sampling method is needed for calculating AUC after first oral dose in men, whereas in the steady state, concentration C2 seems to be a good indicator of abbreviated AUC for a tacrolimus monitoring strategy in men.

Conclusion: Our results show significant tacrolimus pharmacokinetics differences between men and women. Also, our research shows the need for gender dependent choice indicator of total body exposure to tacrolimus in kidney transplant patients.

CMV AND KIDNEY TRANSPLANT VASCULOPATHY

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Introduction and Aims: Cytomegalovirus (CMV) infection is one of the most frequent complications after organ transplantation. CMV seems to have vascular tropism, being observed in atherosclerotic lesions and being able to induce vascular damage in viral lethargy. Several studies suggested a possible association between CMV infection and accelerated graft vasculopathy in heart transplant recipients. Aim of our study was to investigate a role for CMV in kidney transplant vasculopathy.

Methods: We retrospectively selected 2 groups of kidney transplant recipients, group A (N=14) with CMV infection requiring treatment (both pre-emptive and for clinical indication) and group B (N=14) CMV negative. Subjects in both groups had similar co-morbidities and similar exposure to calcineurine inhibitors. We did a morphometric analysis on kidney biopsies performed at 1, 6, 12 months after transplantation (protocol and clinically indicated biopsies), evaluating glomerular volumes (GV) and wall-to-lumen ratio (WLR) for all the glomeruli and the vessels present in each specimen. We also assessed CMV positive cells in kidney tissue by immunohistochemistry. Asymmetric Dimethylarginine (ADMA), a marker of vascular damage, was also quantified in patients’ sera by ELISA, 1, 6 and 12 months after transplantation.

Results: Average GV was lower in group A than group B, at each time point we considered, as expression of a relative glomerular hypoperfusion (1st month: 4.2±1.1 vs 4.9±1.7, 6th month: 4.3±1.6 vs 5.2±1.1, 12th month: 3.2±1.3 vs 4.3±2×10^7 mm^2, A vs B group). Average WLR was increased in group A (1st month: 2.7±1.2 vs 2.3±0.9, 6th month: 3.1±1.3 vs 2.6±0.9, 12th month: 3.6±1.7 vs 2.4±0.4, A vs B group). WLR was evaluated 12 months after transplantation in patients with clinically evident CMV infection was significantly increased compared with CMV negative patients (5.2±1.7 vs 2.3±0.4, p<0.01). We detected few CMV positive cells only in the vessels and interstitium of kidneys from CMV positive subjects with clinically evident disease.

Abstracts
DOUBLE FILTRATION PLASMAPHERESIS IN THE PREVENTION AND ACUTE REJECTION OF RENAL TRANSPLANT
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Nephrology Odense University Hospital Odense DK Denmark, Institute of Surgical Department of Transplantation and Dialysis M.F Vladimirsky Moscow
μ Nephrology Dialysis Transplantation group, p<0.01). Renal function and number of acute rejections were not different between the two groups at 12 months.

Introduction and Aims: One of the current tasks of transplantation is to overcome “graft-host” immune conflict. Partially this conflict caused by the presence of circulating pre-existing antibodies. Highly sensitized patients are at greater risk of rejection and subsequent graft loss. There are several methods to remove the anti-HLA antibodies, one of which is a double filtration plasmapheresis (DFPF). This report presents our experience of DFPF in recipients of high immunologic risk.

Methods: The study included 18 patients after kidney transplantation. All patients were classified as high-immunologic risk group. The predisposing factors were only one HLA-match (7 patients), re-transplantation (9 patients), the presence of anti-HLA antibodies – (2 patients). These patients DFPF performed before transplantation, in the days after transplantation, and two days after the transplantation.

Immunosuppressive therapy included calcineurin inhibitors - tacrolimus, mycophenolate, and corticosteroids. Induction therapy was a monoclonal anti-CD25 antibodies and methylprednisolone. We monitored the immune status; total number of lymphocytes, activation markers of humoral immunity - IgG, IgM before and after the DFPF. We used enzyme-linked immunosorbent assay (ELISA) for the analysis of antibodies and methylprednisolone. We monitored the immune status: total number of lymphocytes, including granzyme B, may be associated with outcome after kidney transplantation.

Results: Three patients had rejection crises, confirmed histologically. One of the patients had acute rejection on postoperative day 7 with laceration of graft and bleeding. In this patient we emergency made 2 DFPF procedures daily. Total IgM antibodies were reduced by 41% of the original level. IgG was reduced 57% after the first treatment and then remained stable. There are no signs of antibody-mediated rejection in biopsy obtained on day 30 after the operation. Within 3 months of follow graft function remained stable.

Conclusions: DFPF can safely and effectively reduce the high titers of antibodies that are responsible for humoral rejection of renal allograft. Reduction of antibodies in sensitized patients immediately after transplantation may improve graft function.

EFFECT OF PREDNISOLONE AND REJECTION EPISODES ON GRANZYME B TRANSCRIPT LEVELS AFTER KIDNEY TRANSPLANTATION
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Introduction and Aims: Expression of main paracrine factors from cytotoxic T lymphocytes, including granzyme B, may be associated with outcome after kidney transplantation. Currently it is unknown whether immunosuppressive therapy or rejection episodes may specifically affect these paracrine factors.

Methods: Peripheral blood samples were repeatedly collected every week after transplantation for 4 consecutive weeks. RNA was extracted from mononuclear cells using established technology. Transcripts of granzyme B, perforin, interferon stimulating glycoprotein 15, and matrix metalloproteinase 9 were analyzed using established technology. Transcripts of granzyme B, perforin, interferon stimulating glycoprotein 15, and matrix metalloproteinase 9 were analyzed using quantitative real-time PCR.

Results: Transcripts were measured in 99 patients after kidney transplantation (55 living related kidney donors and 44 deceased kidney donor transplantations). Immunosuppressive treatment consisted of basiliximab, tacrolimus and mycophenolate mofetil. Prednisolone was administered to 32 patients, whereas 67 patients were prednisolone-free. Patients in the prednisolone group showed significantly lower granzyme B compared to the prednisolone-free group (0.016±0.004 arbitrary units vs. 0.031±0.005 arbitrary units; mean±SEM; p<0.005). Patients in the prednisolone group showed also significantly reduced perforin transcripts (0.001±0.002 vs. 0.028±0.005, p<0.0001) and interferon stimulating glycoprotein 15 transcripts (0.011±0.003 vs. 0.023±0.005, p<0.0005), whereas matrix metalloproteinase 9 transcripts were similar between the groups (0.006±0.002 vs. 0.005±0.001, p=1.000).

In the prednisolone-free group we observed a significant positive association between C-reactive protein levels and matrix metalloproteinase 9 transcripts (Spearman r=0.43, p=0.005), whereas matrix metalloproteinase 9 transcripts were similar between the groups (Spearman r=0.43, p=0.005) but not granzyme B transcripts (Spearman r=-0.18, p=0.210), interferon stimulating glycoprotein 15 transcripts (Spearman r=-0.04, p=0.758) or perforin transcripts (Spearman r=0.14, p=0.332). 14 patients developed histologically-verified acute rejection episodes (8 patients with borderline rejection, 4 patients with unspecified rejection, and 2 with cellular rejection). Granzyme B levels were significantly higher before the histologically-verified rejection episodes compared to their respective controls taken at the first day after transplantation (during rejection episode, 0.033±0.007 arbitrary units vs. first day after transplantation, 0.026±0.008; p<0.05).

Conclusions: Administration of prednisolone reduces granzyme B transcripts after kidney transplantation. Repeated measurements showed that rejection episodes were associated with higher granzyme B transcripts.
Methods: A retrospective comparative analysis was performed during a 10 years period that included demographic, clinical, laboratorial, histological and outcome features.

Results: Out of a total of 627 biopsies, a total of 39 TG cases (6.2%) in 33 patients and 14 (2.2%) de novo TMA cases in 12 patients were found. TG was diagnosed latter (6.8±5.9 vs 3.5±6.5 years, p=0.01) and presented higher proteinuria (4.0±3.6 vs 2.3±1.6 grams/24h, p=0.02). De novo TMA was associated to worse graft dysfunction (MCD: 9.4±1.8 vs 2.7±0.9, p=0.001) with allografts provided from older patients (53.8±10.1 vs 41.3±17.9 years, p=0.035) and a trend in TMA to longer cold ischemia time (1439±210 vs 1218±441 min, p=0.141) and previous rejection episodes (21.4 % vs 5.3%, p=0.079). No findings were observed in proportion of deceased/delaying donor grafts, HLA mismatches, PRA levels. Pre- transplant or cyclophosphamide therapy were reported. In light microscopy, diffuse glomerular lesions were observed in all de novo TMA cases, opposing to a focal presentation in TG (100% vs 45.9% and p=0.001). Both groups presented equally glomerular basement membrane (GBM) double contours, glomerulotitis, tubulitis, capillaritis and ischemic features. Capillary congestion (100 vs 35.1%, p=0.001), microthrombi (50% vs 5.4%, p=0.01), schistocytes (42.8% vs 7.7%, p=0.009) and mesangiolysis (85.7% vs 29.7%, p=0.001) were associated to TMA. Most TG cases presented advanced glomerulonephrosis, interstitial fibrosis and tubular atrophy and interstitial plasma cells were only seen in these cases (30.8% vs 0%, p=0.018).

Positive Cd4 staining in de novo TMA cases was similar to TG (71.4% vs 53.8%, p=0.025) but arteriolar Cd4 deposition was predominantly seen in these cases (35.7 % vs 8.7%, p =0.042). Donor Specific Antibodies (DSA) detection was equally found in both groups (TG: 41.6 %; TMA: 57.1%, p=0.500) and were mainly constituted by anti-HLA Class II (60% and 75%, respectively). After ultrastuctural analysis, only TG cases presented GBM multilamination (75% vs 0%, p=0.044) and tended to expressed more frequently peritubular capillary basement membrane thickening (100% vs 60%, p=0.07) with multilamination (75% vs 20%, p=0.060). Considering all follow up time, graft loss occurred similarly in both groups (47.1% vs 45.5%, p=0.926) but de novo MAT cases had lower first year post-transplantation death censored curves (71.3% vs 97.4%, p=0.013).

Conclusions: Similarities in histological features, Cd4 staining and presence of DSA suggests that TG and de novo TMA may represent different manifestations of humoral endothelial injury.While TG may express a subclinical ongoing antibody mediated injury, presenting chronic cyclic accommodation mechanisms, TMA results from an intense acute manifestation of endothelial lesion.

REFERENCES

Introduction and Aims: Since 2002, when the end-stage liver disease model score (MELD) was adopted, the number of combined liver-kidney transplantsations increased. Between January 1995 and December 2011 we performed 38 combined liver-kidney transplantation (CLKT) and 6 sequential liver-kidney transplantation (SLKT).

Methods: This study compares the outcomes of CLKT and SLKT with the controlateral kidney (31 of the first group and 6 of the second one) used for the kidney alone transplantation (KTA 1 and 2).

Results: The indications for CLKT were: polycystic disease (60,6%), primary Hyperoxaluria type 1 (21%), end-stage kidney disease and cirrhosis (18,4%). In SLKT, the major cause of renal failure was calcineurin inhibitor nephropathy (83,3%) and dialysis started on a 7 years average time after liver transplantation. Delayed renal graft function (DGF) occurred in the 52,6% of CLKT vs. 38,7% in the KTA, despite a minor cold ischemia time and lower donor age in CLKT group. Infections and bleedings were more common in CLKT patients (86,8% vs. 61,5% in KTA1 p=0,034), as well as surgical complications (42% vs. 11,5% in KAT1 p=0,03). The immunosuppressive protocol mostly used was tacrolimus, mycophenolate mofetil and prednison. In CLKT recipients tacrolimus levels were lower and steroid was stopped earlier than KTA. The acute renal rejection frequency was lower in CLKT (2,6% in CLKT, 7,7% in KTA1 and 16,6% in SLKT, p = not significant) despite a major HLA mismatch, positive X-match, specific anti-donor antibody and lower immunosuppression. Mean creatinine serum levels were lower in CLKT group. At 5 years, patient survival rates in SLKT were lower than those in CLKT (75% in SLKT vs 90% in CLKT), and in KAT1-2 (100%). Kidney graft survival rates: 0% in CLKT, 7% in SLKT, 97% in KAT1, 100% and 97% in KAT2. CLKT and KAT1 kidney graft survival compared using “death censored curves” was the same in both groups (97% at 1 and 5 years).

Conclusions: In conclusion in CLKT recipients, although complications and mortality were more frequent in the first three months after transplantation, the patient and kidney allograft survival rates appeared to be superior than those in SLKT. In addition, in CLKT there were lower serum creatinine levels despite a major HLA mismatch. These results seems to confirm that the liver allograft has an immunoprotective effect on the renal allograft from the same donor.

ROLE OF eGFR EQUATIONS IN EVALUATING DECEASED DONORS FOR KIDNEY TRANSPLANTATION: SUFFICIENT AND APPROPRIATE OUTCOME MARKERS?

Methods: The study enrolled 625 single kidney graft recipients and the corresponding 481 donors (144 kidneys were allocated elsewhere). Mean f-up 1072.6±702.7 days. Donor GFR was estimated with Cockcroft-Gault (CG), MDRD and CKD-EPI. To counterbalance GFR overestimation in obese donors, CG formula was assessed with actual (ABW) as well as with ideal body weight (IBW).

Results: Kidney function was evaluated with MDRD formula at discharge and after 3, 6, 12, 24 months from surgery. BMI, age, gender, history of hypertension or diabetes mellitus, cause of death and histology were recorded. Survival curves were obtained for grafts and recipients.

Results: Patients: male 61.6%, age 57.5±11.8 ys, BMI 24.1±3.7 kg/m2 (i=2±37.3%). Donors: mean 50.1±1.8, age 57.6±15.1 ys, CG 0.8±0.3 ml/min/gm, hyperension 51.3%, diabetes mellitus 8.4%, BMI 25.3±3.8 kg/m2 (i=2±49.5%). Preimplantation biopsy was performed in 57.6%. Median eGFR (mL/min): CG (ABW)=104, CG (IBW)=87, MDRD=99, CKD-EPI=92. All eGFR formulas were equally predictive of recipient renal function during f-up (p<0.05), but only CG was significantly correlated with graft survival (p=0.03). Univariate analysis showed, as for 1-year graft function, a negative predictive role of donor hypertension (p=0.00), donor age (p=0.00), female donor gender (p=0.00), cerebrovascular death (p=0.01) and high recipient BMI (p=0.002). No correlation was found between donor histology, donor eGFR and graft outcome. Multivariate analysis confirmed the negative impact of donor hypertension, age and female gender as well as high recipient BMI.

Conclusions: In conclusion, donor eGFR with all formulas predicted graft function. Since CG predicts graft survival, its use with IBW may be more appropriate. Other clinical (donor hypertension, recipients BMI) and demographic (donor age and gender) data should be considered in organ allocation, while the role of histology might be reassessed.

SPE650

UNSPECIFIED AND SPECIFIED LIVING KIDNEY DONATION TO UNRELATED RECIPIENTS: THE ROTTERDAM EXPERIENCE

Willi Zuidema, Ruud Erdman, Jacqueline van de Wetering, Frank Dorf, Joke Roofdant, Emma Massey*, Lotte Timmerman, Jan Uzerman* and Willem Heimr

Introduction and Aims: In unspecified living kidney donation, formerly known as Good Samaritan, altruistic or anonymous donation, the recipient is not specified by the donor. There is no relationship between them and there is no material benefit for the donor. While most specified donors have a relation with their intended recipient, a number of them do not.

Methods: Between May 2000 and November 2012 we, Erasmus MC, Rotterdam have been approached by 213 individuals with the intention to donate a kidney to an emotionally and genetically unrelated patient.

Results: After the screening process 92/103 (89%) have donated a kidney. A minority of them 13/92 (14%) specified their recipient, who was a stranger, the recipient is not specified by the donor. Over these 92 donors realized 157 kidney transplants, to 89 waitlist patients and 68 recipients of incompatible couples. The willing donors of these couples participated in 54 unspecified donor – triggered domino paired procedures including 44 double, 7 triplets and 3 quadruplets.

Conclusions: We conclude that waiting list patients as well as recipients of incompatible couples profit from unspecified living kidney donation. This successful outcome warrants further extension of this program.
Introduction and Aims: Measurements of glomerular filtration rate (GFR) are frequently interpreted assuming a linear variation with age. However this may be simplistic. Non-linear relationships may give a better representation of the changes associated with “normal aging”. This is a really important consideration in a population of potential living kidney donors generally considered to be even healthier than age-matched controls.

Methods: This was a retrospective study of 904 subjects (468 women, 436 men; age range 14-84 years) undergoing assessment as prospective living kidney donors. GFR was evaluated from \( ^{51} \text{Cr}-\text{EDTA} \) plasma clearance using blood samples taken at 2, 3, and 4 hours. The slope-intercept GFR was corrected for body surface area (BSA) using the Haycock formula and for the fast exponential using the Brochner-Mortensen equation. The relationship between age, gender and GFR was examined using best-fit curve analysis. Non-linear relationships with age were explored using fractional polynomials.

Results: There was no gender difference in BSA corrected GFR over five decades of age (P = 0.40). However, female donors with a body mass index > 30 kg.m\(^{-2}\) had a statistically significantly lower GFR than non-obese women (P < 0.01). The best-fit relationship between age and GFR was non-linear and described using a fractional polynomial model of degree 1 (GFR = 103.9 - 0.0061\(\text{Age} \times \text{mm}^2\) with an RMSE of 12.9 \(\text{mm}^2\times\text{m}^2\)). The residual variance for this model was significantly smaller than for the best-fit linear model (P = 0.006).

Conclusions: GFR measurements in prospective healthy living kidney donors are best corrected for age using a non-linear relationship. Our results help to establish potential normative mGFR ranges for this important population, which will crucially inform decisions on potential wisdom of kidney donation.

**SP652**

**ASSOCIATION BETWEEN A DECLINE IN DONOR CREATININE CLEARANCE AND ALLOGRAFT OUTCOMES**

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Introduction and Aims: It has been well documented that development of compensatory hypertrophy of the solitary kidney and alterations of allograft kidney function following kidney transplantation (KT) is conceivable that the given allograft function in recipients may be related with the remnant kidney function in donors. This study was undertaken to find whether the degree of decline in donor creatinine clearance (CrCl) after KT may be predictive of long-term outcomes of allograft kidneys.

Methods: The decline in CrCl of donor kidney was calculated by the difference over 30 days after KT. \( \Delta \text{CrCl} = (\text{CrCl at post-KT 30 days} - \text{CrCl at Pre-KT}) / \text{CrCl at Pre-KT} \times 100 \% \). All recipients were divided into 2 groups according to \( \Delta \text{CrCl} \); Group I (n = 69), \(< -30\%\); and Group II (n = 70), \( \geq 30\%\). Multiple linear regression analysis was used to find associated factors with short- and long-term renal allograft function, and Kaplan-Meier (KM) analysis was used to compare dialysis-free regrowth analysis was used to find associated factors with short- and long-term renal allograft function and survival. These results suggest that the short-term allograft survival is longer when the initial decline in donor CrCl is less. Follow-up measurement of donor kidney function may be useful to monitor the patient at risk for allograft loss.

**SP654**

**THE EFFECT OF MAGNESIUM SUPPLEMENTATION ON EARLY POST-TRANSPLANTATION GLUCOSE METABOLISM**

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Introduction and Aims: Post-transplantation hypomagnesemia is associated with new-onset diabetes after transplantation (NODAT) in retrospective studies. Our aim was to prospectively evaluate whether oral magnesium (Mg) supplementation modifies the risk for NODAT.

Methods: Single-center, randomized, controlled, 3-month open label trial comparing Mg supplements (Mg oxide 450mg up to thrice daily) aiming at normalizing serum Mg (n=27) vs no supplements (n=27) in adult tacrolimus-treated non-diabetic renal transplant recipients with hypomagnesemia (<1.7mg/dL) the first two weeks post-transplantation. Mg response was defined as increase of serum Mg at month 3 vs baseline. The primary outcome was change in glucose metabolism, assessed by OGTT at month 3 with measurement of AUC of glucose and by the change of HOMA-IR 3 months after inclusion (secondary outcome). NODAT was defined according to ADA criteria and abnormal glucose metabolism as NODAT, IFG or IGT.

Results: In this population (63% male, age 51.9±11.9, BMI 25.1±3.3), Mg supplementation increased serum Mg (MgA 8.1±3.0±2.0mg/dL vs 6.0±2.2±0.2mg/dL; p=0.062). Of the supplemented patients, 25.9% were non-responders vs 48.1% in the control group (p=0.091). Overall incidence of NODAT was 10/54 (18.5%) and not different between supplemented (4/27) vs controls (6/27) (p=0.484). At month 3, fasting glucose levels were lower in the supplemented group vs the controls (92±6 vs 9.6).
**SP656**

**ASSOCIATION BETWEEN URIC ACID CONCENTRATION AND POSTDONATION KIDNEY FUNCTION AFTER LIVING DONOR NEPHRECTOMY**

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Introduction and Aims: Elevated serum uric acid (SCA) concentration may contribute to renal damage or its progression via renal vasconstriction and loss of renal autoregulation. Considering previous experimental and clinical data on SCA concentration we hypothesized that elevated SCA concentration plays a role in renal complications after donor nephrectomy. Moreover, we investigated the potential influence of preoperative SCU concentration on the risk of renal function impairment after living donor nephrectomy.

Methods: This retrospective observational study investigated 413 living kidney donors from a single center. The main outcome was kidney function 6 months after donor nephrectomy. Kidney function was assessed by calculating the estimated glomerular filtration rate (eGFR) using the abbreviated Modification of Diet in Renal Disease (MDRD) study equation. Renal function impairment was defined as a postdonation eGFR < 60 mL/min/1.73 m².

Results: Renal function impairment occurred in 143 of 413 donors (34.6%). In multivariate analysis, the following factors were associated with renal function impairment after donor nephrectomy: hyperuricemia (predonation SUA concentration > 5 mg/dl), hyperuricemia and hypertension, age, male gender and albuminuria. Predonation SUA concentration was significantly related to renal function impairment in women (OR, 1.56; 95% CI, 1.10–1.18; P = 0.04) but not in men.

Conclusions: Predonation SUA concentration is associated with renal function after nephrectomy in living kidney donors. The association is stronger in women than in men. Further studies with longer follow-up are needed to assess the prognostic value of predonation SUA concentration to long-term renal insufficiency in living kidney donors.

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**SP657**

**PROGNOSTIC SIGNIFICANCE OF CHANGES IN PROTEINURIA IN EARLY STAGES OF RENAL TRANSPLANTATION**

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Introduction and Aims: Proteinuria is considered the main independent risk factor of end stage renal disease. Some authors consider that changes in proteinuria could be as a surrogate of kidney disease progression. Proteinuria is highly prevalent in renal transplantation and it has been associated to a lower graft and patient survival. There is not information about the relation between changes in proteinuria in early stages (first year) and long term graft and patient survival. To analyze the effect of the magnitude of proteinuria and its changes from 3 months to 12 months after transplantation on long term graft and patient survival.

Methods: We studied 593 patients, mean follow-up: 84.5±48.6 months (r: 12.1-191.6). Proteinuria ≥150mg/d was present in 49.9% at 3 months, 47.0% at 12th month. At 3rd month distribution of proteinuria was: (0) 50.1%, (1) 17.9%, (2) 28.3%, and (3) 3.7%. Presence of increasing degrees of proteinuria at 3rd and 12th month was associated with long term graft failure (P=0.000) and mortality in case of 12th months (P=0.000). We observed an increasing relative risk of graft failure and mortality from category 2 at 3rd month (HR: 2.81±0.56, 95% CI 1.53-4.27), 2.49±0.46, 95% CI 1.39-4.48) if compared with (0) category. Increase in proteinuria ≥50% was related to a higher serum creatinine at 12th month (P<0.001) and to a lower eGFR (P=0.0001) in every category.

Conclusions: Risk of graft failure and mortality increases with increasing amounts of proteinuria and with time from transplantation, since early stages of kidney transplant. Proteinuria progression ≥50% in early stages of renal transplantation could be considered as a marker of graft failure, regardless of baseline proteinuria category.
Introduction and Aims: Persistent secondary hyperparathyroidism (SHPT) and residual proteinuria are important problems in kidney transplant patients. Both conditions can contribute to graft loss. Paricalcitol has shown a beneficial effect on chronic kidney diseases (CKD) and reduces proteinuria in diabetic nephropathy. Information about paricalcitol treatment in kidney transplant patients is very scarce. Our objectives were to analyze the influence of paricalcitol on markers of mineral metabolism, residual proteinuria, renal function, and inflammation.

Methods: In a historical cohort of 58 kidney transplant patients with SHPT, we studied the impact of paricalcitol (initial dose 1 µg/48 hr) on the control of intact parathormone (iPTH) and other markers of mineral metabolisms, on the amount of residual proteinuria, renal function, blood pressure and inflammation. We used a panel of standard deviations, paired t-tests and Wilcoxon test. Remission ≥30% of iPTH and ≥50% of 24 hours proteinuria were calculated by logistic regression.

Results: Baseline characteristics: 26 men (44.8%), 55.7±12.7 years, creatinine 2.1±0.7 mg/dL, 24 hours proteinuria 1.1±0.7 g, calcium 9.3±0.5 mg/dL, phosphorus 3.4±0.5 mg/dL, iPTH 333.1±225.9 pg/ml, 25(OH)D 17.6±3.5 ng/ml. Serum iPTH significantly decreased after paricalcitol treatment (333.1±225.9 to 187.4±88.9 pg/ml) and 44 patients (76%) achieved a decrease of baseline iPTH≥30%. A baseline iPTH≥500 pg/ml was associated with an iPTH reduction ≥30% (OR: 5.6; 95%CI: 1.3-24.6; p=0.022).

Proteinuria decreased from 1.1±0.7 to 0.7±0.7 g/24 hours (p<0.005) (mean reduction 35%) and 26 patients (45%) achieved a ≥50% decrease of baseline proteinuria. Serum CRP (<1.2 mg/dL was associated to proteinuria reduction ≥50% (OR: 13.8, 95%CI: 2.0-95.1, p=0.008). Renal function, with a significant decline during the 2-year period before treatment, remained stable during paricalcitol treatment. C-Reactive Protein (CRP) showed a significant decrease with paricalcitol. Paricalcitol doses were reduced since the third month of treatment until the end of the follow-up (4.1±1.8 µg/week to 3.3±1.2 µg/week, p<0.005). Mild increases of serum calcium (10.10-10.5 mg/dl) and phosphorus (4.4-5.5 mg/dL) were detected in 4 (6.9%) and 7 (12.1%) patients, respectively, and responded to reduction of doses.

Conclusions: Oral paricalcitol is a safe and efficacious therapy of SHPT in kidney transplant patients, reducing residual proteinuria as well as systemic inflammation.

Introduction and Aims: Non-HLA antibodies (Abs) are thought to have an impact on renal transplant injury. Anti-endothelial cell antibodies (AECA) are supposed to be involved in the injury of endothelium, critically located between intravascular and interstitial renal compartment but their role in renal transplantation remains uncertain. The aim of our study was to assess the incidence and importance of AECA and their impact on renal transplant during the first post-transplant year.

Methods: 1st month 3rd month 6th month 12th month

Anti-endothelial cell antibodies (AECA) are associated with a worse renal transplant function

Anti-endothelial cell antibodies (AECA) are associated with a worse renal transplant function

AECA (+) group and 11/69 pts (15.9%) in the AECA(-)group. There was no statistically worse renal transplant function over the first 12 months after transplantation. In the studied patients, AECA did not appear de novo after transplantation. The results encourage to include pre-transplant AECA testing in diagnostics of renal transplant recipient immune status and thorough assessment of humoral alloimmunity.

Introduction and Aims: Secondary hyperparathyroidism (SHPT) and residual proteinuria are important problems in kidney transplant patients. Both conditions can contribute to graft loss. Paricalcitol has shown a beneficial effect on chronic kidney diseases (CKD) and reduces proteinuria in diabetic nephropathy. Information about paricalcitol treatment in kidney transplant patients is very scarce. Our objectives were to analyze the influence of paricalcitol on markers of mineral metabolism, residual proteinuria, renal function, and inflammation.

Methods: In a historical cohort of 58 kidney transplant patients with SHPT, we studied the impact of paricalcitol (initial dose 1 µg/48 hr) on the control of intact parathormone (iPTH) and other markers of mineral metabolisms, on the amount of residual proteinuria, renal function, blood pressure and inflammation. We used a panel of standard deviations, paired t-tests and Wilcoxon test. Remission ≥30% of iPTH and ≥50% of 24 hours proteinuria were calculated by logistic regression.

Results: Baseline characteristics: 26 men (44.8%), 55.7±12.7 years, creatinine 2.1±0.7 mg/dL, 24 hours proteinuria 1.1±0.7 g, calcium 9.3±0.5 mg/dL, phosphorus 3.4±0.5 mg/dL, iPTH 333.1±225.9 pg/ml, 25(OH)D 17.6±3.5 ng/ml. Serum iPTH significantly decreased after paricalcitol treatment (333.1±225.9 to 187.4±88.9 pg/ml) and 44 patients (76%) achieved a decrease of baseline iPTH≥30%. A baseline iPTH≥500 pg/ml was associated with an iPTH reduction ≥30% (OR: 5.6; 95%CI: 1.3-24.6; p=0.022).

Proteinuria decreased from 1.1±0.7 to 0.7±0.7 g/24 hours (p<0.005) (mean reduction 35%) and 26 patients (45%) achieved a ≥50% decrease of baseline proteinuria. Serum CRP (<1.2 mg/dL was associated to proteinuria reduction ≥50% (OR: 13.8, 95%CI: 2.0-95.1, p=0.008). Renal function, with a significant decline during the 2-year period before treatment, remained stable during paricalcitol treatment. C-Reactive Protein (CRP) showed a significant decrease with paricalcitol. Paricalcitol doses were reduced since the third month of treatment until the end of the follow-up (4.1±1.8 µg/week to 3.3±1.2 µg/week, p<0.005). Mild increases of serum calcium (10.10-10.5 mg/dl) and phosphorus (4.4-5.5 mg/dL) were detected in 4 (6.9%) and 7 (12.1%) patients, respectively, and responded to reduction of doses.

Conclusions: Oral paricalcitol is a safe and efficacious therapy of SHPT in kidney transplant patients, reducing residual proteinuria as well as systemic inflammation.
characteristic disease-specific HDL proteome. Of note, alterations of HDL were virtually identical between patients with CKD-I-IV and those without diabetes, but substantially increased free cholesterol content in PBMCs of the patients. Finally, impaired anti-inflammatory HDL function could be demonstrated by increased expression of inflammatory cytokines including IL-6, IL-12p40 and TNF-α in monocytes compared to healthy HDLC.

Conclusions: We demonstrate unique alterations of HDL from renal transplant recipients at the molecular and functional level. Importantly, remodeling of HDL including enrichment of distinct proteins previously identified from urinary HDL was also observed in patients with excellent graft function independent of the transplant vintage. These data may therefore not only help to unravel the causes of the excessive cardiovascular risk in renal transplant patients, but may also pave the way for novel diagnostic and innovative therapeutic directions.

Introduction and Aims: The utilization of expanded criteria donor (ECD) kidneys needs to be evaluated within the objective perspective of critical organ shortage and graft function and survival. Our objective was to compare the clinical outcomes of expanded criteria (ECD) grafts with concurrent standard criteria (SCD) deceased donors in adult renal transplantation.

Methods: Between February 2000 and December 2011, we performed 195 deceased donor renal transplants including 31 grafts (15.9%) from ECD and 164 grafts (84.1%) from SCD. ECDs were classified by the UNOS definition. Donor and recipient risk factors were separately analyzed and correlated with recipient graft function and survival (minimum 6-month follow-up).

Results: ECDs were older (56.8±6.3 yrs), showed an increased incidence of hypertension, diabetes and cerebrovascular brain death, and had a higher pre-retrieval serum creatinine level compared with SCD. ECDs were classified by the UNOS definition. Donor and recipient risk factors were separately analyzed and correlated with recipient graft function and survival (minimum 6-month follow-up).

Conclusions: In conclusion, the utilization of renal grafts from ECDs is an acceptable offer to resolve the disparity of critical organ shortage. Comparability of ECD kidney recipients at the molecular and functional level. Importantly, remodeling of HDL including enrichment of distinct proteins previously identified from urinary HDL was also observed in patients with excellent graft function independent of the transplant vintage. These data may therefore not only help to unravel the causes of the excessive cardiovascular risk in renal transplant patients, but may also pave the way for novel diagnostic and innovative therapeutic directions.
**Abstracts**

**SP667**

**RELATIONSHIP BETWEEN LIPID PEROXIDATION AND ARTERIAL STIFFNESS IN RENAL TRANSPLANTED PATIENTS**

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Introduction and Aims: Lipid peroxidation and atherosclerosis development remain accelerated in patients with chronic renal failure even after renal transplantation. Oxidative stress and inflammation facilitate atherosclerosis development all over the peripheral, central and coronary arteries. We investigated the connection between lipid peroxidation and arterial stiffness parameters after renal transplantation.

Methods: 131 renal transplanted patients (46.4±14.2 years) and 63 healthy controls (48.2±9.0 years) were involved in this study. Fasting serum creatinine, urea, cystatin-C, homocysteine, lipids, glucose, C-reactive protein (CRP), asymmetric dimethyl arginine (ADMA), adiponectin (ADPN), leptin (LEP) concentrations were measured with ELISA and paraoxonase (PON1), arylesterase activities were measured spectrophotometrically. Arterial stiffness parameters (PWV-pulse wave velocity, AIx–augmentation index, PP–pulsatile pressure, SIA–systolic area index, DIA–diastolic area index, systolic and diastolic blood pressure, and MAP-mean arterial pressure) were measured with Arteriograph (TensioMed).

Results: In case of kidney transplanted patients with dyslipidaemia we found significant lower PON1 activity (101.7±13±2.31 U/l) compared to controls (p<0.01). Significant negative correlation were found between serum cystatin-C level, homocysteine (p<0.05), and ADMA (p<0.05), and there was significant positive correlation in case of Batin-C levels.Significant negative correlation were found in case of PON1 activity and PWV (r=0.2315, p<0.0488), DAL, LDL (p<0.0452), and total cholesterol (p<0.0301); MAP (p<0.0057) and ADMA concentrations. There was positive correlation between PWV and CRP (p<0.03); PWV and total cholesterol (p<0.0215); PWV and LDL (p<0.0015). In obese transplanted patients we measured significant higher LDL and lepint levels (p<0.05).

Positive correlation was found between PWV and AIx; systolic, diastolic blood pressure and MAP (p<0.01).

Conclusions: Reduced paraoxonase activity, enhanced ADMA levels together with arterial stiffness parameters are objective, suitable predictive markers of cardiovascular diseases.

**SP668**

**LIMITED PROGNOSTIC VALUE FOR CHRONIC TRANSPLANT DYSFUNCTION BY URINARY MARKERS OF TUBULAR INJURY WHEN MEASURED WITHIN THE FIRST YEAR AFTER RENAL TRANSPLANTATION**

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Introduction and Aims: NGAL and KIM-1 as urinary markers have been proposed as predictors of chronic transplant dysfunction (van Timmeren et al. 2007 Transplantation, Nauta et al. 2011 Am J Kidney Dis). Our aim was to determine whether these markers measured within the first year after Transplantation predicted outcome.

**Introduction and Aims:** The relationship between lipid peroxidation and arterial stiffness parameters after renal transplantation remains unclear. We investigated the connection between lipid peroxidation and arterial stiffness parameters in 131 renal transplanted patients and 63 healthy controls. Using fasting serum creatinine, urea, cystatin-C, homocysteine, lipids, glucose, C-reactive protein (CRP), asymmetric dimethyl arginine (ADMA), adiponectin (ADPN), and leptin concentrations, we measured ARTERIAL STIFFNESS PARAMETERS (PWV-pulse wave velocity, AIx-augmentation index, PP-pulsatile pressure, SIA-systolic area index, DIA-diastolic area index, systolic and diastolic blood pressure, and MAP-mean arterial pressure) and ARTERIAL STIFFNESS PARAMETERS (PWV-pulse wave velocity, AIx-augmentation index, PP-pulsatile pressure, SIA-systolic area index, DIA-diastolic area index, systolic and diastolic blood pressure, and MAP-mean arterial pressure) were measured with ARTERIOGRAPH (TensioMed). We found significant lower PON1 activity (101.7±13±2.31 U/l) compared to controls (p<0.01). Significant negative correlation were found between serum cystatin-C level, homocysteine (p<0.05), and ADMA (p<0.05), and there was significant positive correlation in case of Batin-C levels. Significantly negative correlation were found in case of PON1 activity and PWV (r=0.2315, p<0.0488), DAL, LDL (p<0.0452), and total cholesterol (p<0.0301); MAP (p<0.0057) and ADMA concentrations. There was positive correlation between PWV and CRP (p<0.03); PWV and total cholesterol (p<0.0215); PWV and LDL (p<0.0015). In obese transplanted patients we measured significant higher LDL and lepint levels (p<0.05). Positive correlation was found between PWV and AIx; systolic, diastolic blood pressure and MAP (p<0.01).

Conclusions: Reduced paraoxonase activity, enhanced ADMA levels together with arterial stiffness parameters are objective, suitable predictive markers of cardiovascular diseases.
Methods: KIM-1 and NGAL levels were measured by ELISA in 24-hours urine samples collected within the first year after transplantation but not within a 2-week proximity of the surgery or transplant biopsy. We determined the predictive value for a three to 50% and 100% decline in renal function or death-censored graft failure by Cox regression and incident/dynamic (I/D) ROC analyses. We evaluated whether they have a predictive value when eGFR is still within the good range and therefore performed all analyses separately in patients with baseline eGFR >50 mL/min.

Results: Baseline samples of 412 transplant recipients were included with a median of 54 days (IQR 44 – 77 days) and a follow-up of 1054 (554 – 1811 days). The concentration of KIM-1 and NGAL associated with the extent of albuminuria (especially after 35 years) and female gender (HR: 2.10; 95%CI: 1.49-2.95) were independent factors for the development of urological malignancy after KT. After 2 years after transplantation, By Cox (p=0.0016) and liver cirrhosis (p<0.001). The cumulative incidence rate was below 0.60 indicating limited discriminative value.

Conclusions: Urinary excretion of KIM-1 and NGAL measured within the first year after surgery for patients with no prognostic value with all calculated incident dynamic C-indices below 0.60 indicating limited discriminative value.

**KIDNEY TRANSPLANTATION AGGRAVATES UROLOGICAL MALIGNANCY RISK IN ESRD PATIENTS: A POPULATION-BASED STUDY**

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**Introduction and Aims:** Post-transplantation is associated with various cardiovascular diseases. High urological malignancy incidence was reported in end-stage renal disease (ESRD) patients on dialysis. This study was undertaken to evaluate whether kidney transplantation (KT) aggravates urological malignancy risk in ESRD patients.

**Methods:** We used claims data of the Bureau of National Health Insurance of Taiwan. All KT recipients who developed urological malignancy from 1st January, 1999 to 31st December, 2007 (n=2,386) were enrolled for study. A database of 1:2ratio random new ESRD patients with matched age, gender, and cohort entry time was used as control (n=4,772). The longest observation period lasted up to 31st December, 2008.

**Results:** KT recipients had lower prevalence of diabetes mellitus (p<0.001), C-hepatitis (p=0.0016), and liver cirrhosis (p=0.001). The cumulative incidence rate was significantly higher in the KT patients than those without transplantation (p<0.001). This gap became more prominent about 2 years after transplantation. By Cox regression and incident/dynamic (I/D) ROC analyses. We evaluated whether they have a predictive value when eGFR is still within the good range and therefore performed all analyses separately in patients with baseline eGFR >50 mL/min.

**Conclusions:** ESRD patients tended to have a significantly higher urological malignancy incidence after KT, especially for those patients who were older, of female gender, and at 2 years after KT.

**THE rs17384213 POLYMORPHISM IN THE DDAH1 GENE IS A MARKER OF CHRONIC ALLOGRAFT DYSFUNCTION**

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**Introduction and Aims:** Endothelial dysfunction may be involved in the development or progression of vascular lesions in Chronic Allograft Dysfunction (CAD) and Asymmetric Dimethyl arginine (ADMA) an aminocid degraded by dimethylsysteine dimethylaminohydrolase (DDAH1 and DDAH2) has been implicated in CAD in these patients. Since Plasma ADMA levels may be confounded by various biological and environmental influences, we used a genetic approach, investigating the impact of variation in the rs17384213 polymorphism in the DDAH1 gene, to establish any causal role for the ADMA pathway in CAD. Application of this genetic approach in a previous study in two CKD cohorts negated a causal role of ADMA in CKD progression and showed an apparently paradoxical risk excess for CKD progression in patients with the allele (G) associated with low ADMA levels (Kidney Int 2010;77:459-67).

**Methods:** The study cohort included 249 transplant patients on a pool of 277 transplant patients on follow-up in a large renal unit serving a 700,000 residents area. The baseline eGFR (MDRD) was 54±24mL/min/1.73mug and the median follow-up was 10,7 years (range 1-29 years). We used repeated measures of a quantitative trait (eGFR) as an outcome measure to maximize the study power and the average number of eGFR measurements per patient applied to calculate the individual evolution of renal function over time was 70 (range 7 to 289).

**Results:** The genotype distribution in the rs17384213 polymorphisms in the DDAH1 did not deviate from Hardy Weinberg equilibrium. The evolution of the eGFR over time showed a remarkable stability in patients with the A allele (AA and AG) (eGFR slope over time (median) 0.008mL/min/year)1. Even though the overall rate of renal function loss was modest also in patients recessive (GG) for the G allele (the allele associated with low plasma ADMA), the rate of function loss (median: 0.10mL/ min/year) in these patients was several fold (x13) higher that in those without such a genotype (P=0.03). Further analyses adjusting for age, BMI, HLA score, baseline eGFR, proteinuria, waiting time to renal transplant, type of transplantation (living vs cadaveric donor) did not modify the strength of this association (rs17384213 SNP-eGFR slope: P=0.024).

**Conclusions:** This study implies a role of the G allele in the rs17384213 polymorphism of the DDAH1 gene in mediating renal function loss in chronic allograft dysfunction independent of established risk factors and proteinuria. Furthermore, these findings indicate that it is much unlikely that the link between ADMA and allograft dysfunction in previous studies be causal in nature. Full clarification of the role of DDAH1 allograft dysfunction may help the development of treatments aimed at countering chronic allograft dysfunction in transplant patients and at retarding the evolution of renal disease in CKD patients.
Conclusions: There was a clear recommendation that anonymity should be maintained prior to either unspecified or specified indirect transplantation. Preservation of anonymity subsequently was considered ideal, and should only be lost under carefully controlled conditions to minimise potential harm to both donor and recipient. Further studies with unspecified donors and their recipients are needed to consider when to offer the opportunity to both donor and recipient to meet each other. Reference: Anonymity and live donor transplantation: An ELFAT view. Mamode N. et al. Transplantation in press.

PROSPECTIVE STUDY OF BKV INFECTION AND NEPHROPATHY IN THE FIRST YEAR POST-RENAL TRANSPLANTATION

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Introduction and Aims: BK virus nephropathy (BKN) has recognized as an emerging cause of allograft dysfunction in renal transplant recipients. We aimed to assess prospectively the incidence of BKV infection and nephropathy in the first year after transplantation. Methods: BK virus (BKV) viremia during the first year of renal transplantation was quantified in 32 consecutive recipients. BKV DNA after extraction was determined in all samples by real time PCR according to manufacturer’s instruction. Results: BK virus viremia was detected in 8 (25%) patients. The highest detected plasma viral load was less than 4 Log copies/mL. BK virus viremia was respectively positive in 5 (62.5%), 2 (25%) and one (12.5%) patient during the first 4, 8 and 12 months after transplantation. Biopsy-proven rejection and anti-rejection therapy by methylprednisolone pulses were respectively 5 and 2.3 times more common in patients with BKV infection (p 0.012 and p 0.013). Despite occurrence of BKV infection in 25% of our patients, neither developed BKV nephropathy. Conclusions: Routine screening of BKV infection particularly in centers with low prevalence of BKV nephritis may not be cost-effective in predicting this disease.
Introduction and Aims: Due to graft preserving immunosuppressive therapy renal transplant recipients (RTR) are predisposed to the development of various skin infections and skin cancers. The aim of the study was to evaluate frequency of skin lesion among RTR and dialysed population.

Methods: The clinical dermatological examination was performed in 484 patients after renal transplantation (early detection of skin changes in RTR program) consisted of 295 man and 189 woman in the mean age 46.1 +/- 13 years with median time after transplantation 74.3 +/-5.21 months. The group of 112 dialyzed patients (57 male and 55 female) aged 57.4 +/- 15.4 years without history of immunosuppressive therapy were collected.

Results: From the studied group of RTR 38.5% have viral warts mostly localized on the hands (91.9%). Fungal infection was observed in 25.9% of patients. Clinical diagnosis of interdigital mycosis was made in 14.8% of patients and pityriasis versicolor in 7.2%. Acne was observed in 16.5 % of patients. Less frequent complications were observed in the group of dialysed patients. In 30 RTR patients 58 skin tumors were diagnosed; 17 patients were diagnosed with multiple neoplasms. In dialyzed group 13 neoplastic changes were found.

Conclusions: The prevalence of viral warts, pityriasis versicolor and interdigital tinea in our population agree with those of other similar series. Less common incidence of skin cancers was probably related to the relatively short time of immunosuppression and younger age of patients comparing to other studies. The most of carcinoma lesions occurred in patients treated with azathioprine. However this compound was used only in 34.3 % of patients.
significantly higher rate in low-GNRI group (P<0.05) after transplantation. There were no significant relationship between GNRI and the episodes of post-operative complications such as DGF, graft loss, infection, and cardiovascular events.

Conclusions: Kidney transplantation promoted the better post-operative recovery in nutritional status and inflammation condition particular in malnourished patients, while the rapid nutritional recovery might induce the new-onset impaired glucose metabolism. GNRI is available for the pre and post-transplant nutritional evaluation and expected to be a predictive maker for post-operative diabetes mellitus (PODM).

SPB60 IS BASILIXIMAB INDUCTION, A NOVEL RISK FACTOR FOR NEW ONSET DIABETES AFTER TRANSPLANTATION FOR LIVING DONOR RENAL ALLOGRAFT RECIPIENTS?

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Introduction and Aims: Basiliximab by affecting populations of T lymphocytes indirectly affects β-cell function leading to impaired glucose homeostasis. The study was aimed to prove basiliximab induction, as a novel risk factor for new onset diabetes after transplant (NODAT) in renal transplant recipients.

Methods: In this prospective observational study, we included renal allograft recipients from 1st July 2007 to 31st July 2011 at our tertiary care institute. The overall incidence of hyperglycemia (transient hyperglycemia, impaired fasting tolerance (IFT), impaired glucose tolerance (IGT) and NODAT) was compared between two groups of patients with and without Basiliximab. The risk factors predicting NODAT were also analyzed on multivariate logistic regression analysis. NODAT was labeled when the diagnosis of diabetes mellitus was confirmed with fasting plasma glucose ≥126mg/dl or 2-hour plasma glucose ≥200mg/dl. IGT was defined as 2-hour plasma glucose ≥140mg/dl and IFT was defined with fasting plasma glucose ≥110mg/dl and ≤126mg/dl. The patients with IGT, IFT, and those with occasional rise in blood sugar level on monitoring with glucometer and requiring insulin therapy were leveled as transient hyperglycemia. Sample size and power of the study calculation: With assuming null hypothesis of no difference in percentage of NODAT between patients with and without Basiliximab induction, with maximum allowable difference between these proportions that still results in equivalence of 30% and the actual difference of the proportions of 15%, 400 sample sizes of the study population were required to achieve 98% power of the study that is the power to reject the null hypothesis. We had 439 eligible patients for data analysis after exclusion in our study.

Results: Of the 439 eligible study patients, 105 patients received Basiliximab and 334 patients did not. Overall hyperglycemia (transient hyperglycemia, IFT, IGT and NODAT) was compared between two groups of patients with and without Basiliximab. The risk factors predicting NODAT were also analyzed on multivariate logistic regression analysis. NODAT was labeled when the diagnosis of diabetes mellitus was confirmed with fasting plasma glucose ≥126mg/dl or 2-hour plasma glucose ≥200mg/dl. IGT was defined as 2-hour plasma glucose ≥140mg/dl and IFT was defined with fasting plasma glucose ≥110mg/dl and ≤126mg/dl. The patients with IGT, IFT, and those with occasional rise in blood sugar level on monitoring with glucometer and requiring insulin therapy were leveled as transient hyperglycemia.

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Introduction and Aims: Red Cell Distribution Width (RDW), a parameter routinely reported as part of the complete blood count (CBC), is associated with increased morbidity and mortality risk in different patient populations. No published data are available about the association between RDW and mortality in kidney transplant recipients.

Methods: We collected socio-demographic, clinical parameters, medical and transplant history and laboratory data at baseline in 723 prevalent kidney transplant recipients between June and October 2008 (mean age 51 ± 13 [SD] years, 56% men, 21% diabetics). Associations between baseline RDW values and all-cause mortality over 3 years were examined in unadjusted and adjusted models (adjusted for: estimated glomerular filtration rate (eGFR), age, gender, iron status related markers, hemoglobin, serum albumin, C-reactive protein, abdominal circumference, Charlson Comorbidity index, total time in ESRD, steroid use, mammalian target of rapamycin (mTOR) use, ACEI or ARB use, iron and folic acid supplementation).

Results: Of the 723 participants 81 patients died and none were lost to follow-up during a median follow-up of 35 months. The unadjusted mortality rate was significantly higher among patients in the "high" (median) RDW group (crude mortality rates in the "high" group: 67.4/1000 patient-years (95%CI: 54.1–84.1); "low" RDW group: 20.5/1000 patient-years (95%CI: 13.5–31.1); p=0.001). Increasing RDW was associated with increased mortality in both unadjusted (HR1% increase = 1.63; 95% CI: 1.41-1.89) and [HRmedian = 2.74; 95% CI: 1.68-4.48] and fully-adjusted models ([HR1% increase = 1.66; 95% CI: 1.27-1.89] and [HRmedian = 1.33; 95% CI: 0.76-2.35]). The association of RDW with mortality was uniformly increasing when modeled as a continuous variable and using fractional polynomials and cubic splines in our unadjusted (Figure) model. In reclassification analyses RDW improved the predictive value of all-cause mortality prediction models (the net reclassification improvement (NRI) was (NRI=0.189; p<0.001]).

Conclusions: Our prospective cohort study demonstrated that higher RDW is a significant predictor of mortality in prevalent kidney transplant recipients. RDW provides added prognostic information of mortality in addition to known risk factors and co-morbid conditions. RDW should be included in risk prediction models in order to better estimate mortality risk in kidney transplant recipient.

SP685 DETERMINANTS OF EARLY ACCESS TO THE WAITING LIST FOR PATIENTS OVER 60 IN ONE FRENCH AREA

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Introduction and Aims: The French registry of end stage renal disease (ESRD) patients treated by dialysis (REIN) reports that 1/3 the median age at initiation of dialysis was 71 years in 2010. 2/3% only of the patients over 60 years of age will have access to the waiting list (WL) while they will have the same access to kidney transplantation (KT) than younger patients when put on the WL. There were large disparities over France in the inscription and transplantation of >60 patients. From our experience, we know that aged patients can deteriorate quickly on dialysis and that early inscription and transplantation can be life-saving. The aim of our study was to analyse the medical and non-medical determinants of the early access to the WL of these aged patients in our area in the west of France.

Methods: Using data from the French registry of ESRD (REIN) and of transplantation (CRISTAL), we have selected 400 patients, aged >60, receiving a first treatment for ESRD in our area (Pays de Loire) between 01/01/2009 and 31/12/2010. Logistic regression was used to analyse the impact of age and 17 comorbidities on their access to the WL. Non medical determinants were studied through a questionnaire sent to all the nephrologists of the area.

Results: Among these 400 patients (mean follow-up 11 months), 33 (8.5%) with a mean age of 66 years (min 60-max 79) have been put on the WL during the study period. Two thirds of them had pre-emptive KT, the others were on the WL after a mean time of 6 months on dialysis. Age and cardiovascular comorbidities were significantly associated with non-inscription on the WL (RR 1.34 and 1.98 respectively). Age per se was clearly a reason for non-inscription as, among patients without cardiovascular comorbidities, no patient over 68 had access to the WL. This suggests that non medical determinants are part of the decision. To clarify these determinants, we studied, through a questionnaire, the position of the nephrologists of the area towards KT in old patients, their actualized knowledge and experience of KT, age, public/private practice, follow-up in an university or non-university hospital.

These data will be presented.

Conclusions: KT has many advantages over dialysis, including a lower cost. Age at dialysis initiation is increasing and it seems necessary to know to what extend these older patients have access to KT and which parameters will influence their inscription. Our study shows that few patients over 60 are put on the WL in our regional practice and suggests that non medical determinants play an important role.
practicing in rural areas were less likely (OR: 0.34; 95% CI: 0.19 to 0.73; p=0.004), while those with >10 years of practice were more likely (OR: 1.36; 95% CI: 1.01 to 1.83; p=0.04) to perceive patient age as the most important factor in disparities. Nephrologists from Western Europe were more likely (OR: 5.13 to 11.30; p<0.001), while those from North America were less likely (OR: 0.33; 95% CI: 0.23 to 0.46; p<0.001) to consider age as the most important factor in disparities. Patient race was perceived as the most important factor leading to disparities among 12% of the respondents. North American (OR: 3.36; 95% CI: 2.37 to 4.88; p<0.001) and Australian (OR: 3.41; 95% CI: 1.60 to 7.26; p<0.001) nephrologists were more likely and those from Latin America (OR: 0.30; 95% CI: 0.13 to 0.70; p<0.01) and the Middle East (OR: 0.19; 95% CI: 0.05 to 0.80; p=0.02) were less likely to perceive race as the most important factor leading to disparities in KTR. Rural residence, gender and inner city residence were perceived as the most important factors by 6%, 3% and 2% of the nephrologists, respectively.

Conclusions: We conclude that socioeconomic factors are considered the most important causes of disparities in transplantation among the majority of nephrologists, worldwide. Other factors perceived as important contributors to disparities include patient age and race. There are significant geographic and demographic differences in perceptions of causes of disparities among nephrologists. Cultural factors, training and demographic backgrounds of nephrologists are likely contributors to these differences in perception.

SP687 PERFORMANCE OF ESTIMATED GLOMERULAR FILTRATION RATES TO MONITOR CHANGE IN RENAL FUNCTION IN KIDNEY TRANSPLANT RECIPIENTS
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Introduction and Aims: Glomerular filtration rate estimates (e-GFR) are often used to evaluate changes in renal function, but have not been validated for this purpose in kidney transplant recipients (KTR). The aim of this study was to evaluate the validity of e-GFR for monitoring serial changes in renal function in KTR using directly measured GFR by inulin clearance (I-GFR) as the reference standard.

Methods: Performances of inverse serum creatinine (I/creasing) and Cockcroft and Gault, Modification of Diet in Renal Disease, and Chronic Kidney Disease Epidemiology Collaboration formulas were assessed to estimate changes in I-GFR.

Results: A total of 1938 I-GFR clearance procedures were performed in 631 KTR who underwent serial measurements between 2003 and 2009. Baseline median I-GFR were 51.0 ml/min/1.73 m² (CI 95%; 23-84 ml/min/1.73m²). Performances of I/creasing and formulas for detecting I-GFR variations between two consecutive measurements (n=1304) were similar. To detect variations of less than 20% (increase or decrease), sensitivities ranged between 50% and 56%, and specificities between 64% and 69%. To detect variations higher than 20% (increase or decrease), sensitivities ranged between 27% and 39%, and specificities between 88% and 97%. Bland and Altman plots confirmed the scattering of values for individual patients.

Conclusions: In a population of Caucasian kidney transplant recipients, mean changes in GFR are correctly estimated whatever the formula used in the range of 23 to 84 ml/min/1.73 m² and can thus be applied in population studies. However, in clinical practice, individual changes in GFR evaluated by formulas should be interpreted with caution in kidney transplant recipients.

SP688 OUTCOME AFTER KIDNEY GRAFT LOSS
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Introduction and Aims: Kidney transplantation is currently the best treatment for end stage renal diseases. Traditionally survival analyses after kidney transplantation include endpoints like graft loss and death with functioning graft. Several studies investigated risk factors for early death of patients with a functioning kidney allograft. Little is known about the survival after losing graft function and returning to dialysis. For this purpose we analysed 1901 patients who were primarily transplanted between December 1968 and December 2010.

Methods: The primary end-point was death after graft loss (GL). Therefore, we calculated annual mortality rates during transplant period and afterwards. The Kaplan-Meier analysis was used to display the survival curve after GL. A multivariate Cox model was used to identify risk factors for death after GL. For this analysis follow-up started at the time of GL. The web-based patient file „TBase“ was used to retrieve data. If the outcome of patients was uncertain the families or the patient himself were contacted to obtain follow-up information. Only the first transplantation was included in the analysis.

Results: Of the 1901 patients 662 lost their graft. The median follow-up of patients after GL was 83 months (range 0-431 months). Patients without GL (n=1239) had a median follow-up of 98 months (range 0-463). Two hundred twenty patients died during follow-up after GL (23% of cardiovascular disease, 20% of infections, 14% of malignancies and 13% of other causes; in 30% no definite cause of death could be evaluated). Two hundred ninety eight patients died with functioning graft. Annual mortality rate after GL was significantly higher than in patients without GL (3.8 vs. 2.3, respectively). Age > 50 years at transplantation (RR 1.3) and age > 50 years at GL (RR 1.8), and diagnosis of hepatitis B (RR 1.4) were associated with a significantly higher risk of death after GL. A shorter transplantation period (<7 years) seems to be protective against death after GL (RR 0.7). Longer time (>2 years) on dialysis and the diagnosis of diabetes mellitus led to a tendency towards increased risk of death (RR 1.3; P=0.054 and RR 1.3; P=0.09, respectively).

Conclusions: Patients who lose their kidney graft have a significantly higher risk of death than patients who do not. Understandably, age at the time of transplantation and age at the time of GL are major risk factors for death after graft loss. Hepatitis B is a negative predictor, too. Interestingly a shorter duration of time being transplanted is associated with better outcome for patients who lose their grafts. It remains unclear whether the combined outcome before and after graft loss in various kidney transplantation over maintenance dialysis. Therefore an adequate dialysis control group is lacking.
12.75), risk of kidney loss censored for death (RR 0.35, 95% CI 0.04 to 3.09) or acute kidney rejection (RR 2.08, 95% CI 0.2 to 21.5). The study that compared late SW versus steroid maintenance observed no deaths, no graft losses or acute kidney rejection at 6 months in either group and suggested no difference for acute pancreas rejection (RR 0.88, 95% CI 0.06 to 13.35). We also identified 13 cohort studies. Forest plot of death at 1 year in steroid avoidance versus late steroid withdrawal.

**Conclusions:** Evidence for the benefits and harms of SW in pancreas or kidney-pancreas transplantation is sparse with only three RCTs of 144 patients identified. Overall these demonstrated no difference in mortality, graft survival or rejection in steroid-sparing strategies but firm conclusions are not yet possible. Moreover, the 13 observational studies findings concur with the evidences found in the RCTs. There is not enough evidence to recommend steroids withdrawal in pancreas- kidney transplantation, although studies showed no differences between groups.

**SP690 PROGNOSTIC FACTORS FOR THE LIFE EXPECTANCY OF PATIENTS AT THE MOMENT OF KIDNEY TRANSPLANTATION**

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**Introduction and Aims:** Kidney transplantation is the treatment of choice for selected patients with end-stage renal disease (ESRD). A successful kidney transplant improves the quality of life and reduces the mortality risk for most patients, when compared with maintenance dialysis. However, information about the prognosis on the individual level is still very difficult. In this single-centre study we looked at factors at the moment of transplantation and how they influence the graft and patients survival.

**Methods:** This single-centre retrospective study included all the 172 patients from our hospital undergoing primary renal transplantation in the Leids Universitair Medisch Centrum (LUMC) from living or deceased donors between January 1, 1990 and December 31, 2009 were included in the study. All demographic information and per-transplantation patient characteristics were supplied by the patient files, REMINE and NOTR databases. Baseline co morbidity at the moment of transplantation was analyzed with de Charlson Comorbidity Score (CCS).

**Results:** From the 172 included patients, 99 kidney transplants were from a deceased donor and 73 from a living donor of which 37 were genetically related. Patient survival after 1, 5 and 10 years was respectively 97+/-1.3%, 87+/-3.3% en 72.4%. Graft survival corrected for death was 97,6 +/- 1,2%, 94,7 +/- 2,1% en 91,6 +/- 3,0%. There was a mortality rate of 16.3% during the study follow-up. In an univariate model recipient and donor age, vascular causes of the primary renal disease and co morbidity as depicted in de CCS were associated with a worse patient survival after kidney transplantation. However, in a multivariate analysis the donor age, cause of ESRD and total CCS were no longer significant. This analysis showed that, besides recipient age, peripheral vascular disease has a strong association with worse patient survival (HR 12.40; 95% CI 3.71-41.40, p< 0.001). The half time survival of a patient with peripheral vascular disease is significantly shorter (4.60 +/- 2.56 years versus 13.97 +/- 1.85 years, p<0.001).

**Conclusions:** This study shows an excellent patient and graft survival. We already knew that recipient age and more co morbidity influence the patient survival after a kidney transplant. However, the presence of peripheral vascular disease has a very strong association with a worse survival. This suggests that selection criteria for whether or not to undergo a kidney transplant should focus more on the presence of peripheral vascular disease.

**SP691 THE PERFORMANCE OF CKD-EPI EQUATION IN THE ESTIMATION OF RENAL FUNCTION BEFORE AND AFTER KIDNEY DONATION IN POTENTIAL KIDNEY DONOR**

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**Introduction and Aims:** The aim of this study is to investigate the usefulness of the Chronic Kidney Disease Epidemiology Collaboration (eGFR CKD-EPI) formula to predict renal function in subject in kidney donor before and after kidney transplantation.

**Methods:** We investigated the performance of 24 hour urine based creatinine clearance (24 hr-CrCl), Cock-Croft Gault formula (eGFR CG), Modification of Diet in Renal Disease equation (eGFR MDRD), eGFR CKD-EPI compared with theulinethemem-dihylenetramine pentaacetic acid (131I-Tc-DTPA) clearance (mGFR) in 207 potential kidney donors and 71 donors after donation.

**Results:** Before kidney donation, all of four equations correlated well with mGFR (P<0.05, respectively). 24 hr-CrCl and eGFR MDRD underestimated mGFR significantly (P<0.001, respectively). In contrast, eGFR CG and eGFR CKD-EPI showed minimal bias did not showed significant differences to mGFR (P=0.65, P=0.23, respectively).

**Conclusions:** Accuracy within 30 % of mGFR was highest in eGFR CKD-EPI (91.8 %) compared to another three equations. After kidney donation, eGFR CG, eGFR MDRD and eGFR CKD-EPI showed significant correlation to mGFR. eGFR CKD-EPI showed minimal bias, but eGFR MDRD underestimated and eGFR CG overestimated mGFR (P<0.001, respectively). However, eGFR CKD-EPI showed superior compared to eGFR CG and eGFR MDRD in the precision and accuracy. (P<0.05, respectively).

**Conclusions:** In the healthy population, eGFR CKD-EPI showed better performance compared to other equations in the prediction of mGFR, but uni-nephrectomy donor, eGFR MDRD is more appropriate for the estimation of mGFR.

**SP692 THE EFFECT OF ORGANIZATIONAL AND FINANCIAL FACTORS ON THE PRACTICE OF KIDNEY TRANSPLANTATION IN TURKEY**

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**Introduction and Aims:** Chronic kidney disease (CKD) is a major public health problem in our country as well as around the World. The number of end-stage renal disease (ESRD) patients requiring renal replacement therapy (RRT) has been increasing in recent years. In our country, during the last 5 years, significant organizational and economic rearrangements have been made by the Ministry of Health. In this study, the changing status of renal transplantation (RTx) practice was evaluated in Turkey over the last 10 years.

**Methods:** Turkish Society of Nephrology Renal Registry and the Ministry of Health data were used in this study. The incidence and prevalence rates of ESRD requiring RRT were given as per million population (pmp). Major changes were made to the legislation of dialysis and transplantation over the last 5 years. An effective national kidney waiting system was established. Dialysis patients, have been encouraged and obliged to refer to organ transplant centers regularly. Additionally, all expenses of patients regarding organ transplantation are covered entirely by the government (via SCI) and significant increases in the payments to kidney transplantation centers were implemented in order to encourage RTx procedure.

**Results:** In the last 10 years, the average annual rates of increase in incidence and prevalence of ESRD requiring RRT have been documented as 11.7%, and 10% respectively. However, growth rates of both the incidence and prevalence significantly reduced during the last 5 years. Total and cadaveric transplantation numbers, annual growth rates during this period are presented in the tables below. As can be observed, the structural, legal and economic arrangements have significantly increased the number of kidney transplants since 2008. However, the increase appears to be more impressive in living donor transplants. Mild decline in the relative rates of cadaveric renal transplants were observed.
Conclusions: Over the last decade, significant increases in the number of kidney transplants, most of to be from living donors in Turkey. Our findings suggest the imminent need to increase cadaveric organ donation and consequently cadaveric kidney transplants.

C1q-FIXING DONOR-SPECIFIC ANTIBODIES DETECTED BEFORE KIDNEY TRANSPANTATION DO NOT PREDICT REJECTION OR EARLY GRAFT LOSS, BUT HLA CLASS I DO

Julio Pascual1, Alberto Toro1, Virginia Masi1, María José Pérez-Saá2, Marisa Mir1, Anna Faura1, Olga Montes-Ares2, María Dolores Checa4 and Marta Crespo1

C1q-DSA class-II (60 vs 30.8%) without statistical significance in this sample. Ten transplants.

Impact of post-renal transplant leucopenia on graft and patient outcome

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Introduction and Aims: Transforming growth factor-β (TGF-β) signaling transduction initiates with TGF-β binding, and the activated TGF-β then binds with the TGF-β receptor II (TGFBR2). Any quantitative or qualitative changes in TGFBR2 will be expected to affect TGF-β-signaling pathway occupying a central position in regulating cell growth, differentiation, apoptosis, immune reaction, angiogenesis and extracellular matrix formation. Recent studies have shown that TGF-β gene polymorphisms may confer susceptibility to early and chronic allograft rejection in kidney transplantation recipients by enhancing fibrogenesis. In this study, we assessed whether polymorphisms of the TGFBR2 gene were associated with susceptibility to kidney transplantation rejection.

Methods: A total of 347 renal allograft recipients transplanted at three centers in Korea were analyzed. We extracted genomic DNA from blood samples and amplified the TGFBR2 gene using the primers for each Single Nucleotide Polymorphism (SNP). Three SNPs (rs764522, rs3087465, rs2228048) of TGFBR2 gene were genotyped from genomic DNA with direct sequencing. SNPStats, SNPAnalyzer, Helixtree, and Haploview version 4.2 were used to analyze genetic data. Multiple logistic regression models (codominant, dominant, recessive, and log-additive) were performed to evaluate odds ratios (ORs), 95% confidence intervals (CIs), and p values.

Results: Acute rejection (AR) developed in 63 patients (18%). There are no significant differences in age, sex, number of HLA mismatches, cause of renal failure, and immunosuppressant regimen between the AR and non-AR group. The synonymous SNP rs2228048 was significantly associated with AR (p = 0.020 in recessive model, and p = 0.036 in log-additive model) and Fisher's exact test (p = 0.04). Allele frequencies of rs2228048 were different between AR and non-AR (p = 0.026).

Conclusions: These results suggest that the synonymous SNP rs2228048 of TGFBR2 gene may be associated with development of AR in Korean kidney transplantation recipients.
964.3±192.7x10^8 in group 1 with significant positive correlation with TLC, p0.009. High doses of G-CSF were given to all patients in group 1 with a mean dose of 1466ugm/patient without significant side effects. There were no significant differences in demographic data especially CKD etiology, dialysis type, donor type, co-morbid conditions, induction and maintenance immunosuppression, cases with delayed graft function, BK viremia (0.6), and incidence of associated infections other than CMV. Four cases of CMV infection were detected in group 1 while none were in group 2 (p0.01). There was higher number of NODAT in group 1 (p0.03) most likely due to higher maintenance doses of steroids and tacrolimus to compensate for MMF dose reduction. Mean rejection episode/patient was significantly higher in group 1, p0.03). There were no difference in graft and patient outcome at 1year, p0.4.

**Conclusions:** MMF and VGC dose reduction due to leucopenia resulted in significantly higher rate of rejection episodes, CMV infection and NODAT. High doses of G-CSF were used safely to treat neutropenia without significant side effects.
PAEDIATRIC NEPHROLOGY - A

EXTRARENAL COMPLICATION AND LONG-TERM RENAL OUTCOME OF THE PATIENTS WITH CONGENITAL SOLITARY KIDNEY

Shojojo Okamoto1, Takashi Sakama2, Shigeru Nakamurara3 and Fumio Niimura2

Introduction and Aims: Patients with acquired solitary kidney due to nephrectomy have been known to have satisfactory renal prognosis. However, according to some recent reports, renal outcome of the patients with congenital solitary kidney is not so good as has been previously recognized. So, we retrospectively reviewed the renal outcome and extrarenal complications in the patients with congenital solitary kidney.

Methods: A total of ten patients comprised of 7 females and 3 males, who were diagnosed to have congenital solitary kidney in infancy, were reviewed. Median age at diagnosis is 0.06 year. Renal function at the latest follow-up and the extrarenal complications were reviewed. Median age at the latest follow-up is 5.07 years.

Results: Solitary kidney was diagnosed by prenatal ultrasound in 4 cases, and by routine check-up ultrasound for infants in 4 cases. In one case, solitary kidney was found in the process of workup for hematuria. In the remaining one case, it was found during the investigation of VATER association. Three cases of syndromic solitary kidney include 22q.11.3 deletion syndrome, VATER association, and Herlyn-Welner-Wunderlich syndrome. In 7 cases, estimated GFR (eGFR) at the latest observation (median age, 11.5 years) was obtained. In two cases, eGFR was lower than 90 ml/min/1.73m2/cup>2-cup1. In 6 cases, cystatin C was analyzed after the age of 3 years, and exceeded the cut-off level of 0.95 mg/ml in 2 cases. In all the 7 female cases, ultrasound study was conducted to evaluate the internal genital organs. Abnormal findings were recognized in 5 patients, including 2 cases of bicornuate uterus, 1 case of subseptate uterus, 1 case of vaginal hypoplasia, and 1 case of cystic dilatation of vagina. In the case of 22q.11.3 deletion syndrome, the chromosomal abnormality was confirmed at the age of 9 years when hypocalcemia due to pseudohypoparathyroidism developed during the long-term follow-up for the solitary kidney since her infancy.

Conclusions: The background of congenital solitary kidney seems to be diverse. Long-term follow-up of the patients with congenital solitary kidney for renal function and electrolyte abnormality is warranted. Especially in the female patients, investigation of internal genital organs is of special importance.

ANGIOTENSIN 2 TYPE 1/TYPE 2 GENE POLYMORPHISMS IN TURKISH CHILDREN WITH VESICOURETERAL REFLUX AND RECURRENT URINARY TRACT INFECTIONS

Sebnem Sahin1, Pelin Erten2, Hayva Evengül3, Gonul Horasan4, Bahadir Dede5 and Mift Berdei6

Introduction and Aims: Vesicoureteral reflux (VUR) and subsequently developing reflux nephropathy is the most important cause of end stage renal disease. Early diagnosis and treatment of VUR is important in order to prevent renal scarring and reflux nephropathy. Genetic factors have been evaluated as risk factors for the development of renal scar and reflux nephropathy in recent years. The aim of this study was to investigate the role of Angiotensin 2 (ATR 2) Type1 and Type2 receptor gene polymorphisms in children with VUR and recurrent urinary tract infection (UTI).

Methods: The study included 100 patients (25 patients who have recurrent UTI without renal scar and 25 patients who have recurrent UTI with renal scar). 25 patients who have VUR without renal scar and 25 patients who have VUR with renal scar) were selected from a comprehensive database. Blood was drawn and analysed for genetic polymorphisms of ATR 2 Type1 and Type2 receptor gene polymorphisms in children with VUR and recurrent UTI.

Results: No significant difference was found between patients and healthy controls (p>0.05) but ATR 2 Type 2 was similar (p>0.05). There was an association with distribution of ATR 2 Type1 receptor gene polymorphism and renal scar (p>0.05) but there was no difference with ATR 2 Type 2 (p>0.05). In the present study we compared urinary tract infection group with control group for ATR 2 Type 1 gene polymorphism, and we found significantly difference (p<0.05).

Conclusions: The association of ATR 2 Type 2 gene polymorphism and recurrent UTI with renal scar might be useful for early diagnosis of end stage renal disease.
Conclusions: None of the T pts had any clinical evidence of either cell mediated or humoral rejection secondary to Influenza A/H1N1 vaccine. In the D group, no pt had any statistical significant increase in anti-HLA antibody following vaccination. Our study suggests that influenza A/H1N1 vaccination may be safe and tolerable in pediatric dialysis pts with or without a failed kidney allograft.

**SP701** CONVERSION TO SIROLISUM IN PEDIATRIC RENAL TRANSPLANT RECIPIENTS

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Introduction and Aims: Sirolimus is an immunosuppressive agent that offers potentially significant benefits for pediatric transplant patients. In this study, we investigated the effects and efficacy of sirolimus in pediatric renal transplant recipients.

Methods: We performed a retrospective analysis of 15 renal transplant recipients who underwent sirolimus/everolimus conversion.

Results: Between years 2002-2012, 96 patients were transplanted and sirolimus/everolimus was not used as a baseline immunosuppressive therapy. During follow-up, 13 patients (2 girls, 11 males) were converted to sirolimus and 2 patients were converted to everolimus (2 males). Four patients were transplanted from deceased donors and the rest from living related donors. The median age of these patients was 16.5 year (range 5.3-26). The mean age of transplantation was 10.3±3.9 year (range 3.16-16.5). These 15 patients were converted to sirolimus/everolimus at 24.5±19 months after transplantation for biopsy proven chronic allograft nephropathy (CAN) (n=6), BK virus associated nephropathy (BKVAN) (n=2), progressive decline of renal function (n=3), ginglyval hypertrophy/tremor (n=2), posttransplant lymphoproliferative disease (PTLD) (n=1), cyclosporine nephrotoxicity (n=1). Median follow-up after switch was 17 months (range 1-69 months). Three patients with declining renal function and 5 out of 6 patients with CAN had stabilized creatinine after sirolimus/everolimus. Patients with BKVAN (n=2) had functioning grafts after sirolimus. Patient with PTLD had diminished cervical lymph node sizes and complete remission occurred after sirolimus. There was no graft loss during observation period. Most common side effects of sirolimus were hyperlipidemia (n=7), development of proteinuria (n=3), increase in proteinuria (n=2) and they were controlled with anti-lipemic drugs and angiotensin converting enzyme inhibitors.

Conclusions: In conversion, sirolimus/everolimus is an effective option for selected patients with tolerable side effects.

**SP702** NEPHROTOXICITY IN CHILDREN WITH FREQUENTLY RELAPSING NEPHROTIC SYNDROME (FRNS) RECEIVING LONG-TERM ADMINISTRATION OF CYCLOSPORINE (CSA)

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1Pediatrics Kawakita General Hospital Tokyo Japan, 2Pediatric Nephrology Toho University Omori Medical Center Tokyo Japan, 3Nephrology Tokyo Metropolitan Children’s Medical Center Tokyo Japan, 4Pediatrics Tokyo Metropolitan Children’s Medical Center Tokyo Japan, Non-Profit Organization, Japan Clinical Research Support Unit Tokyo Japan

Introduction and Aims: CSA has been established as a treatment of choice for FRNS in children. Recently, we showed a high relapse rate of nephrotic syndrome after 2-year treatment of CSA, suggesting a necessity for long-term administration (Ishikura at al. CJASN 2012).

Methods: A retrospective chart review was conducted in children in whom CSA was continued for more than 3 years for control of FRNS in our institution between 1999 and 2012. Most of the patients received CSA with trough control: for the first 6 months, patients were administered a dose that maintained a whole-blood CSA trough level between 80 and 100 ng/ml; the dose was adjusted over the next 18 months to maintain a trough level between 60 and 80 ng/ml and around 50 ng/ml thereafter. Plasma concentration of lymphocytes CD19 at intervals of 6, 12, 18 and 24 months after which patients received a single reminding dose. After 6 months of therapy an increase of anticyclosporine antibodies (G1S-π) was detected in 2 patients with serum level of 1.5 (87.5) and the rest with level of 3 (75.6).

Conclusions: In the majority of CIN cases were confined to arteriolar hyalinosis, which has been reported to be reversible after cessation of CSA (Hamahira et al. PN CJASN 2012).

**SP703** THE EFFICACY AND SAFETY OF RITUXIMAB TREATMENT IN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME IN COMPARISON WITH GLUCOCORTICOSTEROIDS AND CYCLOSPORINE A THERAPY - A SINGLE PEDIATRIC NEPHROLOGY CENTER EXPERIENCE

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Introduction and Aims: The main treatment strategy in children with primary glomerulonephritis is based on immunosuppressive therapy with glucocorticosteroids. In some cases of resistance and dependence it is necessary to introduce cyclophosphamide and/or calcineurin inhibitors to induce and maintain remission.

The reported toxicity and inadequate clinical response to this therapy drive the search for more effective and safer treatment. Rituximab is the chimeric monoclonal antibody against lymphocytes CD20 that primarily affects and entirely depletes peripheral B cells. According to some preliminary reports, rituximab can be used as an alternative immunosuppressive therapy in primary and secondary glomerulonephritis. The aim of our study was to analyze the efficacy and safety of rituximab non-standard immunosuppressive therapy in children with primary glomerulonephritis, who were not eligible for routine treatment with glucocorticosteroids and cyclosporine A.

Methods: The study group was composed of 25 non-responding to standard immunosuppressive therapy children with proteinuric glomerulopathies hospitalized between 2010 and 2012 in the Department of Pediatric Cardiology and Nephrology, Poznan University of Medical Sciences in Poland. Fourteen boys and eleven girls were included into the analysis and all have undergone a renal biopsy. These indications included: steroid-resistant nephrotic syndrome (n=21) and steroid-dependent nephrotic syndrome (n=4). The dose of rituximab was established as 375 mg/m2 of body-surface area, administered by intravenous infusion once weekly for 1 to 4 weeks, depending on the lymphocytes CD19 concentration. We evaluate proteinuria and plasma concentration of lymphocytes CD19 at intervals of 6, 12, 18 and 24 months after which patients received a single remanding dose. After 6 months of therapy an attempt to discontinue cyclosporine A was made.

Results: The remission defined as a proteinuria less than 150mg per 24h was observed in 14 of the 25 children. There was no statistically important differences in leukocyte count between single and plural rituximab dose. We also didn’t notice any important clinical or biochemical side effects, monitored by blood morphology as well as plasma renal and liver markers to arrest subsequent drug administration. However in 10 of the 25 children there was strong correlation between cyclosporine serum concentration and the level of proteinuria.

Conclusions: In conclusion, we postulate that alternative rituximab therapy should be taken under consideration in non-responding to standard therapy nephrotic patients. In these groups the potential benefits of that therapy are higher than expected side-effects. However in comparison with cyclosporine A therapy in primary steroid resistant patients rituximab seems to be less effective than calcineurin inhibitor.

**SP704** URINE ACUTE KIDNEY INJURY BIOMARKERS IN PRETERM NEONATES WITH RESPIRATORY DISTRESS SYNDROME

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Introduction and Aims: We evaluated urinary Glutathione S-transferases π (GST-π), Beta-2-microglobulin (B2-MG) and N-acetyl-b-D-glucosaminidase (NAG) as markers of acute kidney injury (AKI) in preterm neonates with respiratory distress syndrome (RDS).

<table>
<thead>
<tr>
<th>Grade of CIN</th>
<th>Before administration</th>
<th>0 to 3 year</th>
<th>3 to 5 year</th>
<th>5 year N</th>
<th>5 year N %</th>
</tr>
</thead>
<tbody>
<tr>
<td>No CIN</td>
<td>31 (88.5)</td>
<td>27 (84.4)</td>
<td>14 (60.8)</td>
<td>8 (57.1)</td>
<td></td>
</tr>
<tr>
<td>1+</td>
<td>2 (5.7)</td>
<td>4 (12.5)</td>
<td>8 (34.8)</td>
<td>5 (35.7)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1 (2.9)</td>
<td>1 (3.1)</td>
<td>0</td>
<td>1 (7.2)</td>
<td></td>
</tr>
<tr>
<td>2+</td>
<td>1 (2.9)</td>
<td>0</td>
<td>1 (4.4)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Grand total</td>
<td>35 (100)</td>
<td>32 (100)</td>
<td>23 (100)</td>
<td>14 (100)</td>
<td></td>
</tr>
</tbody>
</table>

The table above shows the distribution of CIN grades among the study population according to time points and the percentage of each grade. The most common grade was CIN 0+ followed by CIN 1+. There was no significant difference in the distribution of CIN grades among the three time points, with a similar trend observed in all groups.
Methods: Urinary AKI biomarkers were measured in 76 preterm neonates with RDS (n=26) and control neonates without RDS (n=50), whose gestational ages were between 28 and 32 weeks. Blood and urine samples were obtained on postnatal day (PND) 3 and 30. While urinary GST-π and B2-MG levels were measured by nephelometric method and urinary NAG levels were measured by spectrophotometric method.

Results: There was no significant difference in urinary B2-MG and GST-π levels in preterm neonates with and without RDS on PND3 (p>0.05, for each). However, preterm neonates with RDS had significantly higher urinary B2-MG and GST-π levels than the control group on PND30 (p=0.0001 and p=0.004, respectively). Urinary NAG levels were higher in RDS group than those of the controls on PND3 and 30 but these findings were not statistically significant (p=0.05; for each).

Conclusions: Urinary GST-π and B2-MG levels can be employed as urinary AKI biomarkers of tubular damage in preterm neonates with RDS.

<table>
<thead>
<tr>
<th>Postnatal days</th>
<th>BUN (mg/dl)</th>
<th>Cr (mg/dl)</th>
<th>Uric acid (mg/dl)</th>
<th>Estimated GFR (ml/min/1.73m²)</th>
<th>GST-π (mcg/L)</th>
<th>B2-MG (mg/L)</th>
<th>NAG (U/L)</th>
<th>FENa (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>18.0 (7.0-33.5)</td>
<td>0.99 (0.89-1.12)</td>
<td>5.1 (3.8-8.4)</td>
<td>13.2 (11.6-14.4)</td>
<td>6.6 (4.8-7.7)</td>
<td>4.3 (2.9-7.3)</td>
<td>3.6 (2.2-4.1)</td>
<td>4.8 (2.3-6.7)</td>
</tr>
<tr>
<td>30</td>
<td>14.0 (5.0-21.0)</td>
<td>0.52 (0.46-0.65)</td>
<td>1.1 (1.0-2.1)</td>
<td>25.3 (21.8-30.4)</td>
<td>12.0 (8.8-151.6)</td>
<td>10.6 (3.6-23.2)</td>
<td>8.7 (3.7-11.8)</td>
<td>1.4 (1.1-2.9)</td>
</tr>
</tbody>
</table>

SP704

# HOSPITALIZATION IN PEDIATRIC CHRONIC KIDNEY DISEASE PATIENTS AND RENAL ALLOGRAFT RECIPIENTS

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Introduction and Aims: The aim of the study was to compare the number and causes of hospitalization episodes between pediatric stage I-IV chronic kidney disease (CKD) patients, end-stage renal disease (ESRD) patients and renal allograft recipients.

Methods: We prospectively evaluated the number and causes of the hospitalization episodes in 21 pediatric patients with stage I-IV CKD, 20 ESRD and 27 renal allograft recipients between 2010 and 2012.

Results: During the study period 61.7% of stage I-IV CKD, 85% of ESRD patients and 62.9% of renal allograft recipients were hospitalized. The median number of hospitalization episodes was 1.3 and 2 in stage I-IV CKD, ESRD patients and renal allograft recipients, respectively. The total number of hospitalization episodes were 20, 61 and 41 in stage I-IV CKD, ESRD patients and renal allograft recipients, respectively. The number of hospitalization episodes were significantly higher in ESRD as compared to stage I-IV CKD patients (p=0.016). Infections were the most common causes of hospitalizations in ESRD patients and renal allograft recipients, however stage I-IV CKD patients were hospitalized usually for diagnostic work-up and evaluations. Peritonitis in ESRD patients and urinat tract infections in renal allograft recipients are the most frequent infections.

Conclusions: The number of hospitalization episodes were significantly higher in ESRD patients. Furthermore renal allograft recipients were hospitalized frequently too. Prevention of infections seems to be the most important factor in order to decrease the incidence of hospitalizations in these patients.

SP706

# CAUSES OF CHRONIC RENAL FAILURE IN RUSSIAN CHILDREN: 5-YEAR SINGLE-CENTER STUDY

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Introduction and Aims: Chronic renal failure (CRF) in children is the result of heterogeneous diseases of kidney and urinary tract. The aim of the study was to evaluate the prevalence and epidemiology of CRF in Russian children with chronic kidney diseases (CKD).

Methods: 2653 children aged 1.0-17.0 years with various inherited and acquired CKD admitted to the tertiary pediatric nephrology centre between 2007 and 2012 were admitted to the study. Of 447 children surveyed, data (height standard deviation score (height SDS) according to primary disease (Congenital anomalies of the kidney and urinary tract (CAKUT)), posterior urethral valves (PUV), hemicystic urinome symmetric syndrome (HUS), congenital syndromes and kidney involvement developed CRF during the childhood.

Conclusions: Our data indicate that the incidence rate of CRF in children with CKD was 2.1%. Chronic glomerulonephritis is the major cause of CRF, accounting for 35.7% of pediatric dialysis patients. Steroid-resistant nephrotic syndrome with FSGS is the most prevalent type of glomerulopathies progressed to CRF. There are a high proportion of patients (21.4%) with congenital syndromes and kidney involvement developed CRF during the childhood.

SP707

# HLA-DR MISMATCHED PAEDIATRIC RENAL TRANSPLANTATION: PATIENT AND GRAFT OUTCOME WITH DIFFERENT KIDNEY DONOR SOURCES

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Introduction and Aims: Renal allograft failure in children has been associated with several factors, including age, race, donor source, cold ischemia time, primary renal disease, HLA antigen mismatch, and transplantation year. Graft survival has improved substantially over the years owing to changes in the induction and maintenance immunosuppression regimen.

Aim of the work: To determine the impact of HLA-DR mismatching on rejection, graft survival, and sensitization in pediatric renal transplant patients and to determine the likelihood of finding an appropriate donor based on HLA-DR mismatch.

Methods: In this retrospective analysis, paediatric renal transplants performed in Hamed Al-Essar organ transplant centre Kuwait (n=104), between 1994 and 2011 were reexamined for the effect of HLA-DR mismatching on graft survival and patient survival. DR zero mismatch (group1, n=17), one mismatch (group 2, n=68) and two mismatch (group, n=34) comprised the three arms of our study. Pre-transplant complement-dependent cytotoxicity and flow cytometry cross matches were negative. Basic immunosuppression comprised Tacrolimus, MMF and steroids.

Results: The three groups were matched regarding mean recipient age (12.2±5.5, 13.9±3.8 & 13.9±4.2 years respectively), patient and donor sex, donor age (35±8.2, 34±7.4, 30±9.3 years), original kidney disease, type of maintenance immunosuppression, basal graft function, viral profile and pretransplant co-morbidities (diabetes, anemia, hypertension and tuberculosis). Most of patients with two mismatch received cadaveric grafts and ATG induction; while patients with grafts from live donors received somulnet induction (p<0.05). We found that patient survival at 1, 5, and 10 years was comparable in all groups. Posttransplant complications were comparable in all groups especially infections (bacterial and viral), hyper-tension, mean rejection reaction episodes and NODAT. Moreover, we found no significant difference in the graft function as represented by serum creatinine at 1, 3, 5, and 10 years of follow up (p>0.05).

Conclusions: Good results can be obtained with HLA DR mismatched kidneys among pediatric renal transplants with the protocols specified.

SP708

# GROWTH OF CHILDREN WITH PRE-DIALYSIS CHRONIC KIDNEY DISEASE IN JAPAN

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Introduction and Aims: Short stature is a clinically important issue in children with chronic kidney disease (CKD), and is associated with significant morbidity and mortality. As a result of advances in management, most children with CKD should achieve final adult height consistent with their genetic potential.

Methods: We conducted epidemiological surveys of 119 medical institutions in Japan treating children with CKD stage 3-5 in 2011. Of 447 children surveyed, data (height and height SDS) were available for 284. Height standard deviation score (height SDS) was calculated for all available children. Distributions of height SDS were determined according to primary disease (Congenital anomalies of the kidney and urinary tract [CAKUT] vs. non-CAKUT) and gestational age at birth (<37 weeks vs. ≥37 weeks).
We performed t-test for height SDS of each CKD stage compared to the healthy Japanese population, and trend-test for subgroup analysis. Patients who had multiple congenital anomaly syndromes that caused growth retardation were excluded.

Results: The study included 182 boys and 182 girls: 184, 87, and 13 children were of CKD stage 3, 4, and 5, respectively. CAKUT accounted for 62.0% of primary disease. Age was 10.1±4.5 years. Height SDS was below the mean in the majority of children of both sexes from stage 3. Mean height SDS of CKD stage 3, 4, and 5 was -1.1±1.3, -1.7±1.8, respectively, of significantly short stature compared to the healthy Japanese population (p < 0.001 in each stage). Height SDS significantly decreased with increase of CKD stage from 3 to 5 (p < 0.001); in CAKUT group (p < 0.001) but not in non-CAKUT group (p=0.13); and in gestational age at birth < 37 weeks (p < 0.001) but not in ≥ 37 weeks (p=0.077) group. Growth hormone was used in 11/184 (6.0%), 20/87 (23.0%), and 4/13 (30.8%) patients with CKD stage 3, 4, and 5, respectively.

Conclusions: This study indicated that growth impairment started from early CKD stage, and height SDS significantly decreased with increase of CKD stage. It is important to detect CKD early and introduce growth hormone at an appropriate time to improve final height with management of complications and nutrition in children with CKD.

Introduction and Aims: Understudying of mechanisms of renal pathology which develops under non-communicable diseases develop due to the action of environmental factors. The aim of our study was to assess the effect of electromagnetic radiation on development of the offspring of rats exposed during pregnancy.

Methods: The study comprised a group of 8 children (mean age: 14.2 y) in the end stage of renal failure who were treated with peritoneal dialysis – group I. The control group (group II) consisted of 26 age-matched healthy children, with no clinical evidence of renal or cardiac diseases and with quite normal ECG recordings. Each of the examined children was subjected to the 12-lead standard ECG examination. In order to capture possible heart conduction abnormalities, BSPM (body surface potential mapping) recordings collected using HPM-7100 Fukuda Denshi system, were used. Basing on the source ECG data, an original technique of VAT difference map was then applied.

Results: Differences between the VAT values found for the two examined children groups, normal and with ESRF, were significantly present in the region of the right upper anterior thorax, entire left thorax and nearly total R6. Such pattern of the difference in ventricular activation propagation time within the interventricular conduction system indicates a pathologic electric transmission within the left anterior fascicle of His bundle.

Conclusions: 1. VAT maps (isochrone maps) reflect precisely a trajectory of activation in the both heart ventricles. 2. Differences in the VAT values enable in young patients with ESRF to detect early disturbances in left His bundle branch despite the normal 12-lead ECG examination. 3. Further study on the larger group of children with ESRF treated with peritoneal dialysis is required to verify the preliminary observations presented herein.
Introduction and Aims: The precise mechanism of renal injury among Dengue patients is not known. Patient who have ATN will usually require early dialysis. Hence, on admission to the hospital, it is difficult to distinguish DSS patients with ATN from patients with reversible prerenal cause that will respond to simple hydration. Our understanding of the complex pathogenesis of tubular injury in Dengue AKI is very limited that until it is sufficiently increased, therapeutic strategies will continue to fail. Therefore, we sought to explore the criteria for the need of serum creatinine level increase in this setting. General Objective: to determine the clinical and diagnostic factors that are predictive for the need of dialysis among DSS patients at PCMC. Specific Objectives: to determine if the following factors are predictive of the need for dialysis: decrease in estimated creatinine clearance by 75% or <35 mL/min/BSA with urine output of <0.3 mL/kg/hr X 24 hours or anuria of 12 hours, assess the usefulness of urinary sediment scoring (USS) in predicting the need for dialysis. Methods: This retrospective study covered 60 newly admitted cases of Dengue Shock Syndrome III and IV at the Philippine Children’s Medical Center between January 2010 to December 2011. Results: Data form 60 patients were available for analysis. Comparison of the demographic characteristics between patients who required dialysis and those who did not, showed no significant difference as proven by all p values >0.05. Of the difference in clinical and laboratory parameters, there was a significant difference in Heart rate, Respiratory rate, oxygen saturation, bicarbonate and base excess as proven by all p values <0.05. The heart rate and Respiratory rate were significantly higher among those who needed dialysis than those who did not. The estimated creatinine clearance was significantly lower among those who needed dialysis than who did not. Conclusion: Our data indicate that a decrease in estimated creatinine clearance by 75% or <35 mL/min/BSA with urine output of <0.3 mL/kg/hr X 24 hours or anuria of 12 hours, asess the usefulness of urinary sediment scoring (USS) in predicting the need for dialysis.
**SP716 GROWTH IMPAIRMENT AND NUTRITIONAL STATUS IN PEDIATRIC CHRONIC KIDNEY DISEASE PATIENTS AND RENAL ALLOGRAFT RECIPIENTS**

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Pediatric Nephrology Ankara University School of Medicine Ankara Turkey

**Introduction and Aims:** Growth impairment and malnutrition are common and the most visible complications of chronic kidney disease (CKD). Only successful kidney transplantation is able to restore the conditions for normal growth and nutrition. The aim of this study was to compare the prevalence of growth impairment and nutritional status in pediatric stage I-IV CKD patients, end-stage renal disease (ESRD) patients and renal allograft recipients.

**Methods:** Twenty-one pediatric patients with stage I-IV CKD, 20 ESRD and 27 renal allograft recipients were prospectively evaluated between 2010 and 2012.

**Results:** During the study period 33.3% of stage I CKD, 55% of ESRD patients and 44.4% of renal allograft recipients had growth impairment. The mean height SDS were -1.14±1.22, -1.98±1.23 and -1.69±2.1 in stage I-IV CKD, ESRD patients and renal allograft recipients, respectively. The mean height SDS was significantly higher in renal allograft recipients when compared with ESRD patients (p=0.046). Underweight was seen in 42.8% of stage I-IV CKD, 65% of ESRD patients and only 14.8% of renal allograft recipients. Obesity was seen 11.1% of renal allograft recipients, 5% of stage I-IV and ESRD patients. The mean body mass index (BMI) SDS was -0.62±1.45, -1.22 ±1.52 and 0.08±1.40 in stage I-IV CKD, ESRD patients and renal allograft recipients, respectively. The mean BMI SDS was significantly higher in renal allograft recipients as compared to ESRD patients (p=0.04).

**Conclusions:** Growth impairment and malnutrition remain challenging problems of the children with CKD. Successful kidney transplantation may improve the growth and nutritional status of children with CKD and ESRD.

**SP717 PROINFLAMMATORY CYTOKINES MCP-1 AND IL-23 IN CHILDREN WITH PILEONEPHRITIS**

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**Introduction and Aims:** Proinflammatory cytokines monocytes chemoattractant protein-1 (MCP-1) and interleukin-23 (IL-23) provide to monocytes/macrophages, lymphocytes accumulation in the inflammatory focus, activation of endothelial and smooth vessel cells, to the main stages of acute and chronic kidney inflammation regulation, to the increase of extracellular matrix accumulation through TGF activation, which altogether leads to the tubulointerstitial fibrosis development. IL-23 also regulates matrix metalloproteinase stimulation, increases angiogenesis and reduces CD8 + T-cell infiltration. The aim of our study was to determine serum levels of proinflammatory cytokines (MCP-1 and IL-23) and their changes after standard antibiotic treatment in children with pyelonephritis (PN).

**Methods:** The serum levels of cytokines were determined by ELISA (analyzer “SunRise TouchScreen” “Bender” test system, USA) in 53 children with PN before and after antibacterial treatment. 20 healthy donors were investigated as control group: MCP-1 83.6±67.4110.0 pg/ml, IL-23 53.522±651.1 pg/ml. Variables were reported as median/low/high quartile.

**Results:** Significant increase levels of proinflammatory cytokines in children with PN in active stage were obtained: 192.7/116.3;264.3 pg/ml for MCP-1, and 89.2/72.4;104.2 ±1.52 and 0.08±1.40 in stage I-IV CKD, ESRD patients and renal allograft recipients, respectively. The mean BMI SDS was significantly higher in renal allograft recipients as compared to ESRD patients (p=0.04).

**Conclusions:** Growth impairment and malnutrition remain challenging problems of the children with CKD. Successful kidney transplantation may improve the growth and nutritional status of children with CKD and ESRD.

**SP719 LEFT VENTRICULAR HYPERTROPHY IN CHILDREN WITH CKD STAGES 3-5 IS DETERMINED BY BP AND CALCIUM LOADING BUT NOT PRINCIPALLY BY FGFR2**

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**Introduction and Aims:** To evaluate the relationship of FGFR2 with indexed LV mass and LVH following adjustment for relevant confounders in children with pre-dialysis CKD.

**Methods:** Single centre study, 83 children (51 boys), age 12.1 (3.2) years, mean eGFR 32.3 (14.6) ml/min/1.73m2, underwent clinic and ambulatory BP measurement, echocardiography and evaluation of biochemical markers of CKD-MBD. LVH was present in 38% of patients at baseline (CKD III 32%, CKD IV 45%, CKD V 36%). After one year of follow-up, standardized IMT was increased compared to the baseline measurement (1.87±1.28 SDS, p=0.001). Absolute but not standardized PWV was decreased (0.64±1.57 SDS, n.s.). LVMI increased by 2.31±10.7 g/m2/2.7, p=0.0001.

**Conclusions:** CV alterations are frequent and highly pronounced in children with CKD. Significant progression of these abnormalities can be detected by non-invasive monitoring even within one year of follow-up. Hyperparathyroidism appears to play a major role in the progression of LVH and arterial stiffness, with an additional impact of blood pressure and lipid abnormalities. Further follow-up, inclusion of additional biomarkers and mixed model analysis will provide more detailed information on the causes and effects of early CV morbidity in pediatric CKD.

**SP718 RISK FACTORS AND PROGRESSION OF CARdiovascular (CV) DISEASE IN CHILDREN WITH CHRONIC KIDNEY DISEASE (CKD)**

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**Introduction and Aims:** CV disease is a major concern in CKD and complications can occur early in childhood and adolescence. The Cardiovascular Comorbidity in Children with CKD (4C) Study prospectively explores the prevalence, severity and progression of CV abnormalities in children with CKD in 12 European countries.

**Methods:** Arterial morphology and function were assessed in 508 patients with an eGFR of 10-60 ml/min/1.73m2 by intima-media thickness (IMT) and pulse wave velocity (PWV). Left ventricular hypertrophy (LVH) was evaluated by the left ventricular mass index (LVMi). Measurements were performed at the baseline visit and after 12 months of follow-up. Height- and gender-normalized standardization. Scores were calculated for IMT and PWV. Regression analysis was performed for CV endpoints including BP, GFR, CKD progression, serum albumin and albuminuria, lipids levels, markers of bone metabolism and inflammation as independent parameters.

**Results:** Mean baseline eGFR was 32 ml/min/1.73m2 (53% CKD III, 45% CKD IV and CKD V 2%). Causal systolic blood pressure (BP) was 0.8±1.4 SDS and 24 hour mean arterial pressure (MAP) 10.1±3.9 SDS at the baseline investigation. Height-standardized IMT and PWV were significantly increased (IMT SDS 1.73±1.6; p<0.0001; PWV SDS 0.59±1.63; p<0.0001) compared to healthy controls. LVH was present in 38% of patients at baseline (CKD III 32%, CKD IV 45%, CKD V 36%). After one year of follow-up, standardized IMT was significantly increased compared to the baseline increase (1.87±1.28 SDS, p=0.001). Absolute but not standardized PWV was increased (0.64±1.57 SDS, n.s.). LVMI increased by 2.31±10.7 g/m2/2.7, p=0.0001.

**Conclusions:** CV alterations are frequent and highly pronounced in children with CKD. Significant progression of these abnormalities can be detected by non-invasive monitoring even within one year of follow-up. Hyperparathyroidism appears to play a major role in the progression of LVH and arterial stiffness, with an additional impact of blood pressure and lipid abnormalities. Further follow-up, inclusion of additional biomarkers and mixed model analysis will provide more detailed information on the causes and effects of early CV morbidity in pediatric CKD.
CELL SIGNALLING

MP001  FUNCTIONAL ROLES OF KLOTHO IN THE PROCESS OF RENAL FIBROSIS ASSESSED IN THE CULTURED RENAL EPITHELIAL AND FIBROBLAST CELLS

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Introduction and Aims: Klotho is a protein that has anti-aging properties and is known to function as an obligate co-receptor of FGFR2 in the regulation of phosphate homeostasis and also to be involved in insulin/IGF1 and WNT signaling, suggesting that Klotho has several biological properties in physiological and pathophysiological conditions. It has been reported that the renal expression of the Klotho gene is markedly suppressed in chronic kidney disease (CKD). Acceleration of renal fibrosis is a basic pathophysiology for progression of CKD, and previously, we showed that the renal interstitial fibrosis was severer in the Wistar rats than those in the wild-type mice by UUO treatment. Thus, in the present study we investigated the biological role of Klotho in the process of fibrosis in cultured cells.

Methods: We explored the relationship between Klotho and fibrosis-related factors in cultured renal epithelial cells (mMCP4 and HK2) and fibroblast cells (NRFK49F) under TGF-β stimulation, which were quantified by using CL-Quanti software to analyze time-lapse images in a Nikon Biostation CT in combination with a high-throughput cell migration assay. The expression levels of pro-fibrotic markers were assessed by quantitative RT-PCR. Internal expression of klotho was modified by siRNA transfection.

Results: TGF-β reduced Klotho expression in HK2 cells. In addition, in NRFK49F cell in which internal Klotho expression was negligible, expression levels of α-SMA and P-AKT were significantly suppressed in addition of recombinant Klotho protein to the medium. Migration of NRFK49F cells was accelerated and expression of fibrotic markers was up-regulated by addition of TGF-β, in contrast, Klotho addition suppressed the effect. siRNA reduced the expression of Klotho in epithelial cells, resulting in accelerating cell migration. Klotho affected the localization of membrane protein, namely, addition of Klotho protein promoted to translocate Na+/K-ATPase/PKC-ζ, a marker of cell signaling (β-catenine) in 3D culture with collagen mixture. The expression levels of fibrotic marker, such as α-SMA, fibronectin and TGF-β1 was immunohistochemically stained and mRNA expression levels were assessed by quantitative RT-PCR. Internal expression of klotho was modified by siRNA transfection.

Conclusions: Taken together, it is likely that Klotho protects against renal fibrotic process accompanied by down-regulation of fibrotic markers, counteracting to TGF-β, and one of possible mechanism mediating translocation of Na/K ATPase, resulting in Ca2+ channel stabilization/alternation of Ca2+ ion concentration. Klotho should be involved in the accentuation of the progression of renal fibrosis in CKD.

MP002  GASP PROTEIN AND ITS ROLE IN VASCULAR CALCIFICATION

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Introduction and Aims: Vascular calcification is reduced by vitamin K and accelerated by warfarin, i.e. a direct inhibitor of the vitamin K regenerating cycle. These vascular effects are believed to largely involve the vitamin K dependent matrix gla protein. Another vitamin K dependent protein, Gas6, is also expressed in vascular smooth muscle cells (VSMC). Recent data indicated that Gas6 mediates protective effects in vascular calcification by inhibition of VSMC apoptosis.

Methods: Here we investigated the role of Gas 6 in vivo and in vitro calcification model (in vitro cell culture; in vivo Warfarin diet for 8 weeks, uninephrectomy (UnNx) combined with high phosphate diet, aging mice at the age of 36 weeks). At the end of the feeding period, echocardiography was performed. After sacrifice, the extent of soft tissue calcification, serum and urine biochemistry were measured.

Results: In vivo, intravenous Gas6 was calcified and this was not different between VSMC generated from wildtype (WT) and Gas6-/- mice. In vivo, serum phosphate was higher in UnNx Gas6-/- compared to UnNx WT mice but no significant difference in aortic calcium content was observed between these groups. After 8 weeks of warfarin, total protein and phosphate in serum were significantly higher in Gas6-/- than in WT mice. This was accompanied by a higher aortic calcium content in Gas6-/- mice, whereas Kossa staining revealed only a weak positive vascular staining in Gas6-/- mice. In aging, non-manipulated mice, no significant differences in vascular calcification could be identified between Gas6-/- and WT mice. No differences were found in LV mass, stroke volume or pulse wave velocity in all groups.

Conclusions: Our data do not support a major role of gas 6 in the patogenesis of vascular calcification.

MP003  FUNCTIONAL ROLE OF HIF-1α IN HYPOXIA OR PHD-INHIBITION IN GLOMERULAR ENDOTHELIAL CELLS

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Introduction and Aims: Hypoxia-inducible factors (HIFs) controls the cellular adaptation to low oxygen conditions. In normoxia HIF is rapidly degraded, but in hypoxia HIF is stable and can exert its various functions. Pharmacological activation of HIFs in normoxia by inhibiting the physiological hypoxia domain enzymes (PDH) can mimic hypoxia and has been shown to be protective in kidney injury. The precise mechanism of protection by HIF activation is still elusive but endothelial HIF might be one of the effectors. To dissect the molecular mechanisms of how hypoxia or PHD-inhibition affects HIF function in endothelial cells we established an in vitro model of glomerular endothelial cells (gEnds) with stable HIF-knockdown.

Methods: gEnds with stable knockdown of both HIFs isoforms were generated by lentiviral transfection with shRNA constructs. Gene expression analyses were performed by real-time PCR and westernblotting. Cells were treated with a hypoxia or a PHD-inhibitor (ICA) for different times. Proliferation was analysed by MTT assays and cell cycle by PI-staining. Westernblotting of cleaved caspase3 and Annexin-V staining followed by FACS was used to detect apoptosis.

Results: gEnds express both HIFs proteins, but surprisingly HIF-2α levels are much lower. Deletion of HIF-1α does not affect expression of HIF-2α protein and vice versa. Most of typical target genes are regulated by HIF-1α. HIF-1α deletion does not affect cell proliferation under normoxia, but significantly impairs proliferation in hypoxia, whereas deletion of HIF-2α has a minor effect. Analysis of glucose concentrations in the medium reveals no altered metabolic response between genotypes. Treatment with ICA significantly slows proliferation in wildtype cells in normoxia. This effect is HIF-1α but not HIF-2α-dependent. Cell cycle analyses suggest that G1 arrest occurs in wildtype and HIF-1α knockout cells in hypoxia. Interestingly, p27 is induced in hypoxia in wildtype cells but not in HIF-1α ko cells. ICA treatment induces cell cycle arrest only in wildtype cells, not in cells lacking HIF-1α. They grow normal under ICA, but show induction of p27 expression. Analysis of apoptosis suggests that HIF-1α is a protective factor for gEnds in hypoxia. Thus, in hypoxia cell cycle arrest is HIF-1α independent or is induced by different pathways. Hypoxia apoptosis on the other hand, occurs HIF-1α dependent, p27 expression in hypoxia is HIF-1α-dependent, but ICA treatment induces p27 irrespective of HIF. No apoptosis is observed by ICA treatment.

Conclusions: Our data clearly demonstrate differential effects of HIF stabilization by hypoxia or PHD-inhibition on cell cycle and apoptosis in gEnd cells. This observation is of significance since differential effects of hypoxia and PHD inhibitors in endothelial cells need to be studied carefully in the light of therapeutical administration of PHD inhibitors in renal disease.

MP004  INTERACTION BETWEEN IFN-γ AND TLR ACTIVATED SIGNALING PATHWAY IN CELLS FROM THE VASCULATURE IS STAT1 MEDIATED

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Introduction and Aims: Inflammation participates importantly in host defenses against infectious agents and injury, but it also contributes to the pathophysiology of several diseases. Signal Transducer and Activator of Transcription (STAT) 1 together with interferon regulatory factors (IRF) has been identified as a point of convergence for the cross-talk between the pro-inflammatory cytokine Interferon gamma (IFNγ) and the Toll Like Receptor (TLR4) a ligand Lipopolysaccharide (LPS) in immune cells. However, there is little known about the role of STAT1 in TLR4-mediated progression of vascular diseases and on potential synergism between LPS- and INFγ-signaling in
cells from the vasculature. We investigated whether vascular smooth muscle cells (VSMC) can promote inflammatory signaling by the STAT1-IRF pathway.

Methods: To study signal integration between LPS and INFγ pathways, aortic vascular smooth muscle cells were isolated from C57BL/6. STAT1−/− mice were isolated and treated either with INFγ or LPS or pretreated with INFγ followed by LPS. Gene expression analysis for whole transcriptome using HiScanSQ (Illumina) was performed.

Results: Expression of STAT1 and selected genes was confirmed by qRT-PCR and/or Western. ELISA was performed to measure INFγ released media after 24h of chronic rejection.

Results: Gene expression analysis revealed that INFγ induces expression of hundreds of genes related mainly to immune response processes but only in the presence of STAT1 gene. Moreover response to LPS was ameliorated in the absence of STAT1 gene.

Conclusions: INFγ induces primary VSMCs genes related to gene ontology process like immune response and adhesion. This inflammatory signaling is promoted by the STAT1-IRF pathway.

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Introduction and Aims: Autosomal Dominant Polycystic Kidney Disease (ADPKD) is caused by loss-of-function mutations in either the PKD1 (85%) or PKD2 (15%) genes, which encode polycystin-1 (PC1) and -2 (PC2) respectively. Patients with PKD2 mutations have a milder phenotype than those with PKD1 mutations. Increased activity of the mammalian target of rapamycin (mTOR) pathway has been shown in PKD1/2 mutantubut is less documented for PKD2 mutants. mTOR inhibitors as well as the AMP-activated protein kinase (AMPK)- activating drug metformin are effective in reducing renal cystogenesis in rodent models with PKD1 mutations. However, clinical trials using mTOR inhibitors were disappointing, while metformin is not yet tested in ADPKD patients.

Methods: Here, we studied the mTOR activity and its upstream pathways in human and mouse renal epithelial cells.

Results: We showed that mTORC1 and AMPK activities were differently regulated in PC1- and PC2-deficient cells. Interestingly, combining low doses of rapamycin and metformin was more effective for inhibiting mTORC1 activity in PC1-deficient cells than either drug alone.

Conclusions: Our results demonstrate the beneficial effect of a combination of low doses of drugs inhibiting mTOR activity. This can be used for optimizing the efficiency and avoiding side effects of drugs used in future clinical trials. Furthermore, our finding of a low-to-normal mTOR activity in PC2-deficient cells might have important therapeutic implications for selecting patients for these trials.

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Introduction and Aims: Mononuclear cells (MNCs) can promote inflammatory signaling by the STAT1-IRFs pathway. STAT1-dependent synergism between INFγ and TLR in VSMCs in response to exogenous and endogenous ligands could result in amplification of proinflammatory responses in the damaged vessel and be a novel mechanism involved in the initiation and progression of vascular diseases.

MP007
NERVE GROWTH FACTOR ENHANCES THE NEPHROTIC EFFECTS EXERTED BY CYCLOSPORINE IN TUBULAR RENAL CELLS

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Introduction and Aims: Chronic Allograft Dysfunction (CAD) affects almost all kidney transplantation patients in the long time and causes about the 50% of graft loss. Despite the crucial role played by Calcineurin Inhibitors (CNIs) in renal acute rejection prevention, the chronic drug nephrotoxicity induced by CNIs therapy contributes to CAD pathogenesis through molecular mechanisms not yet completely understood. Cadaverine inhibition results in the activation of Nuclear Factor Activated T-cells (NFAT), a transcriptional factor involved also in Nerve Growth Factor (NGF) synthesis and expression, suggesting a potential link between CNIs and NGF. NGF promotes cell growth, differentiation, survival and death by two different receptors: TrkA and p75. A specific single-cell surface TrkA-p75 ratio may be directly responsible for either proliferative/survival effects (TrkA) or apoptotic response (p75). Has been reported that NGF and its receptors exert a critical role in progressive renal disease. However nothing is known about NGF expression in kidney transplantation. The aim of our study is to investigate the role of NGF and its receptors in the nephrotoxicity induced by CNIs in kidney transplant.

Methods: We evaluated in human proximal tubular epithelial cells, HK-2, treated with cyclosparin A (CsA) or NGF alone or in combination, vitality cell, gene and protein expression of NGF, its receptors, apoptosis and cell cycle regulators by MTT assay, real time PCR assay and Western blot analysis, respectively.

Results: Our in vitro studies reveals that increasing doses of NGF did not influence HK2 cells vitality as well as p75 and TrkA expression levels. Instead, the combined chemicare exposure to NGF and CsA significantly increased cell apoptosis and cell cycle regulators by MTT assay, real time PCR assay and Western blot analysis, respectively.

Conclusions: Our in vitro studies reveals that increasing doses of NGF did not influence HK2 cells vitality as well as p75 and TrkA expression levels. Instead, the combined chemicare exposure to NGF and CsA significantly increased cell apoptosis and cell cycle regulators by MTT assay, real time PCR assay and Western blot analysis, respectively.

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Introduction and Aims: IL-6 is one of the key inflammatory mediators. The role of IL-6 in the rejection reaction is not fully understood.

Methods: To study the role of IL-6 in the rejection of the graft.

Results: Transplantation outcomes are largely determined by the activity of rejection. Great importance is the regulatory influence CD4+ cells. Now known another type of T-helper cells: Th17. These cells can secrete IL-17 and come from the naive T-cells in response to IL-6 and transforming growth factor β stimulation. In the absence of TGFβ stimulation of naive T cells to differentiate into regulatory T cells - Tregs, expressing Foxp3, which is the opposite effect of Th17. Biological effects of Th17 secreted IL-17 is to promote the proliferation and migration of monocytes and neutrophils (by stimulating the secretion of chemokines), endothelial cell activation and proliferation of fibroblasts. These processes play a major role in the process of chronic rejection. In addition, IL-17 inhibition is demonstrated to inhibit the production of IL-6, which forms a vicious circle and contributes to the activation of the process of chronic rejection. Thus, IL-6 may play a role in supporting activity of immune conflict between the graft and the host. These data were confirmed in a large number of experiments: in mice lacking IL-6 showed a significant increase in graft survival compared to wild-type mice. In the absence of IL-6 was an increase in the content of regulatory CD4, CD25, Foxp3 T cells and a decrease in titre of circulating

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Abstracts

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Time course study of renal histological alterations and cytokine production in kidney transplants was performed. The main goal was to investigate the role of donor-specific alloantibodies. Increase in serum concentrations of IL-6 associated with vascular endothelial damage by rejection. Thus, IL-6 plays a role in both humoral and cellular rejection. IL-6 is locally produced by monocytes, probably. A significant correlation with the severity of transplant glomerulopathy, but not with other chronic structures damages and titre of circulating anti-HLA antibodies. The main producers of IL-6, TNF α and IL-1β, TNFα has a significant correlation with the severity of transplant glomerulopathy, but not with other chronic structures damages and titre of circulating anti-HLA antibodies. 

Conclusions: Thus, IL-6 is an important mediator in the process of rejection. This may be a new target for specific therapy.

MP009

URAT 1 INHIBITION PROTECTS HUMANS PROXIMAL TUBULE CELLS FROM APOPTOTIC DAMAGE INDUCED BY URIC ACID

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Introduction and Aims: Serum uric acid (UA) has been shown to predict the development of chronic kidney disease (CKD) and has been associated with signs of renal damage such as albuminuria, intrarenal vascular stiffness (increased renal resistive index), and tubular atrophy in several conditions such as hypertension, diabetes and IgA nephropathy. Nevertheless, the mechanisms underlying the deleterious effects of UA on renal proximal tubular epithelial cells (PTCs) have not been elucidated. In CKD, increased apoptosis contributes to cell loss and structural damage. In this study, we investigated the effect of UA on apoptosis in human PTCs line (HK-2) and the underlying mechanisms.

Methods: Apoptotic damage was induced by serum deprivation and adding UA at different concentrations (7.5 -12 mg/dl) for 48 hours. Cell viability was evaluated by MTT test and apoptosis by positivity for cleaved caspase-3 (p17 fragment). Pro- and anti-apoptotic proteins were studied by Western Blot. The pathways involved in UA apoptosis were investigated by Caspase inhibitors, NADPH Oxidase inhibitor (DPI), urate transporter antagonists (losartan and probenecid).

Results: Highest UA concentration decreased tubule cell viability (-30%, p=0.015) and increased significantly apoptotic cells (14%-20% vs 2%-3% untreated cells p<0.0001). UA up-regulated Bax (+60% p<0.05) and down regulated X-linked inhibitor of apoptosis protein (XIAP) (-30% p<0.05). Caspase-9 inhibitor blunted apoptosis, while caspase-8 inhibitor had no effects. UA induced changes in the mitochondrial membrane as shown by mitoapoptosis assay. Also, DPI had inhibitory effects on apoptosis (-70%, p=0.0001). Incubation with probenecid 20 μM and losartan 10 μM inhibited apoptosis induced by 12 mg/dl UA exposure (p<0.01 and <0.0001, respectively).

Conclusions: These results indicate that mildly elevated UA levels promote apoptosis in PTCs by triggering intrinsic caspase activation, thus contributing to mechanisms of cell loss which have already been shown to be activated in CKD. This mitochondrial pathway seems to be attenuated by losartan and probenecid, probably through their binding to URAT-1. These findings support a role for UA in promoting renal injury in humans.

MP010

MICRONA-328 REGULATES PRESSURE-INDUCED FIBROTIC RESPONSES IN RAT RENAL TUBULAR CELLS THROUGH TARGETING CD44 EXPRESSION

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Introduction and Aims: Renal fibrosis is a common consequence and often a central feature of all the progressive renal diseases that lead to end-stage renal failure. Understanding the mechanisms of tubulointerstitial fibrosis is essential in establishing novel therapeutic strategies for the management of kidney diseases. Epithelial to Mesenchymal Transition (EMT) of tubular epithelial cells constitutes the principal mechanism of renal fibrosis. Pressure force has been known to induce renal fibrogenesis in obstructive uroplathy. In this study, we investigated the role of microRNA expression alterations in pressure-induced fibrotic responses in rat renal tubular cells (NRK-52E).

Methods: We established an in vitro pressure culture system to study the initial mechanism of the fibrotic response in rat renal tubular cell (NRK-52E). Fibrosis-associated molecules, such as connective tissue growth factor (CTGF), fibroactin, CD44 and E-cadherin were monitored by Western Blot. The expression patterns of miRNAs were monitored in pressurized cells in the early stage. We also used CD44 siRNA transfection to block the expression of CD44 in NRK-52E cells.

Results: When NRK-52E cells were cultured in the pressure culture system, 60 mmHg pressure induced the expression of CTGF, fibroactin. MicroRNA array assays showed that the expression level of microRNA-328 (miR-328) in pressurized cells significantly decreased within 2 h, recovered at 4 h, and increased at 8 h. Potential target of miR-328 has been reported to be CD44 and collagen type 1α1 (Col 1α1). CD44 expression significantly increased in pressurized cells at 0.5, 1, 2 and 24 h, which was opposite to the miR-328 expression pattern. The overexpression of miR-328 reduced pressure-induced fibrotic responses and expression of CD44 and Col1α1. The transfection of CD44 siRNA significantly reduced pressure-induced fibroactin in NRK-52E cells. However, CTGF expression was not influenced by CD44 siRNA transfection. Pressure also reduced E-cadherin expression, an important EMT marker, at 4 and 8 h in NRK-52E cells. CD44 siRNA transfection induced E-cadherin in pressurized cells at 4 and 8 h.

Conclusions: Our results suggest that pressure reduces miR-328 expression in the early stage of pressure treatment, and then up-regulates CD44 expression. CD44 up-regulation may play an important role in decrease expression of E-cadherin. Therefore, miR-328 mediated CD44 up-regulation plays a role in pressure-induced EMT in renal tubular cells.

MP011

GREMLIN AGGRAVATES HYPERGLYCEMIA-INDUCED PODOCYTE INJURY BY A TGFβ/SMAD DEPENDENT SIGNALING PATHWAY

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Introduction and Aims: Gremlin is a bone morphogenic protein (BMP) antagonist and is elevated in diabetic kidney tissues, which is associated with disease progression. Although the mechanisms are unclear, in the early course of diabetic nephropathy (DN), podocyte are injured. We studied protein and gene expression of gremlin in mice podocytes cultured in hyperglycemia ambient. The role of gremlin on podocyte markers (nephrin and synaptopodin) and the likely signaling pathways involved were determined.

Methods: Expression of gremlin was visualized by confocal microscopy. Recombinant mouse gremlin and small interfering RNA (siRNA) targeting to gremlin 1 identified the role played by gremlin on podocytes. Study of canonical (smad2/3) and non-canonical (p38MAPK and JNK1/2) transforming growth factor beta (TGFβ)/smad mediated signaling, revealed the putative signaling mechanisms involved. Smad2/3 siRNA and TGFβ receptor inhibition (SB431542) were used to probe canonical TGFβ/smad signaling in gremlin-induced podocyte injury. Apoptosis of podocytes was measured by FUELI assay.

Results: Gremlin expression was enhanced in high glucose cultured mouse podocytes, and was localized predominantly in the cytoplasm and negligibly on the cell membrane. Not only expression of nephrin and synaptopodin were decreased on treatment with gremlin, but also synaptopodin rearrangement and nephrin’s relocation were evident. Targeting gremlin and smad2/3 by siRNA, and inhibition of TGFβR (SB431542) attenuated podocyte injury. Inhibition of canonical TGFβ signal can block the injury of gremlin on podocytes.
Conclusions: In conclusion, gremlin was clearly elevated in high glucose cultured mouse podocytes, and likely employed endogenous canonical TGF-β1/Smad signaling to induce podocyte injury. Targeting gremlin by siRNA may be clinically useful in the attenuation of podocyte injury.

OUABAIN INDUCES KIDNEY INJURY VIA MODULATION OF NEPHRIN AND SIK1 EXPRESSION IN GLOMERULAR PODOCYTES

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Introduction and Aims: Endogenous ouabain (EO) has been associated to reduced renal function in naïve hypertensive patients and has been identified as a powerful biomarker of acute kidney injury (AKI). Ouabain-induced AKI occurs through downregulation of podocyte protein Nephrin leading to glomerular damage. These data have been replicated by incubating cultured podocytes with nanomolar doses of ouabain, which induce podocytopenia and consequent glomerular damage. Nephrin and SIK1 protein expression in kidney injury.

Methods: Immunohistochemistry experiments were conducted in isolated glomeruli from kidney biopsy samples. Expression of nephrin and SIK1 was investigated using immunofluorescence microscopy.

Results: SIK1 is localized in rat and human glomerular podocytes (immunohistochemistry) where a positive correlation is observed between Nephrin and SIK1 protein expression in humans (r=0.781, p<0.001, n=33). Rat cultured podocytes incubated with 10−7M ouabain show reduced Nephrin and SIK1 protein levels. Isolated glomeruli from congenic MNS and NB rats, carrying the mutant beta adducin, predisposed to glomerular damage, show reduced Nephrin and SIK1 protein expression.

Conclusions: The direct relationship between Nephrin and SIK1 protein expression in different settings suggests that SIK1 may functionally participate in Nephrin signaling pathway involved in ouabain glomerular podocyte damage and kidney injury.

OUABAIN INDUCES KIDNEY INJURY VIA MODULATION OF NEPHRIN AND SIK1 EXPRESSION IN GLOMERULAR PODOCYTES

Rat cultured podocytes with nanomolar doses of ouabain induce podocytopenia leading to glomerular damage. These data have been replicated by incubating cultured podocytes with nanomolar doses of ouabain, which induce podocytopenia and consequent glomerular damage. Nephrin and SIK1 protein expression in kidney injury.

Conclusions: The direct relationship between Nephrin and SIK1 protein expression in different settings suggests that SIK1 may functionally participate in Nephrin signaling pathway involved in ouabain glomerular podocyte damage and kidney injury.

PODOCYTES

β

RETINOIC ACID REGULATES PODOCYTES DEDIFFERENTIATION AND REGENERATION

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Introduction and Aims: Injury to the podocytes results in proteinuria and often leads to progressive kidney disease. Podocytes as highly differentiated cell with unique architecture, loss of maturation biomarkers, cell apoptosis, and de-differentiation are characteristic of the lesion. Retinoic acid (retinoic acid, RA) in the field of podocyte disease treatment may also be crucial, besides to promote the differentiation and maturation of podocytes, leads to reducing proteinuria and attenuate renal fibrosis. We will demonstrate retinoic acid regulate podocytes maturity and differentiation maybe also mediated by Wnt and Notch pathway to restore cell structure and function of in glomerular lesions.

Methods: We used mouse immortalized podocytes for the in-vitro study, by setting all-trans retinoic acid group, puromycin injury group, the all-trans retinoic acid and puromycin co-stimulate group respectively. And further validated in vivo on SD rats

With Adriamycin induced nephropathy as podocytopathy and FSGS model by performing Real-time PCR, western blot analysis and immunohistochemistry and immunofluorescence.

Results: We observed the structure and function of cytoskeletal proteins in podocytes with puromycin injury and all-trans retinoic acid by immunofluorescence showed that in the PAN-podocytes the synaptopodin expression being significantly downregulated can be restored by intervention of all-trans retinoic acid (P<0.05), and reform the F-actin cytoskeleton along fiber filaments. With intervention of retinoic acid to Adriamycin induced nephropathy rat model, the results showed that the podocyte differentiation markers: cytoskeletal proteins synaptopodin, SD complex protein podocin and nephrin expression levels in disease states reduced compared with normal rats significantly (P<0.05). Retinoic acid intervention on adriamycin nephropathy rats led to mild to moderate proteinuria, compare with the massive proteinuria in ADR rat. The proteinuria excretion and renal function deterioration and kidney/body weight ratio of retinoic acid intervention on rats with Adriamycin nephropathy were significantly improved (P<0.05). Furthermore, our results showed that rats with adriamycin nephrosis activated the Wnt/β-catenin pathway target genes (Axin2), and the Notch pathway target genes (Hes1, HeyL), expression significantly with compare with the WT rats.

In conclusion, gremlin was clearly elevated in high glucose cultured mouse podocytes, and likely employed endogenous canonical TGF-β1/Smad signaling to induce podocyte injury. Targeting gremlin by siRNA may be clinically useful in the attenuation of podocyte injury.
Methods: We cultured predipocyte cell line 3T3-L1 cells, which were differentiated with 500 μM IBMX, 250 nM dexamethasone, 10 μg/ml insulin after 90% confluency. Treatment with p-cresol was performed in various concentrations (0–200 μM). Cell proliferation was determined by cell count and Brd-U cells. The maturity of adipocyte was investigated by oil red O staining and by real-time PCR to see the mRNA expression of PPARγ. Apoptosis was measured by ELISA kit. We also examined glucose uptake in the presence and absence of insulin using radiolabeled 2-deoxyglucose.

Results: In the cell count experiment, the number of 3T3-L1 adipocyte treated with 200 μM p-cresol was significantly decreased at day 3 and day 7, while no significant decrease was observed in 20 μM or less p-cresol treatment. Brd-U antibody detection showed similar results suggesting that p-cresol disturbed normal cell cycle. Oil red O staining at day 7 showed that the number of mature as well as immature adipocytes was decreased by the treatment with 200 μM p-cresol. As consistent with this finding, apoptotic cell number at day 7 was increased by the treatment with 100–200 μM p-cresol. In addition, 200 μM p-cresol decreased mRNA expression of PPARγ, a main regulator of the differentiation, even when corrected with GAPDH mRNA level. Since the number of mature adipocytes decreased, β labeled 2-deoxyglucose uptake was remarkably inhibited by 200 μM p-cresol in the presence and absence of insulin.

Conclusions: High concentration of p-cresol disturbed normal cell cycle, induced apoptosis, inhibited the differentiation of predipocyte into mature adipocyte, and decreased glucose uptake at basal and after insulin stimulation. These findings indicate that the accumulation of uremic toxins may induce the reduction of fat mass, insulin resistance, malnutrition, and eventually poor prognosis in chronic dialysis patients.

Introduction and Aims: Insulin resistance is associated with higher prevalence of cardiovascular disease (CVD) in chronic kidney disease (CKD) patients. Previously, we have reported that mesenchymal stem cells (MSCs) from CKD mice were functionally incompetent in terms of proangiogenic capacity. The purpose of this study is to determine whether insulin resistance contributes to uremia-induced dysfunction of MSCs.

Methods: Primary bone marrow-derived MSCs were generated from C57Bl/6J mice. A uremic toxin, p-cresol, was treated at a concentration that is similar to the blood level in dialysis patients. Results: MSCs treated with p-cresol showed significantly lower expression of vascular endothelial growth factor (VEGF), VEGF receptor-1 (VEGFR1), and stromal cell-derived factor (SDF)-1x. Insulin-stimulated tyrosine phosphorylation of insulin receptor β subunit was not different between control and p-cresol-treated MSCs. However, insulin-induced tyrosine phosphorylation of insulin receptor substrate (IRS) 1, association of p85 subunit to the IRS1, and IRS1-associated phosphatidylinositol 3-kinase (PI3K) activity were significantly decreased in p-cresol-treated MSCs when compared with control cells. In parallel, p-cresol treatment was associated with increased inhibition of insulin phosphorylation of IRS1 and IRS2 at 6/16 residue. Insulin-stimulated serine phosphorylation of Akt was also reduced significantly in p-cresol-treated MSCs. In contrast, insulin-induced activation of ERK remained unchanged by p-cresol. Inhibition of PI3K/Akt, but not the MEK/ERK pathway, using U0126, an inhibitor of phosphorylation of extracellular signal-regulated kinase (ERK). U0126, an inhibitor of ERK pathway, prevented insulin-stimulated phosphorylation of insulin receptor. U0126 greatly diminished Akt phosphorylation, which is an important step in the activation of PI3K/AKT pathway. Therefore, insulin resistance in the presence of p-cresol may involve the suppression of PI3K/AKT, but not the MEK/ERK pathway.

Conclusions: Our results, together with previous reports, suggest that low levels of uremic toxins may contribute towards the development of insulin resistance, which is a major problem in patients undergoing chronic dialysis.

Introduction and Aims: Oxidative stress and inflammation are closely associated with renal fibrosis, and the microRNAs (miRNAs) are key modulators in renal fibrosis. The purpose of this study was to investigate the effect of miRNA-192 and miRNA-93 on renal fibrosis in CRF rats.

Methods: CRF rats were induced by 5/6 nephrectomy. The rats were randomized into three groups: control, miRNA-192 and miRNA-93 injection groups. At the end of the experiment, kidney tissue samples were collected and analyzed for miRNA expression, collagen deposition, and renal function.

Results: In the miRNA-192 and miRNA-93 injection groups, the expression of TGF-β1 and Smad3 was significantly down-regulated compared to the control group. Additionally, the collagen deposition and renal function were significantly improved in the miRNA-192 and miRNA-93 injection groups compared to the control group.

Conclusions: The miRNA-192 and miRNA-93 injection groups significantly inhibited renal fibrosis and improved renal function in CRF rats.

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Conclusions: The miRNA-192 and miRNA-93 injection groups significantly inhibited renal fibrosis and improved renal function in CRF rats.
ARB may halt the deleterious process of dyslipidemia via normalization of regulators.

Abstracts

**MP019**

**INHIBITION OF OXIDATIVE STRESS DOES NOT PREVENT RENAL TUBULAR CYTOTOXICITY INDUCED BY CISPLATIN**

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Introduction and Aims: Drug nephrotoxicity is a serious health and economic problem affecting approximately one out of four among the 100 most used drugs in intensive care units. Cisplatin-induced acute kidney injury is characterized mostly by proximal and distal tubular damage. The death phenotype depends on the concentration of cisplatin to which cells are exposed. Necrosis appears as a response to high concentrations, whereas apoptosis to low concentration of the drug. Oxidative stress has been shown to be implicated in cisplatin cytotoxicity and nephrotoxicity, both in vitro and in vivo. However, the role of oxidative stress in the different forms of cell death induced by increasing concentrations of cisplatin has not been assessed nor has it been studied the subcellular sources of cisplatin-induced oxidative stress under these distinct phenotypical and biochemical scenarios. We aimed at testing the ability of the different antioxidants, a NADPH oxidase inhibitor (DPI), and the SOD mimetic tempol to prevent oxidative stress to identify molecular targets to minimize nephrotoxicity.

Methods: A human proximal tubule cell line (HK2) was treated with cisplatin (0-1000 μM) in the presence or absence of 0.03 mM 4-hydroxy-TEMPO (tempol) and 3 μM DPI. Biochemical and phenotypic characteristics evoked by pro-apoptotic and pro-necrotic concentrations of cisplatin were studied in the presence and absence of the antioxidants in order.

Results: Our results show a dose-dependent effect of cisplatin on lipid peroxidation and H2O2 production in HK2 cells, in agreement with previously published data in vivo and in vitro. Surprisingly, the effect of high doses of cisplatin on lipid peroxidation is more strong that the effect on H2O2 production. DPI significantly, but partially, reduced lipid peroxidation. Tempol completely prevented the lipid peroxidation produced by pro-necrotic concentrations of cisplatin concentrations. DPI and tempol exerted a moderate protective effect against cell death through the range of cisplatin concentrations, being slightly more pronounced on pro-apoptotic than on pro-necrotic concentrations. Cisplatin had a concentration-dependent cytotoxic effect, measured as the number of viable cells and these antioxidants do not minimize this effect.

Conclusions: Our data show that most of the oxidative stress induced by cisplatin is originated from mitochondrial NADPH oxidase activity, as lipid peroxidation and H2O2 production is clearly reduced by the NADPH oxidase inhibitor DPI. These results suggest that oxidative stress is not the only important mechanism behind cisplatin cytotoxicity; and that oxidative stress participates more in the death by apoptosis than in that caused by necrosis. The inhibition of the oxidative stress does not prevent the cytotoxicity induced by cisplatin in renal tubular cells.

**MP020**

**THE FARNESOID X RECEPTOR LIGAND PREVENTS CISPLATIN-INDUCED RENAL INJURY BY ENHANCING THE ORPHAN NUCLEAR RECEPTOR SMALL HETERODIMER PARTNER**

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Introduction and Aims: The farnesoid X receptor (FXR) has been shown to be largely expressed in liver, intestine, and kidney. In the present study, we investigated whether 6-ethyl chenodeoxycholic acid (6-ECDCA or INT-747), a semisynthetic derivative of chenodeoxycholic acid (CDCA), modulate small heterodimer partner (SHP) in human proximal tubular (HK2) cell lines and cisplatin-induced renal injury rat model.

Methods: The mice were treated with cisplatin alone (20 mg/kg, single injection, i.p.; Platosin-Pharmachemie; Haarlem, Netherlands; n = 9) or cisplatin + FXR ligand (30 mg/kg/day, for 7 days, oral; Santa Cruz, Califonia, USA; n = 9). In another series of experiment, HK-2 cells were treated with cisplatin (50 μM), with or without FXR ligand.

Results: Cisplatin induced the protein expression of SHP on HK2 cell and cisplatin-treated rat, which is attenuated by FXR ligand treatment. Furthermore, FXR ligand attenuated renal injury in HK2 cell strain compared with cisplatin-treated rats. FXR ligand also attenuated the protein expression of transforming growth factor β1 (TGF-β1), inflammatory markers and cytokines, and fibrosis markers in cisplatin-treated rats. The increased ratio of proapoptotic protein Bax and anti-apoptotic protein Bcl2 in cisplatin-treated rats also is attenuated by FXR ligand treatment. The cisplatin induce NF-κB expression in HK2 cell which is attenuated by FXR ligand pretreatment. In SHP deletion state by siRNA, the protein expression TGF-β1 and p-JNK was not attenuated, while overexpression of SHP induce decreasing of protein expression of TGF-β1 and p-JNK by FXR ligand treatment in HK2 cells.

Conclusions: In conclusion, FXR ligand, 6-ECDCA prevents cisplatin-induced renal injury by enhancing the orphan nuclear receptor small heterodimer partner.
**ROLE OF CIASTATIN AGAINST CISPLATIN-INDUCED NEPHROTOXICITY AND INFLAMMATION IN RATS**

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**Introduction and Aims:** Cisplatin is a major antineoplastic drug for the treatment of solid tumors, but its nephrotoxicity is a major complication and a dose limiting factor for anticancer therapy. Several evidences have shown that inflammation contribute to the pathogenesis of cisplatin-induced acute renal failure. We have found that clastatin, a renal dehydroepiandrosterone 1 inhibitor has protective effects on cultured proximal tubular epithelial cells from cisplatin-induced damage. In this study, we have investigated the potential use of clastatin as nephroprotector on cisplatin induced renal injury and inflammation in rats.

**Methods:** Male Wistar rats were divided into 4 groups: control rats, cisplatin-control rats, cisplatin-treated cisplatin-injected rats. Nephrotoxicity was assessed 5 days after cisplatin treatment, by measuring serum creatinine, blood urea nitrogen (BUN), serum collagen IV (collagen IV) and tumor necrosis factor-β (TNF-β). TUNEL-positive apoptotic cells and PCNA-positive mitotic cells were counted. Inflammation was assessed by electrophoretic mobility assay (EMSA), enzyme-linked immunosensor assay and immunohistochemical studies.

**Results:** Cisplatin-treated rats showed significant increases in BUN, creatinine, and proteinuria and decreased the glomerular filtration rate compared when with control rats. Cisplatin rats also exhibited severe morphological changes such as necrosis and extensive vaculization of the proximal tubule and inflammatory mediators were increased. Clastatin significantly prevented partial or totally these changes in renal function and ameliorated histological damage in cisplatin injected animals. Clastatin also reduced serum tumor necrosis factor-alpha and IL-6 levels, nuclear factor Β activation and ED1 (monocytes/macrophages) positive cells.

**Conclusion:** This study provides evidence that clastatin reduces in vivo cisplatin nephrotoxicity by preventing inflammation and might represent a novel strategy in the prevention of cisplatin-induced acute renal injury.

**MP025**

**EPIDERAL GROWTH FACTOR RECEPTOR (EGFR) INHIBITION WITH ERLOTINIB ATTENUATES CIASTATIN-INDUCED NEPHROTOXICITY IN RATS**

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**Introduction and Aims:** The effects of blocking the EGFR pathway in acute kidney injury (AKI) are controversial. Therefore, we investigated the renoprotective effect of erlotinib, a tyrosine kinase inhibitor that can block EGFR activity, on cisplatin-induced acute kidney injury in rats.

**Methods:** Male Wistar rats were divided into 4 groups: control rats, cisplatin-control rats, cisplatin-treated cisplatin-injected rats. Nephrotoxicity was assessed 5 days after cisplatin treatment, by measuring serum creatinine, blood urea nitrogen (BUN), serum collagen IV (collagen IV), and alanine aminotransferase (ALT). TUNEL-positive apoptotic cells and PCNA-positive mitotic cells were counted. Inflammation was assessed by electrophoretic mobility assay (EMSA), enzyme-linked immunosensor assay and immunohistochemical studies.

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**Conclusion:** This study provides evidence that clastatin reduces in vivo cisplatin nephrotoxicity by preventing inflammation and might represent a novel strategy in the prevention of cisplatin-induced acute renal injury.

**MP024**

**ACTIVATION OF THE INFLAMMASOME IN CISPLATIN-INDUCED ACUTE KIDNEY INJURY; PROTECTION BY CASPASE INHIBITION**

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**Introduction and Aims:** We have demonstrated that there is increased caspase-1, IL-1α, IL-1β, and IL-18 in cisplatin-induced acute kidney injury (Cis-AKI). As caspase-1, IL-1α, IL-1β, and IL-18 are activated in the inflammasome, the aim of the study was to further investigate the inflammasome in cisplatin-induced AKI and also to determine whether caspase inhibitor protects the inflammasome in proximal tubules of Cis-AKI in vitro.

**Methods:** Fresh isolation of proximal tubules and cisplatin treatment (in vitro);

Proximal tubules were freshly isolated from kidney cortex of male C57BL/6 mice using collagenase digestion and Percoll centrifugation. After recovery period, proximal tubule cells were incubated with different concentrations of cisplatin (final concentration 10 and 50 μM) and QVD-OPH (50 μM).

**Results:** Mice injected with cisplatin (25 mg/kg) developed AKI on day 3. On quantitative PCR of whole kidney, levels of NALP3 mRNA expression were increased on day 3. On immunoblot of whole kidney, there were a 2-fold increase in IL-1β (15 kDa) and a 3-fold increase in IL-18 (15 kDa) on day 2 respectively. IL-1β and IL-18 were significantly increased in both groups of cisplatin-treated AKI.

**Conclusions:** In conclusion, components of the inflammasome are increased in both whole kidneys in vivo, and PT treated with cisplatin in vitro. Caspase inhibition protects against Cis-AKI through inhibition of proinflammatory and proapoptotic cytokines.

**MP025**

**REGULATION OF MOUSE GLomerular FILTRATION BY THE INTEGRIN-LINKED KINASE (ILK) IN CisPLATIN INDUCED NEPHROTOXICITY**

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**Introduction and Aims:** The guanine 3,5-cyclic monophosphate (cGMP)-dependent signalling pathway plays an important role in the regulation of glomerular filtration, since vasodilation appears when NO activates soluble guanylyl cyclase (sGC) which produces cGMP, which activates cGMP-dependent protein kinases (PKG).

**Methods:** Control (WT) and conditional ILK-deleted mice (cKO) were treated or not with single dose of cisplatin (CIS, 20 mg/kg intraperitoneal) and placed in metabolic chambers for 3 days. Urine volumes and creatinine levels were analyzed and changes in cortical sGC and PKG protein levels and their activity were studied.

**Results:** Observed enhanced urine volume and creatinine clearance in cKO mice compared with controls, as a consequence of increased cortical sGC and PKG protein levels and activities. CIS induced a decrease in glomerular filtration rate, measured as creatinine clearance, and this decrease was significantly less marked in CIS-cKO mice due to its higher tissue contents of sGC and PKG compared with WT.

**Conclusions:** We propose ILK as a major player in the glomerular physiology and pathology. The increased cGMP-dependent glomerular filtration due to the lack of ILK could be targeted to prevent nephrotoxicity in cancer patients undergoing treatment with platinum-derived chemotherapeutic agents.

**Abstracts**

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doi:10.1093/ndt/gft125 | 1305
Results: Western blot of activated caspase-3 and cytochrome c release. Cisplatin (0-1000 μM). Cell viability/proliferation was assessed by the MTT method. The cell death mode was determined by DEVDase (caspase activity) and western blot of activated caspase-3 and cytochrome c release.

Conclusions: The aim of this work was to gain further insight into the effect of caspase 9 in the apoptosis and necrotic mechanisms underlying cisplatin's cytotoxicity. Tubular (HK2) and Jurkat cells (overexpressing Bcl2, a negative mutan of Bcl2) and silencing diminished Gremlin-induced gene overexpression of profibrotic factors and ECM and EMT markers, by western blot/confocal microscopy or Real-time PCR. The effect of renal fibrosis was determined by evaluation of key profibrotic factors, expression of syndecan 4 was significantly reduced (p<0.005) in podocytes grown in high glucose.

Introduction and Aims: Increased transient receptor potential canonical family (TRPC) channel member 6 and syndecan 4 have been associated with altered podocyte function and diabetes mellitus. We investigated whether the expression of TRPC6 and syndecan 4 are altered in hyperglycemia. Human immortalized podocytes grown in the presence and absence of high glucose. In addition, podocytes were cultured with 10% fetal bovine serum (FBS) and 5% FBS with 10 μM calpeptin (pH 7.4) for 24 h.

Results: The expression of TRPC6 mRNA was significantly higher (p<0.05) while the expression of syndecan 4 was significantly reduced (p<0.05) in podocytes grown in the presence of high glucose compared to controls. Tempol significantly ameliorated the altered expression of TRPC6 (p<0.05) and syndecan 4 (p<0.05) by glucose, indicating that oxidative stress was the underlying mechanism. L-glucose did not change either TRPC6 or syndecan 4 expression significantly.

Conclusions: High glucose concentrations cause different changes of mRNA expression of TRPC6 and syndecan in podocytes due to oxidative stress.

Introduction and Aims: Proteinuria, especially albuminuria, mainly caused by podocyte injury and ensuing filtration barrier failure, predicts progression and renal outcomes in human glomerular diseases. Cadmium (Cd) is an important industrial and environmental heavy metal pollutant that with chronic, low-level patterns of exposure the kidney is the primary target of toxicity. It is not known if low-level exposure to Cd induces an irreversible dysfunction in glomerular podocytes, which have a significant role in establishing the selective permeability of the kidney filtration barrier.

Methods: In this study, we analyzed the association between blood and urinary Cd levels and kidney abnormalities (serum creatinine level, urine creatinine clearance and albuminuria) in a rodent model. Adult male Sprague-Dawley rats were daily subcutaneously infused with 0.3 mg/kg CdCl2 for up to 12 weeks. In vitro toxic effects and cellular mechanisms of Cd were examined on cultured murine podocytes. Results: The results showed that significant elevated serum creatinine level and raise of albuminuria were associated with increased serum and urine Cd concentration by continuous infusion in rats. Histological confirmation of podocyte injuries was done by transmission electron microscopy (showing Cd-induced podocyte foot process effacement) and immunohistochemistry exam of augmented cleaved caspase 3 staining. This study further examined in vitro toxic effects and cellular mechanisms of Cd on cultured murine podocytes. We showed that treatment with low concentration CdCl2 (500, 48hrs) markedly increases intracellular Cd concentration in cultured podocytes. Accumulation of Cd in podocytes resulted in increased reactive oxygen species production, endoplasmic reticulum stress (indicated by elevated CHOP and GRP94 expression), inhibition of the survival pathway Akt and Erk, and finally led to cellular apoptosis.

Conclusions: This observation suggests that low concentration Cd exposure causes kidney injuries by inducing endoplasmic reticulum stress and apoptosis in glomerular podocytes.

Introduction and Aims: Gremlin is a developmental gene upregulated in chronic renal diseases associated to extracellular matrix (ECM) accumulation but its direct role in the regulation of renal fibrosis is still unclear. In endothelial cells, gremlin induces angiogenesis via vascular endothelial growth factor receptor-2 (VEGFR2) pathway. Our aim was to investigate the receptor and mechanisms involved in gremlin-mediated fibrogenic events in renal cells.

Methods: Human tubular epithelial cells (HK2) and renal fibroblasts were studied. Cells were treated with gremlin form 10 min, followed by a cross-linking procedure, then total proteins were isolated and immunoprecipitated with an anti-VEGFR2 antibody, the covalently-linked Gremlin complexes were analyzed by Western blotting. The effect of renal fibrosis was determined by evaluation of key profibrotic factors, ECM and EMT markers, by western blot/confocal microscopy or Real-time PCR.

Results: In tubular epithelial cells and fibroblasts gremlin binds to VEGFR2, as shown by complex formation, and activates VEGFR signalling, demonstrated by increased VEGF2 tyrosine phosphorylation. As gremlin is a BMP antagonist, we evaluated the involvement of BMPs in the activation of VEGFR2. In the presence of BMPs (BMP-2, 4 or 7) gremlin-induced VEGFR2 activation was not modified, showing BMPs-independent effect. In human tubular epithelial cells gremlin induced profibrotic and ECM-related factors, such as TGF-β1, and induced phenotypic changes to myofibroblast-like morphology, including loss of epithelial markers and induction of mesenchymal markers. VEGFR2 blockade by pharmacological inhibition or gene silencing diminished Gremlin-induced gene overexpression of profibrotic factors and changes in EMT markers.

Conclusions: We propose that gremlin, by VEGFR2, increased profibrotic events and therefore could contribute to renal fibrosis.

Introduction and Aims: Vascular calcification is the leading cause of coronary artery disease and one of the most serious complications in hemodialysis patients. Recent
Therefore, we explored whether LaCl₃ inhibits AGEs-induced osteoblastic uremia. These findings inquire the elucidation of the beneficial role of HO-1 in found a small beneficial effect of hemin treatment in oxidative stress-induced apoptosis however, affects endothelial cell viability to a larger extent in uremic conditions. We There is no differential HO-1 upregulation after exposure to hemin. Oxidative stress, however, affects endothelial cell viability to a larger extent in uremic conditions. We found a small beneficial effect of hemin treatment in oxidative stress-induced apoptosis in uremia. These findings inquire the elucidation of the beneficial role of HO-1 in

**Methods:**

**Results:**

**Conclusions:**

We demonstrated for the first time that AGEs induced NF-κB activation in these cells. LaCl₃ significantly inhibited AGEs induced NF-κB activation in these cells.

**LaCl₃**

**Methods:** Rat VSMCs were cultured and administered with 100mg/ml glyceraldehyde-derived AGEs or bovine serum albumin (BSA). VSMCs were co-incubated with 10 mM LaCl₃, neutralizing RAGE antibody, 10μM BAY11-7082, an inhibitor of NF-κB, cytoskeleton, neutralizing anti-RAGE antibody as well. Co-incubation of LaCl₃ significantly inhibited AGEs induced NF-κB activation in these cells.

**Results:** Administration of AGEs markedly increased ALP mRNA and protein expression in VSMCs. AGEs also induced ROS generation, which was abolished by LaCl₃. Furthermore, AGEs induced ALP mRNA and protein expressions were blocked by LaCl₃. Furthermore, AGEs induced ALP mRNA expression were abolished by BAY11-7082, NAC and anti-RAGE neutralizing antibody as well. Co-incubation of LaCl₃ significantly inhibited AGEs induced NF-κB activation in these cells.

**Conclusions:** We demonstrated for the first time that AGEs-induced osteoblastic differentiation was blocked by LaCl₃ through the inhibition of RAGE-ROS-NF-κB pathway in VSMCs. These observations suggest that Lanthanum may be a useful therapeutic tool for the prevention of vascular calcification in hemodialysis patients.

**Heme Oxygenase 1 Expression in Human Umbilical Artery Endothelial Cells (HUAECS) in Uremic Versus Healthy Serum Conditions**

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**Introduction and Aims:** Heme oxygenase 1 (HO-1) is an inducible heme-degrading enzyme, known for its protective antioxidant, anti-inflammatory and anti-apoptotic effects in atherogenesis and plaque stabilization. Increased inflammation and oxidative stress have been described to contribute to the accelerated atherosclerosis seen in CKD. We investigated the effect of oxidative stress on endothelial cells in uremic compared to healthy serum conditions and studied inducibility of HO-1 and its effects in control as well as short and persistent oxidative stress conditions.

**Methods:** HUAECs were conditioned in 30% human serum (pooled either from 40 hemodialysis patients or 10 healthy volunteers) for 72 hours, followed by exposure to either increasing concentrations of peroxynitrite (0.10, 0.25, 0.50 and 1.00 mM) for 5 minutes or SIN-1 (7.5 mM for 4 hours. Additionally, HUAECs were pretreated with 50 μM Hemin during 6 hours. After incubation for 6 hours, HO-1 expression was evaluated by RT-PCR and western blot. Cell viability 30 minutes after peroxynitrite exposure was evaluated by MTT assay. Cell apoptosis after 8 hours of SIN-1 incubation with or without hemin preincubation (50 μM) was evaluated by western blot for caspase-3.

**Results:** Equal HUAEC cell viability was measured by MTT when cells were conditioned in uremic and healthy serum. Hemin treatment did not affect cell viability and induced a 10- to 20 fold increase in HO-1 protein in both conditions. SIN-1 induced a mild increase of HO-1, which was 1.5-fold higher in uremic conditions. Peroxynitrite treatment reduced cell viability by 23% in healthy serum and by 43% in uremic serum (P<0.05 vs. control between 0.1 - 0.5 mM). SIN-1 treatment induced apoptosis in urmic conditions 3 hours after exposure to peroxynitrite.

**Conclusions:** Uremic serum per se does not affect cell viability or HO-1 expression. There is no differential HO-1 upregulation after exposure to hemin. Oxidative stress, however, affects endothelial cell viability to a larger extent in uremic conditions. We found a small beneficial effect of hemin treatment in oxidative stress-induced apoptosis in uremia. These findings inquire the elucidation of the beneficial role of HO-1 in uremia.

**Curcumin and Valproic Acid Relieve the Adriamycin-Induced Injury on Podocyte**

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**Introduction and Aims:** Our previous study showed that curcumin and valproic acid could alleviate adriamycin-induced rat kidney injury, so we aimed to investigate whether curcumin and valproic acid could protect podocyte from injury by adriamycin.

**Results:** We found that curcumin and VPA could improve podocyte proliferation and have different effects in different doses, especially when curcumin dose was at 0.125ug/ml (p<0.01), whereas curcumin (p<0.05) and VPA (p<0.01) pretreatment could reduce cell motility to the normal level. In the control group, the F-actin filaments were distributed as stress fibre-like bundles along the axis of the cell, and adriamycin-treating for 24 hours led to significant F-actin filaments depolymerization, and curcumin and VPA could attenuate adriamycin-induced podocyte actin rearrangement. Besides, RT-PCR results showed that adriamycin-treating group in different doses all could increase wnt1 mRNA expression significantly (p<0.01), the group pretreated with curcumin could also increase wnt1 mRNA expression (p<0.05), while wnt1 mRNA expression was decreased in VPA group (p<0.05). Our Western Blot results indicated that p-mTOR protein was downregulated in curcumin group and upregulated in VPA group.

**Conclusions:** Our study demonstrated that curcumin and VPA could improve podocyte proliferation, reduce motility and rearrange actin in adriamycin-treated podocyte. Meanwhile, we found that wnt/beta-catenin pathway and mTOR pathway could affect above changes as well.

**Differentially Expressed Genes and Their Associated Networks in Clear-Cell Renal Cell Carcinoma (RCC)**

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**Introduction and Aims:** Clear cell renal cell carcinoma (ccRCC) is the predominant RCC subtype. Microarray gene expression profiling has been used in the past by various groups to identify novel markers of the disease. We hypothesized that a meta-analysis of publicly available gene expression datasets of ccRCC may identify a
list of the common deregulated genes (DEGs), which should have higher potential to be used as novel tumor markers.

**Methods:** In the Oncomine platform, genes deregulated in ccRCC relative to the corresponding normal tissue were filtered by a corrected Q value cut-off and concept filters. The identified genes that were common among 5 different microarray datasets were chosen as the candidate markers and their performance to discriminate between cancer and normal tissue was measured by ROC test. Their networks were analyzed by Ingenuity Pathway Analysis (IPA). Further Gene Ontology (GO) enrichment, KEGG pathways and Transcription Factor Target analyses were performed for the most common DEGs. The Caki-2 and ACHN ccRCC cell lines were used in order to validate the expression of the most common DEGs. The AB8/13 undifferentiated podocyte and HEK293 cells were used as controls.

**Results:** We concluded in 93 commonly up-regulated and 76 commonly down-regulated genes in ccRCC vs. normal tissue. The top 10 up-regulated molecules were NDUFA4L2, PLIN2, NNMT, ENO2, AHNAK2, NETO2, CA9, VWF, COL23A1 and EHD2, and the top 10 down-regulated molecules were NPHS2, CALB1, RALY1, KCNJ1, KNG1, SERPINA5, CLDN8, SLC12A3, CA10 and ATP6V0A4. Their expression levels were validated with qRT-PCR in the Caki-2 and ACHN ccRCC cell lines, compared to the AB8/13 undifferentiated podocyte and HEK293 cells. The top canonical pathways included the antigen presentation pathway, the inositol metabolism and the pentose phosphate pathway among others. The common DEGs participate in biological functions such as cancer, inflammatory response, renal and urological disease, reproductive system disease and respiratory disease. The top molecular and cellular functions were cell-to-cell signaling and interaction, cellular function and maintenance, molecular transport, cellular growth and proliferation and carbohydrate metabolism.

**Conclusions:** The present study highlights the most responsible genes for the formation of ccRCC and their associated networks. These genes could be used as predictive markers for the disease.
**GENETIC DISEASES AND MOLECULAR GENETICS**

**MP034 EFFICACY OF ECULIZUMAB IN ATYPICAL HEMOLYTIC UREMIC SYNDROME (aHUS) PATIENTS WITH OR WITHOUT PRIOR TRANSPLANT**

Christophe Legendre1, David Cohen2, Yahou Delmas3, Thorsten Feldkamp4, Denis Fouque5, Richard Furman6, Osama Gaber7, Larry Greenbaum8, Timothy Goodship9, Hermann Halter10, Maria Hetheliou11, Maryvonne Hourmant12, Christoph Licht13, Bruno Moulin14, Neil Sheerin9, Antonella Trivelli15, Camille L. Bedrosian16 and Chantal Loirat17

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**Introduction and Aims:** Post-transplant aHUS recurrence leads to graft failure within 1 yr (year) in 60% of patients (pts). Case reports suggest that eculizumab (Ecu) rescues ongoing complement-mediated thrombotic microangiopathy (TMA) and prevents resulting graft loss in pts with post-transplant aHUS recurrence.1,2 Methods: Ecu efficacy and safety were evaluated in 2 open-label, single-arm, 26-week phase 2 trials with long-term extensions in aHUS pts age ≥12 yrs. Outcomes in non-transplant (NTP) and prior transplant (TP) AHUS pts with progressing TMA or long disease duration and 2 yrs of ongoing Ecu treatment were analyzed. Results: Ecu improved renal function in NTP and TP (Table). Baseline eGFR was not predictive of eGFR change in any group. Shorter time from aHUS clinical manifestation predicted greater eGFR gain in all groups (P<0.03). Conclusions: Ecu is effective in preserving renal function in NTP and TP and preventing graft loss in TP due to aHUS. These data support early Ecu treatment to prevent ESRD in NTP and TP and prophylactic treatment in pts undergoing transplant.

**MP035 EFFICACY OF ECULIZUMAB IN ATYPICAL HEMOLYTIC UREMIC SYNDROME (aHUS) PATIENTS WITH OR WITHOUT A HISTORY OF DIALYSIS**

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**Introduction and Aims:** Eculizumab (Ecu), a terminal complement inhibitor, is the only approved treatment for aHUS, a life-threatening disease characterized by chronic uncontrolled complement activation and systemic thrombotic microangiopathy (TMA). Up to 65% of patients (pts) develop end-stage renal disease (ESRD) or die within 1 year of diagnosis.1 Outcomes in pts with progressing TMA and/or Eculizumab plasma exchanges/infusions (≥1 wk at screening) who received 2 years of ongoing Ecu treatment were analyzed based on baseline dialysis status. Methods: Ecu efficacy and safety were evaluated in a single-arm, open-label trial with a 26-wk trial and long-term extension in 17 pts age ≥12 years with progressing TMA. Results: Median Ecu treatment duration was 124 wks and 93 wks for dialysis and nondialysis pts, respectively. Baseline characteristics and Ecu efficacy at 2 years were similar in pts with or without dialysis at baseline (Table). Ecu improved platelet counts and renal function in both pt groups. Four of 5 pts (80%) on dialysis at baseline eliminated dialysis and 1 of 12 pts (8%) not on dialysis at baseline started dialysis at wk 64. Ongoing Ecu was safe and well tolerated in both populations. Conclusions: Ecu inhibited hemolysis TMA and improved renal function in both pt groups. These data provide evidence for the benefit of Ecu treatment on renal outcomes in aHUS pts, including those on dialysis, regardless of renal function at the start of treatment.

**Table. Baseline characteristics and 2-year efficacy outcomes in Eculizumab-treated aHUS patients with or without dialysis at baseline.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Dialysis Pts (n=12)</th>
<th>Nondialysis Pts (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (y)</td>
<td>31 (21–47)</td>
<td>32 (17–68)</td>
</tr>
<tr>
<td>Gender, male (%</td>
<td>57%</td>
<td>70%</td>
</tr>
<tr>
<td>Race, Caucasian (%)</td>
<td>5%</td>
<td>10%</td>
</tr>
<tr>
<td>No identified complement mutation or autoantibody (%)</td>
<td>1 (9%)</td>
<td>3 (29%)</td>
</tr>
<tr>
<td>Prior platelet transfusion, n (%)</td>
<td>2 (17%)</td>
<td>4 (26%)</td>
</tr>
<tr>
<td>Clinical manifestation of aHUS to screening, mean (SD)</td>
<td>23.6 (4.1)</td>
<td>30.6 (16.5)</td>
</tr>
<tr>
<td>eGFR at baseline, mean (SD), mL/min</td>
<td>7.0 (4.7)</td>
<td>13.0 (11.7)</td>
</tr>
</tbody>
</table>
| Table 1. Baseline characteristics and 2-year efficacy outcomes in Eculizumab-treated aHUS patients with or without dialysis at baseline.**

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LT12 MP037 POSTPARTUM ATYPICAL HEMOLYTIC UREMIC SYNDROME IN A YOUNG ADULT TREATED WITH ECULIZUMAB

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Introduction and Aims: Atypical hemolytic uremic syndrome (aHUS) is a rare, life-threatening disease caused by uncontrolled chronic activation of alternative pathway, resulting in systemic microvascular thrombosis, organ ischemia and organ damage. Prognosis is poor: up to 65% of patients require dialysis, have permanent kidney damage or die despite plasma exchange/plasma infusion (PE/PI).

Methods: Case presentation We describe the case of a 23-year-old female who after a pre-eclampsia induced premature delivery showed signs of thrombotic microangiopathy (TMA).

Results: The patient was admitted with tonicoclonic seizures, anasarca edema and high blood pressure while laboratory investigation revealed acute renal failure (creatinine 4.9 mg/dl), thrombocytopenia (platelets 40 x 10^9/L) with elevated lactate dehydrogenase, LDH (3245 IU/L) with presence of schistocytes on blood smear. She was initially diagnosed with thrombotic thrombocytopenic purpura (TTP) and intensive PE was initiated twice daily. She also received dialysis for 1 month. Three months after initial admission, the patient was discharged with non-dialysis dependent renal failure (creatinine 2 mg/dl) and without signs of hemolysis. In the next three months, the patient was readmitted with signs and symptoms of TMA. Further investigations showed a negative Coombs test and detectable ADAMTS13 activity excluding TTP. The patient was diagnosed with aHUS. A renal biopsy was performed that showed TMA; the patient later developed signs of cardiomyopathy (left ventricular ejection fraction 25%). Due to failure of PE and dialysis to reverse TMA, the patient was started on eculizumab (complement inhibitor), which improved clinical and laboratory parameters. During long-term eculizumab treatment renal and cardiac functions were restored and TMA manifestations reversed. No further clinical symptoms and signs of TMA have been observed. The patient currently remains under chronic eculizumab treatment, without complications.
Abstracts

allows simultaneous investigation of multiple genes in a time- and cost-efficient manner

Methods:
We present a novel genetic testing approach in patients with aHUS and determine the need for any other invasive treatment.

Conclusions: Chronic eculizumab treatment can rapidly block complement activation, successfully reverse systemic TMA and improve organ function in aHUS patients.

Results: Our data corroborate that many patients carry an alteration in more than one gene which may aggravate the clinical phenotype in line with a mutational load model.

Conclusions: Genetic testing for all susceptibility factors is necessary. Its complexity makes interpretation challenging and requires an interdisciplinary approach in diagnostics and treatment of patients with aHUS and related disorders.

Introduction and Aims: We present a case of post-partum atypical hemolytic uremic syndrome (aHUS) - without identified complement gene mutation – that presented complete recovery of renal function (availing dialysis), after early treatment with eculizumab (6 months follow-up).

Methods: A 41-year-old primigravida, without previous medical history, uneventful obstetric history. Delivery was by cesarean section at 37 weeks for cephalopelvic disproportion. After delivery, the patient presented to the emergency room with progressive weakness and distal edema. The blood test showed acute kidney failure (creatinine 9 mg/dL; blood urea nitrogen-BUN 133 mg/dL; proteinuria 1664ng/24h), non-immune hemolytic anemia (hemoglobin 4.1 g/L; lactate dehydrogenase - LDH 2312 U/L; histoplasmin undetectable; peripheral smear showed schistocytes, direct Coombs test negative) and thrombocytopenia (platelets 35000/L). At that point the patient required support treatment with blood transfusions (2 units) and frozen plasma. After ruling out other causes (ADAMTS 13 activity 43%; Shiga-toxin negative; normal autoimmune study) she was diagnosed with post-partum aHUS.

Six sessions of plasma exchange (PE) were conducted and two hemodialysis sessions were required due to over hydration. Her renal dysfunction and hemolysis signs persisted. Renal biopsy confirmed thrombotic microangiopathy. Eleven days after first symptoms, we decided to begin treatment with C5 inhibitor: eculizumab (Soliris®; weekly dosage of 900 mg intravenously for four weeks) previous prophylaxis therapy with pneumococcos vaccine and benzyl-penicillin.

Results: A few days after first doses the hemolysis was reverted and kidney function progressively improved (avoiding dialysis). At five days, she changed to maintenance treatment at 900 mg biweekly. Follow-up: six months after initiation of treatment, patient maintains normal renal function (creatinine 0.9 mg/dL) without proteinuria, without new episodes of hemolysis. Genetic analysis showed no mutations in the alternative complement pathway regulators.

Conclusions: We propose individualizing treatment with C5 inhibitor to aHUS, and suggest that with some patients a low dose of the drug could be used for maintenance based on the complete clinical improvement with the first doses, environmental trigger defined and absence of genetic alteration. In summary, to our knowledge, we report the first case of post-partum aHUS treated successfully with eculizumab, early treatment may prevent the progression to end stage renal disease.

Introduction and Aims: Hemolytic uremic syndrome (HUS) is characterized by hemolytic anemia, thrombocytopenia, and impairment of renal function, and is the most common cause of acute renal failure in childhood. Most cases occur secondary to infection with Shiga toxin-producing bacteria. About 10% of HUS patients are classified as atypical (aHUS) with a generally poorer prognosis. Genetic complement abnormalities play a major role in aHUS and lead to uncontrolled overactivation of the alternative complement pathway. While the glomerular vascularature of the kidney is the main target, about 20% of patients additionally show extrarenal involvement (CNS or multivisceral). There is increasing evidence for a multiple-hit scenario in aHUS with complex inheritance, i.e. mutations in genes encoding complement regulatory proteins or complement activators predispose to aHUS rather than being causative per se.

According to the guidelines of the European Pediatric Study Group for HUS (Arieta et al., Pediatr Nephrol. 2007), genetic testing of CFI, CFI, MCP, THBD, CPD and C3 is indicated in all patients with aHUS, even if plasma levels are normal. Genotype-phenotype correlations make genetic testing an essential part of clinical management; the genetic predisposition often determines the prognosis after the initial HUS episode and post renal transplantation. While patients with CFI mutations usually have the worst prognosis, the outcome of patients with MCP mutations is relatively good. Early intensive plasmapheresis should be started as early as possible and appears to have a beneficial effect, except in MCP-mutated patients.

Methods: We present a novel genetic testing approach in patients with aHUS and related disorders (e.g., MPGN II) based on Next-Generation Sequencing (NGS) that allows simultaneous investigation of multiple genes in a time- and cost-efficient manner.

Introduction and Aims: Atypical hemolytic uremic syndrome (aHUS) and related disorders are genetict conditions that present a challenge for the clinician. The identification of genetic alterations in aHUS allows personalized treatment approaches, leading to improved outcomes.

Methods: We report on a patient diagnosed with aHUS and B3GNT5 mutations. A 63-year-old female presented with renal failure, microangiopathic hemolytic anemia, and fever. Genetic testing revealed a B3GNT5 mutation, which is associated with aHUS.

Results: The patient was treated with eculizumab, achieving improvement in renal function and hemolysis.

Conclusions: Genetic testing in aHUS can provide insights into personalized treatment approaches, leading to improved outcomes.

Introduction and Aims: aHUS is a complex genetic disease. The identification of genetic alterations in aHUS allows personalized treatment approaches, leading to improved outcomes.

Methods: We report on a patient diagnosed with aHUS and B3GNT5 mutations. A 63-year-old female presented with renal failure, microangiopathic hemolytic anemia, and fever. Genetic testing revealed a B3GNT5 mutation, which is associated with aHUS.

Results: The patient was treated with eculizumab, achieving improvement in renal function and hemolysis.

Conclusions: Genetic testing in aHUS can provide insights into personalized treatment approaches, leading to improved outcomes.
significant upregulation of UPR markers in the mutant mice both at the mRNA and the protein level. Finally, UPR activation was evident in biopsies of patients carrying mutation COL4A3-G134E.

Conclusions: Collectively, our results suggest that ER stress can arise from defective localization of collagen IV chains in human podocytes exerting a strong intracellular effect and may thus represent a contributing factor for TBMN and AS pathomechanism. These results further imply that UPR activation due to underlying collagen mutations may potentially have a strong impact on disease progression. Importantly, this could pave the way for novel therapeutic interventions for various collagenopathies such as the use of chemical chaperones to improve or ameliorate disease symptoms.

Results: We found distinct sets of miRNAs that were specifically expressed both in tubular and glomerular ARPCs. Among miRNAs modulated specifically in ARPCs, we found several miRNAs that were predicted to target genes involved in the regulation of WNT/β-catenin, WNT5A, SLC6A9, and HOXAX9 and that could be one of the key regulators of the stem cell identity, including self-renewal and cell fate decision. In particular, miR-195 and miR-1225-5p regulated the expression of important markers of renal progenitors, such as CD133 and PAX2, and important genes involved in the repair mechanisms of ARPCs, such as TLR2. We demonstrated that the expression of both the renal stem cell markers CD133 and PAX2 depends on lower miR-195 levels and that the increase of miR-195 levels improved capacity of tubular ARPCs to differentiate into adipocyte-like and epithelial-like cells. Finally, we foresee that the low levels of miR-1225-5p were responsible for high TLR2 expression in tubular ARPCs.

Conclusions: Therefore, together, miR-1915 and miR-1225-5p seem to regulate important traits of renal progenitors: the stemness and the repair capacity, and could be used, in the future, to modulate the features of renal progenitors for therapeutic purposes.

**Functional Studies of SLC2A9 (GLUT9) Variants Associated with Plasma Uric Acid Levels**

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2Lille 2 University

Introduction and Aims: SLC2A9 (GLUT9, also called GLUTX or URAT1) is a new voltage-sensitive urate transporter expressed in the liver, the kidney and other tissues. It was cloned by homology with the GLUT family, but has been shown to transport urate.

Methods: GLUT9 variants were prepared by site-directed mutagenesis and expressed in Xenopus laevis oocytes by injection of cRNAs. 48 hours later they were subjected to 14C-urate uptake (n=30 oocytes, 3 batches). Surface expression was assessed by immunostaining.

Results: The uptake assay revealed decreased 14C-urate flux for all mutants compared to wild-type GLUT9 (70±1% decrease for L75R; 86±8% for T125R; 58±21% for R198C; 72±14% for R808W; and 69±9% for P414R for human mutants and 80±5% for C210F; p=0.01 for all compared to wildtype). Expression at the cell surface was preserved for all variants, SNP V253I showed decreased 14C-urate uptake by 41±22% (p=0.05) and decreased surface expression.

Conclusions: All GLUT9 mutants displayed decreased 14C-urate transport flux without affecting the cell surface expression. This suggests that these causative GLUT9 missense mutations directly interfere with urate transport mechanisms. Moreover, a non-synonymous single-nucleotide polymorphism (SNP) V253I, present with a frequency of 22.3% in the population, has been associated with low plasma uric acid level in genome-wide association studies. A loss-of-function mutation, C210F, has been identified as causative for the kidney stone formation and it is one of the most common inherited causes of hyperuricemia. A decrease in plasma uric acid levels and increased risk of uric acid kidney stones and uric acid nephropathy have prompted us to study all variants systematically.

**Functional Studies of SLC2A9 (GLUT9) Variants Associated with Plasma Uric Acid Levels**

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Introduction and Aims: Uromodulin-associated kidney disease (UAKD) is a heritable renal disease in humans caused by mutations in the uromodulin (UMOD) gene. Clinical symptoms of UAKD are very heterogeneous and can comprise hyperuricemia, gout, alteration of urine concentrating ability, and inconsistently progressively renal failure and histological kidney alterations like glomerular and tubular cysts, interstitial nephritis and fibrosis. Clinical symptoms of UAKD result from dysfunction of cells of the thick ascending limb of Henle (TALH), which is caused by maturation and trafficking defect of mutant uromodulin protein retained in the hyperplastic endoplasmic reticulum of TALH cells. So far, therapeutic strategies to treat UAKD focus on treatment of hyperuricemia and gout, which don’t prevent disease progression. Improvement of maturation of mutant uromodulin protein depends on the chemical chaperones sodium-4-phenylbutyrate (4-PBA). In vivo was reported independently by two groups. Therefore, the aim of our study was to assess the putative therapeutic effect of 4-PBA in a recently established Umod-mutant mouse model of UAKD in vivo.

Methods: 4-PBA was orally administered by the drinking water at a dosage of 1 g 4-PBA/kg body weight per day over a period of two months on homozygous Umod mutant male mice and their wild type littermates, beginning at an age of two months. The control groups received no 4-PBA in the drinking water. The following parameters were assessed: intake of drinking water and food, blood and urine electrolytes, parameters of kidney function and urinary uromodulin excretion, kidney morphology. In parallel, effect of 4-PBA was tested using immortalized murine proximal tubular epithelial cells (MTC cell line) stably transfected with wild type Umod and mutant Umod4227T constructs, respectively.

Results: In homozygous Umod mutant mice treated with 4-PBA, kidney dysfunction with increased blood urea concentration, increased urine excretion, decreased urine osmolality, decreased fractional excretion of sodium and decreased uromodulin excretion were present. Compared to the control group, no amelioration of clinical symptoms and morphological kidney alterations were present in the 4-PBA treatment group. Incubation of 4-PBA on MTC cells stably expressing and secreting mutant uromodulin protein resulted in an increase of mature uromodulin protein in the supernatant. However, this increase was not due to ameliorated mature protein maturation and trafficking but was due to an increased uromodulin expression and it was also present in Umod4227T transfected cells.

Conclusions: While 4-PBA was reported to ameliorate maturation and trafficking defect of mutant uromodulin in vitro, no beneficial effect of 4-PBA administration was detected in vivo in a mouse model of UAKD.

**MIR-1915 and MIR-1225-5P Regulate the Expression of CD133, PAX3 and TLR2 in Adult Renal Progenitor Cells**

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1Department of Emergency and Organ Transplantation University of Bari Bari Italy, 2Consorzio CARSO Valenzano Ba Italy, 3University of Salento Lecce Italy

Introduction and Aims: Adult renal progenitor cells (ARPCs), were recently identified in the tubular compartment and in the Bowman’s capsule and it was demonstrated that renal progenitors from both locations were positive for PAX2, CD133, CD24 and exhibited multipotent differentiation ability. Recent studies indicated that microRNAs (miRNAs), a class of noncoding small RNAs that participate in the regulation of gene expression, may play a key role in stem cell self-renewal and differentiation. Distinct sets of miRNAs are specifically expressed in pluripotent stem cells but not in adult tissues, suggesting a role for miRNAs in stem cell self-renewal. We compared miRNA expression profiles of ARPCs with that of renal proximal tubular cells (RPTCs) and of mesenchymal stem cells (MSCs) with the aim to found distinct sets of miRNAs that were specifically expressed both in tubular and glomerular ARPCs and to obtain the whole-genome miRNA expression profiles of ARPCs.

Methods: miRNA global expression profiles were obtained by Agilent microarray technology. Real-time PCR was used for the verification of microarray results. miRNA targets were predicted by miRBase 17.0, TargetScan 5.2, PiqTar and RNA22 1.0 algorithms. Mimic transfection, cell immunofluorescence, western blot and flow cytometric analysis were used for validation of miR-1915 and miR-1225-5p effect on CD133, PAX2 and TLR2 expression.

Conclusions: miR-1915 and miR-1225-5p showed decreased surface expression and decreased miR-1915 and miR-1225-5p levels improved capacity of ARPCs to differentiate into adipocyte-like and epithelial-like cells. Finally, we demonstrated that the expression of both the renal stem cell markers CD133 and PAX2 depends on lower miR-1915 levels and that the increase of miR-1915 levels improved capacity of tubular ARPCs to differentiate into adipocyte-like and epithelial-like cells. Finally, we foresee that the low levels of miR-1225-5p were responsible for high TLR2 expression in tubular ARPCs.
Introduction and Aims: Uromodulin-associated kidney disease (UAKD) is an autosomal dominant disease caused by mutations of the uromodulin (UMOD) gene. Our study explored genotype-phenotype correlations by examining the relationship between the type of UMOD mutation and the age of onset for end stage renal disease (ESRD).

Methods: Extensive bibliographic research was employed to ascertain patient-level data of all UAKD patients published up to October 2011. Data included gender, age at onset of hyperuricemia, gout and ESRD, as well as the UMOD genotype. Kaplan Meier analysis and Cox Proportional Hazards Models fitted with shared gamma frailty terms to adjust for within-family correlations were used to model time to event.

Results: Thirty-one peer reviewed publications reporting 202 patients from 74 families with 59 different UMOD mutations were included. The median ages at onset of hyperuricemia, gout, and ESRD were 24, 40, and 56 years, respectively. Males developed gout and ESRD significantly earlier than women (P=0.02 and P=0.035, respectively, shared frailty model). A particular group of 18 families with no mutation identified in UMOD mutations (Figure). Age at onset of ESRD was significantly lower for UMOD mutations located within the epidermal growth factor domains 2 and 3 (range 45 to 52 years) compared to the Cysteine-Rich domains (range 60 to 65 years; P=0.05 by shared frailty model).

Conclusions: The UMOD genotype is related to the clinical phenotype of UAKD. Certain genotypes are associated with an earlier age of onset of ESRD, with mutations affecting epidermal growth factor domains being associated with the most severe clinical phenotypes. However, hyperuricemia and gout were found not to be predictive of the advance of ESRD. Our findings may assist in counseling of patients.

Metallothioneins as Markers for Biological Organ Age in Preimplantation Kidney Biopsies

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Introduction and Aims: Structure and function of the kidney deteriorate with age and age-related diseases contribute to this process, leading to the high frequency of end-stage renal disease in the elderly. The difference between chronological and biological age is a main problem in determining donor kidneys for transplantation. The ideal situation would be to match the functional capacity of a donor kidney to the patient's renal requirements. Therefore the identification of markers for biological organ age is a strong clinical need.

Methods: Age-regulated gene expression changes in 37 zero hour kidney biopsies from donors with no clinical signs of AKI at the time of explantation were determined using microarray technology followed by ANOVA and SAM analysis. Expression changes of selected genes were confirmed by quantitative real-time PCR. In situ hybridization was used to localize mRNA expression in zero hour biopsies. Functional aspects were subsequently performed in 24 probands who had no pathogenic mutation identified in COL4A5, and as first-tier in 4 families with unequivocal autosomal inheritance of CKD.

Results: COL4A5, COL4A4 or COL4A3 pathogenic mutations were found in 40 families (40/65; 62%). XLAS was confirmed in 29 males and 34 females from 21 families (21/40; 52.5%). Two probands carried the same COL4A3 missense mutation c.4342G>C (p.Gly1448Arg). Autosomal recessive ARAS was molecularly confirmed in 8 patients from 6 families (6/40; 15%). A single COL4A3 or COL4A4 pathogenic mutation was identified in 27 patients from 13 families (13/40; 32.5%), as well as in 10 relatives of 3 probands with ARAS. Seven probands carried the same COL4A3 missense mutation c.1291G>C (p.Gly407Arg). Eight of the remaining 25 families had no pathogenic mutations identified in any of the 3 genes, while in 17 families the study was limited to COL4A4. The diagnosis of XLAS or ARAS could be genetically confirmed in all 10 patients who showed the typical ultrastructural GBM features of AS.

Conclusions: The proportion of families with pathogenic mutations in COL4A4 was lower than expected, possibly due to broad clinical inclusion criteria. The GBM ultrastructural changes are important diagnostic clues to XLAS and ARAS. Mutational analyses of COL4A4/COL4A3/COL4A5 is an essential diagnostic tool in these families.

Metallothionein isoforms in elderly kidney predisposes to a reduced anti-stress response capacity.

Molecular Characterization of 65 Portuguese Families with Clinical Diagnosis of Collagen Type IV Glomerulopathies

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Introduction and Aims: Collagen type IV glomerulopathies include Alport syndrome (AS) and thin basement membrane nephropathy (TBMN). AS is a childhood onset progressive chronic kidney disease (CKD) associated with sensorineural hearing loss and typical ocular signs. TBMN manifests by hematuria, usually without significant proteinuria or progressive CKD, and is not associated with extra-renal complications. While thinning of the glomerular basement membrane (GBM) occurs in TBMN and AS, alternating GBM thinning and thickening as well as lamellation with electron-dense bodies are characteristic of AS. X-linked AS (XLAS) is caused by COL4A3 and COL4A4 mutations. Autosomal AD and many cases of TBMN are due to COL4A3 or COL4A4 mutations. Approximately 85% of AS families are X-linked. AIM: To describe the molecular pathology of AS and TBMN in Portugal.

Methods: Sixty-five unrelated families with a clinical diagnosis of AS or TBMN were enrolled in a multicenter study. Mutational analysis of COL4A3 was performed by direct PCR sequencing and Multiplex Ligation-dependent Probe Amplification (MLPA) in 61 probands. Direct PCR sequencing of COL4A3/COL4A4 was subsequently performed in 24 probands who had no pathogenic mutation identified in COL4A5, as well as in 1 family with unequivocal autosomal inheritance of CKD.

Results: COL4A5, COL4A4 or COL4A3 pathogenic mutations were found in 40 families (40/65; 62%). XLAS was confirmed in 29 males and 34 females from 21 families (21/40; 52.5%). Two probands carried the same COL4A3 missense mutation c.4342G>C (p.Gly1448Arg). Autosomal recessive ARAS was molecularly confirmed in 8 patients from 6 families (6/40; 15%). A single COL4A3 or COL4A4 pathogenic mutation was identified in 27 patients from 13 families (13/40; 32.5%), as well as in 10 relatives of 3 probands with ARAS. Seven probands carried the same COL4A3 missense mutation c.1291G>C (p.Gly407Arg). Eight of the remaining 25 families had no pathogenic mutations identified in any of the 3 genes, while in 17 families the study was limited to COL4A4. The diagnosis of XLAS or ARAS could be genetically confirmed in all 10 patients who showed the typical ultrastructural GBM features of AS.

Conclusions: The proportion of families with pathogenic mutations in COL4A4 was lower than expected, possibly due to broad clinical inclusion criteria. The GBM ultrastructural changes are important diagnostic clues to XLAS and ARAS. Mutational analyses of COL4A3/COL4A4/COL4A5 is an essential diagnostic tool in these families.

Thin Basement Membrane Nephropathy Due to Heterozygous COL4A3/COL4A4 Mutations Is a More Frequent Cause of ESKD Compared to Alport Syndrome

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Introduction and Aims: Alport syndrome (AS) is a severe hereditary hematuric nephritis, associated with deafness, eye defects and early progression to ESKD. About 85% of all AS cases are X-linked due to mutations in COL4A5, while the rest are autosomal recessive due to homozygous or compound heterozygous COL4A3/COL4A4 mutations. ARAS. Thin basement membrane nephropathy (TBMN) is the leading cause of familial hematuria (FH) worldwide and is mostly explained by heterozygous COL4A3/COL4A4 mutations. TBMN should no more be considered as a benign condition, since about half of these patients progress to chronic renal failure after the age of 50 years, and about 30% reach ESKD by the age of 70 years, according to our data in the Greek-Cypriot population. This study in a catchment area of 600,000 people, aims to compare AS and TBMN in terms of ESKD cases.
Methods: Since 1991 we identified more than 120 families with familial hematuria of different causes. We assessed and compared the number of ESKD cases in TBMN families (only for them that a heterozygous COL4A3 or COL4A4 mutation was found) and AS families.

Results: We have identified nine AS families referred to our public hospitals: four XLAS families with nine living patients (71%) and five ARAS families with four living patients (29%). COL4A5-P628L was found in two of the XLAS families. Only six of these living patients reached ESKD. We have found a heterozygous COL4A5or COL4A4 mutation in 213 patients in 27 families. Mutation COL4A5-G1334E was found in 16 families and it accounts for 155 patients. Of these 213 patients, 21 have reached ESKD. Interestingly, we observe that Greek-Cypriot patients with ESKD due to TBMN (21 patients) outnumber by 3.5 times those who reach ESKD due to AS (6 patients).

Conclusions: This observation demonstrated again that TBMN is not a benign condition with excellent prognosis, as usually mentioned in the previous literature. Further investigations are needed in other populations to confirm this epidemiological finding, while work is in progress to identify putative genetic modifiers that are responsible for the adverse outcome in a subset of TBMN patients.

Introduction and Aims: Molecular genetics (MG) allows now for accurate diagnoses and elimination of uncertainties based on EM findings alone in patients with familial hematuria (FH) and especially the Alport syndrome (AS). AS used to be diagnosed only if thickened and lamellated glomerular basement membranes were present, while thinning was thought characteristic of benign FMH due to heterozygous COL4A3/A4 mutations. This may not always be the case. Methods: Long term follow up, laboratory studies to include renal biopsies with EM and MG since 1991, are used to study patients with FH. PCR-RFLP is used to identify carriers of previously found mutations. Results: MG has yielded 9 COL4A3/A4 mutations with 213 live heterozygous carriers in 28 families. The initial phenotype is isolated MH starting in childhood. Most families however, include members (65%), who later develop additional proteinuria, hypertension and CKD, usually after the age of 50. Presently, 21 patients [10%], have reached ESRD. On the opposite, 20% of carriers reached 70 yo with only MH. Occular abnormalities are absent. The histopathology is TBMN with superadded FSGS in members who develop proteinuria, CKD and ESRD. In homozgyosity or compound heterozygosity, these 9 COL4A3/A4 mutations may be responsible for 5 patients with classical autosomal recessive AS, reaching ESRD in late adolescence with deafness and ocular changes. 46 other carriers with FH, belonging to 8 different families, proved to be caused by one of two missense, X-linked, COL4A5 AS mutations. These were: G624D in six families and P628L in two families. CKD developed in hemizygous males and 11 such males reached ESRD between 31 and 61 yo. Several other affected males exhibiting TBMN, remain well in their late 50's. Affected heterozygous females show only MH.

Conclusions: MG studies confirm that some COL4A5 AS mutations may be expressed with TBMN and variable degrees of CKD. It should therefore be Known that X-linked COL4A5 AS mutations show a wide phenotypic spectrum with a) classical AS, characterized by early onset ESRD, neurosensory deafness and ocular defects from serious nonsense COL4A5 mutations, b) males who develop late onset ESRD and late onset deafness and c) hypomorphic, missense, COL4A5 mutations, such as G624D and P628L, that in hemizygous males exhibit MH, TBMN, mild CKD or late onset ESRD. Therefore, when investigating ‘benign FMH’, these two and other similar X-linked COL4A5 mutations should always be looked for.

Introduction and Aims: The calcium-sensing receptor (Casr) has an important role in regulating calcium homeostasis via parathyroid (PT) gland and kidney tissues. Casr is also expressed in several other tissues where its role is less understood. Previous studies suggested that-chondrocyte-specific mice under the Col2a1 promoter display a very severe phenotype with embryonic lethality. We revisited the function of Casr in chondrocytes by utilizing a different conditional Casr mouse model.

Methods: We generated a conditional Casr-deficient mouse model targeting exon 3 using the Cre/Lox system. We obtained Cre transgenic mice driven by the chondrocyte-specific Col2a1 promoter and developed chondrocyte Casr-deficient mice (Ch Casr-/-).

Results: Ch Casr-/- mice were viable and were born at the expected Mendelian ratio displaying growth retardation starting at 3 to 4 days of age. Life expectancy was decreased with 3 to 5 weeks. Serum chemistry studies revealed significant hypercalcemia and hyperphosphatemia in the setting of significantly elevated PTH levels at 3 weeks of age (310±373 vs. 128±18 μg/ml, P<0.01). Necropsy revealed enlarged parathyroid glands in Ch Casr-/- mice. Bone histology featured osteomalacia. Urine studies showed hypercalciuria and hyperphosphaturia. Quantitative PCR for Casr from xiphoid tissue showed significantly decreased Casr expression (RQ value 1 ±0.2 vs 5.8±1, P<0.01). Immunohistochemistry suggested intact expression of Casr in the PT gland. We utilized the mT/mG (membrane-Tomo/membrane-Green) Cre reporter mouse to test the tissue specificity of Col2a1 expression. Preliminary data suggest that Col2a1 is expressed at least in kidney, heart and parathyroid tissues besides chondrocytes.

Conclusions: Casr-deficient mice driven by the Col2a1 promoter are viable exhibiting a less severe phenotype than previously observed by others using conditional deletion of Casr. Ch Casr-/- mice display significant growth retardation, hypercalcemia and hyperparathyroidism. Our preliminary data suggest that Col2a1 is expressed in several tissues besides chondrocytes. Data on chondrocyte proliferation and differentiation in the setting of Casr deficiency utilizing Adenovirus-mediated Cre deletion in culture will be presented.

Introduction and Aims: Idiopathic calcium nephrolithiasis (ICN) is a multifactorial disease. The importance of hereditary factors in ICN has emerged from several studies of familial renal stones. Whole genome scanning technologies have revealed unexpectedly heterogeneous structural variation in the human genome. Several studies have been resulted in increasing recognition of the critical role of structural genetic variation in modulating gene expression and disease phenotype. Structural genetic variants are mostly represented by copy number variants (CNVs). Rare CNVs have been implicated in the pathogenesis of several multifactorial diseases. It is not known whether CNVs similarly contribute to the pathogenesis of ICN.

Methods: We performed CGH-array analysis in a case study family with clinical and familiar characteristics very peculiar. The proband, 49 years old, since 19 has formed calcium oxalate and calcium phosphate renal stones; he expelled about 275 calculi both spontaneously and by lithotripsy. The metabolic phenotype revealed intermittent hypercalciuria and phosphaturic tubulopathy. He belongs to a family with consanguinity (his parents are second cousins and both affected by nephrolithiasis). In this family ICN is transmitted in an apparently dominant fashion, with males less frequently but more severely affected than females. CGH-array analysis has been performed in the proband and in eight family members. We designed a quantitative assay (by Real Time PCR) to validate CNVs from the proband and in eight family members.

Results: A duplication of 308 kb region of the Xq22.2 chromosome has been detected in the proband and in the affected mother, maternal aunt and cousin. This CNV is not present in the main CNV databases and we found only five duplications overlapping it in a cohort of 14375 controls. Thus, we focused in a deep investigation of the detected CNV to better define its possible role in ICN pathogenesis. To this aim, we firstly confirmed CGH-array findings by qPCR and we next performed a CNV-profiling screening on a cohort of 85 ICN patients. We interestingly found that 5 individuals carried a duplication overlapping the CNV found in the case-study family. Thus, considering our control cohort, this can significantly indicate a strong association with ICN (p=6.3310^{-17})

Conclusions: Our results show for the first time that a novel CNV can be a susceptibility genetic variant for the pathogenesis of ICN.
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**Introduction and Aims:** High urinary calcium excretion is a well known risk factor for calcium-based stone formation. Our study investigated the association of rare allele variants with extremes of urinary calcium excretion by sequencing 40 candidate genes, mostly known to affect urinary calcium excretion, in participants from the Nurses Health and the Health Professionals Follow-up Studies.

**Methods:** A total of 960 individuals were selected based on availability of 24-hour urine collection data and degree of urinary calcium excretion (high versus low). DNA sample pooling, droplet-based target gene amplification, barcoding and high-throughput sequencing were utilized for target sequencing.

**Results:** Approximately 64% of samples (n=615) showed both successful target amplification and sequencing data exceeding 20-fold deep sequence coverage. A total of 261 novel non-synonymous coding variants were identified. None of the rare gene variants with minor allele frequencies < 2% showed increased frequency in the high versus low urinary calcium groups; they were mostly observed in single individuals. When more common variants with allele frequencies over 2% were analyzed, an association of the rare gene CLAUDIN14 with high urinary calcium excretion (OR 5.20 versus 29/710 haplotypes, P value = 0.003) was suggestive. The significance of this finding was diminished after correction for multiple comparisons.

**Conclusions:** Claudin14 has previously been shown to be associated with nephritis in an ex vivo analysis of the HGMEC. In addition, several mouse models, the CLDN14-deficient and the kidney-specific calcium-sensing receptor-deficient models, have suggested an important role for Claudin14 in regulating urinary calcium excretion. These data suggest an important role for Claudin14 in urinary calcium excretion. Gene expression studies in larger sample sets will be necessary to confirm our findings for Claudin14 in this study. Analysis of non-synonymous variants in clusters, implicated functional pathways and tubular regions for kidney stone formation, will be presented.

**A FAMILY WITH NPHS2 HOMOZYGOUS p.R229Q VARIANT IN BOTH AFFECTED AND UNAFFECTED FAMILY MEMBERS: THE MISSING EVIDENCE**

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**Introduction and Aims:** Steroid-resistant nephrotic syndrome (SRNS) represents a common cause of ESRD. In its genetic form, the most frequently mutated gene is NPHS2, mutations of which are inherited in an autosomal recessive fashion. One of its variants, the c.686G>A polymorphism (p.R229Q) in heterozygous state and in association to an NPHS2 mutation was found to cause late-onset SRNS. Homozygous p.R229Q was also described in patients with late-onset SRNS, but its pathogenicity remained questionable.

**Methods:** Here we present a 37-year-old man diagnosed with nephrotic-range proteinuria in infancy, FSGS at the age of 20 years who progressed to ESRD by the age of 33.

**Results:** Mutational analysis of the NPHS2 gene revealed the p.R229Q variant in homoyzgous state. Nevertheless, his father and brother were both homozygous for the p.R229Q variant either, with normal renal function. We performed ophthalmologic examination revealed the “morning glory” disk anomaly in the right eye with radial vessels and a central tuft of white glial tissue. The tilted disk was surrounded by a ring of pigmented chorioretinal changes in his left eye. Based on these characteristic ocular abnormalities, the PX2 gene was sequenced. A de novo, heterozygous frameshift mutation (c.674delG, p. V226fs) was found. This mutation could entirely explain both the renal and the ocular involvement.

**Conclusions:** The NPHS2 homozygous p.R229Q variant in itself may not cause FSGS. It may exert an epistatic effect which can explain its enrichment in SRNS. Nevertheless, patients carrying homozygous p.R229Q should be screened for the causative mutation in a second generation.

**ASSESSING BLEEDING RISK OF RENAL ANGIOIMYOLIPOMATA (AMLs) IN TUBEROUS SCLEROSIS COMPLEX (TSC)**

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**Introduction and Aims:** Renal AMLs have been reported to occur in up to 80% of patients with TS (1) and are a major cause of morbidity and mortality in adults (2,3). In a large RCT, an mTOR inhibitor, Everolimus has been proven to shrink AMLs (4) and is therefore likely to prevent bleeding. We urgently need to delineate risk factors for AML haemorrhage to target Everolimus therapy. We have previously reported that AMLs larger than 3cm that are growing are at risk (5). We have examined a larger cohort of people with TSC to determine the prevalence & risk factors for bleeding.

**Methods:** From 1996 to 2012 the UK TSC Renal Registry collected data by questionnaire on 251 patients. 110 (43.8%) were men & 141 (56.2%) women, 168 patients (67%) had at least one AML and 148 patients had bilateral AMLs (59%). Mean age current years (Range 13-83).

**Results:** In 69 age at TSC diagnosis was 0-9 years in 71%, 10-19 in 12% & as an adult in 16%. Maximum size of the largest AML in males (4.8 cm +/-4.1 SD) was no different from females 5.5 cm +/-3.8. In patients without haematuria half had AML size of less than 3 cm and half AML over 3 cm. However in the 22.6% of patients who had haematuria it was twice as common in females (68.4%) as males (31.6%). Mean age of occurrence haematuria was 34.9 years (+/-13.3 SD, range 6 – 58), which was not significantly different from the age of the whole group. In 17 with known AML size of bleed was the mean 5.8cm (range 1.8-13), in males – 4.3+/-.2cm (range 1.8-13) and in females 7.1+/-.3cm (range 2-13). There was no size difference between males & females. 76% of patients at the time of their bleed had an AML size >= 3 cm. Of the 77 patients in whom renal measurements of 118 AMLs are available, 92 (78%) grew & 26 (22%) did not. Average AML growth rate was 0.51cm/year. Growth rate did not correlate with age, AML size or sex.

**MP057** **EFFECT OF EVEROLIMUS ON RENAL ANGIOMYOLIPOMA (AML) IN PATIENTS WITH TUBEROUS SCLEROSIS COMPLEX (TSC) BEING TREATED FOR SUBEPENDYMAL GIANT CELL ASTROCYTOMA (SEGA)**


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**Introduction and Aims:** Assess the effect of everolimus (EVE), an oral mTOR inhibitor, on renal AML growth in pts with TSC being treated for SEGA.

**Methods:** EXIST-1 (NCT00789898), a prospective, double-blind, randomized, placebo-controlled, phase 3 trial evaluated EVE in pts with SEGAs associated with TSC. An exploratory analysis was performed in a subset of pts who also had ≥1 target AML (lesion longest diameter ≥1 cm) at baseline. EVE was initiated at 4.5 mg/m²/day and titrated to attain a blood trough level of 5-15 ng/mL based on tolerability. EVE exposure was defined as a reduction in sum of all target lesions ≥50% relative to baseline. With no new lesions ≥1 cm in diameter on imaging, EVE exposure ≥20% from the lowest value obtained for the pt, and no AML-related bleeding of grade ≥2 (CTCAE, version 3.0). Adverse events (AEs) were assessed every visit and graded using CTCAE.

**Results:** EVE was superior to placebo (PBO) for the primary endpoint of SEGA response rate (p = 0.001). As of 02-03-2011 treatment was ongoing for 97.4%/79.5% of pts in the EVE/PBO arms, respectively, in the overall population. 30 pts (38.5%) in the EVE arm and 14 pts (35.9%) in the PBO arm had ≥1 AML ≥1 cm in longest diameter at baseline. In this pt subset the mean dose intensity was 6.1 mg/m²/day (EVE) and 5.6 mg/m²/day (PBO). Median exposure duration was 38 wks for EVE and 44 wks for PBO. Median exposure rate was 53.9% (95% CI 34.3-71.7%) in the EVE arm (16/30) vs 0.0% (95% CI 0.0-23.2%) in the PBO arm (0/14). After 48 wks of treatment 100% of pts in the EVE arm and >80% of pts in the PBO arm had ≥1 target AML shrinkage compared to 16.7% in the PBO arm (n=6). AEs were consistent with the known safety profile of EVE in TSC. Grade 3-4 AEs occurred in 20.6% (N=30) of patients (EVE arm) and 7.1% (1/14) of pts (PBO arm). Only 0.7% (2/230) of grade 3-4 AEs in the EVE arm were suspected to be drug treatment related.

**Conclusions:** EVE treatment elicited AML response with an acceptable safety profile in patients with AML and SEGAs associated with TSC.

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**MP058** **PHARMACOKINETICS AND EXPOSURE-SAFETY RELATIONSHIP OF EVEROLIMUS IN PATIENTS WITH RENAL ANGIOMYOLIPOMA (AML) ASSOCIATED WITH TUBEROUS SCLEROSIS COMPLEX (TSC) OR SPORADIC LYMPHANGIOLEIOMYOMATOSIS**

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**Introduction and Aims:** Renal AML associated with TSC are a leading cause of morbidity and mortality in affected pts. The randomized, double-blind phase 3, EXIST-2 (NCT01099400) study showed that everolimus (EVE) was superior to placebo for the primary endpoint, renal AML response rate (P<0.001), which was defined as the proportion of pts with confirmed ≥50% reduction in sum of volumes of all target AML relative to baseline and yielded a safety profile consistent with previous reports. This analysis examines the relationship between EVE concentration and safety. **Methods:** Pts with ≥1 AML were randomized (2:1) to EVE 10 mg daily (n=79) or placebo (n=39). EVE concentrations were measured at wks 2, 4, 12, 24, and 48 during the double-blind treatment period. EVE blood concentrations pre-dose (Cmin) and 2 hours post-dose (C2h) in whole blood were determined by liquid chromatography-mass spectroscopy (WuXi App Tec, Shanghai, China), with a lower limit of quantification of 0.3 ng/mL. The incidence of clinically notable adverse events (AEs) was reported by level of Cmin (<10, 10-25, and ≥25 ng/mL) and C2h (<40, 40-80, and ≥80 ng/mL). The relationship between EVE exposure and time to the first onset of stomatitis and infection events was also investigated using a Cox regression model.

**Results:** Median Cmin (range) at wks 2, 4, 12, 24, and 48 after treatment start was 6.6 (0.6-19.0), 7.0 (1.4-22.2), 7.5 (1.0-32.6), 6.7 (0.6-52.8), and 6.9 (2.5-50.0) ng/mL, respectively. Median C2h (range) at these same time points was 31.5 (4.9-75.4), 28.2 (4.3-75.9), 34.4 (10.5-77.9), 38.9 (5.4-98.6), 29.0 (10.0-71.2). There were no consistent trends in the relationships between incidence of clinically notable AEs and Cmin or C2h. Higher Cmin or C2h was not indicative of a higher probability/risk for stomatitis and infection events of all grades within the Cmin and C2h ranges observed in this trial. Hazard ratios (95% confidence interval [CI]) comparing Cmin <10 ng/mL vs 10-25 ng/mL for stomatitis and infections were 1.06 (0.45-2.51) and 0.61 (0.19-1.98), respectively. Hazard ratios (95% CI) comparing C2h <40 ng/mL vs 40-80 ng/mL for stomatitis and infections were 1.04 (0.49-2.22) and 0.48 (0.15-1.59). Median Data in the Cmin group ≥25 ng/mL and in the C2h group >80 ng/mL were not interpretable due to the small sample size.

**Conclusions:** Median Cmin and C2h appeared to be stable over time and were within the observed in previous EVE studies with the same dose. There were consistent trends in the relationships between clinically notable AEs and the level of Cmin or C2h exposure. However, the results must be interpreted with caution due to the small sample size.

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**MP060** **THE MUTATIONAL ANALYSIS OF THE ACTN4 IN PATIENTS WITH FOCAL SEGMENTAL GLOMERULOSCLEROSIS USING HRM METHOD**

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**Introduction and Aims:** Nephrotic syndrome (NS) is characterized by proteinuria, hypalbuminemia and edemas. There are four most important genes that condition the formation of hereditary nephrotic syndrome (ACTN4, CD2AP, NPHP5 and TRPC6). The gene ACTN4, which encodes protein α-actinin 4, is responsible for the autosomal dominant form of focal segmental glomerulosclerosis (FSGS).

**Methods:** The mutational analysis of the gene ACTN4 was performed on the set of 48 patients with FSGS/MCD. There were 17 males and 31 females, mean age 34.2 ± 16.5 years at the time of diagnosis 35.9 ± 18.2. Data were not available in 7 patients. Four patients were steroid sensitive and 31 patients were steroid resistant. Data were not available in 9 patients. As steroid resistant were defined patients who did not respond to prednisone (dose 1mg/kg) during 6 months of therapy. To investigate the prevalence and possible effect of some substitutions found in FSGS/MCD patients we were also looking for these changes in 155 patients (100 males and55 females, mean age 46.7 ± 14.5) with IgA nephropathy (IgAN) and 56 patients (34 males and 22 females).
Abstracts

Expression analysis was performed by next generation sequencing. For validation of controls were recruited. After isolating RNA from PBMCs, high throughput miRNA miRNAs in CKD, we now performed genome-wide miRNA expression profiling. In order to identify aberrantly regulated miRNA-mediated dysregulation of gene expression centrally contributes to initiation are crucial components of post-transcriptional gene regulation. Although (P<10^-10) between hemolysis patients and control subjects. Gene ontology analysis of potential candidate genes identified dysregulated biological processes such as “regulation of immune system process”, “immune response”, “response to external and endogenous stimulus”, “cell proliferation involved in kidney development” or “cytokine production”. Finally, annotation of candidate genes to the genetic association database identified genes which are associated with renal (e.g. DUSP6, DUSP1, TLR1, CAT) and immune disease (e.g. HSPA1A, IL1B, DUSP1, MYD88). The results of our research could be used in the diagnosis in patients with FSGS/MCD, MGN and IgAN. Supported by the grant project PRVOUK- P25/1F1/2.

**MP061 RENAL AGENESIS AND HYPOPLASIA IN HUMANS ARE NOT ASSOCIATED GLIAL CELL LINE-DERIVED NEUROTROPHIC FACTOR**

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Introduction and Aims: Congenital abnormalities of the kidney and urinary tract (CAKUT) are frequently observed in children and represent a significant cause of morbidity and mortality. Renal agenesis/hyoplasia account for a significant portion of these anomalies, and a genetic contribution to its cause is being increasingly recognized. Such as, Glial cell-derived neurotrophic factor (GDNF) plays an important role in renal development, serving as a trophic factor for outgrowth of the ureteric bud and its continued arborisation.

Methods: Twenty-five unilateral renal agenesis and twenty-five renal hyoplasia (without renal scar) patients were analyzed by direct DNA sequencing of all exons and exon-intron boundaries of GDNF gene.

Results: The study consists of 25 renal agenesis (17 male and 8 female) and 25 renal hyoplasia (14 male and 11 female) patients. The mean age of the renal agenesis patients were 9.1 years. The 8 patients of renal agenesis had right and 16 of them had left renal agenesis. And also the mean age of patients with renal hyoplasia were 8.8 years. 10 have right and 15 of them have left renal hyoplasia among renal hyoplasia patients. The GDNF mutations were not found any of patients.

Conclusions: These results suggest that genomic alteration GDNF is not a major mechanism leading to renal agenesis and hyoplasia. Analysis of a larger series of patients will be necessary to validate the association of the GDNF mutation with renal development defects.

**MP062 mirPhoNING IN CKD**

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Introduction and Aims: microRNAs (miRNAs), which are small, non-coding RNAs, are crucial components of post-transcriptional gene regulation. Although miRNA-mediated dysregulation of gene expression centrally contributes to initiation and progression of a broad spectrum of human diseases, surprisingly little work was performed in nephrology on this topic. In order to identify aberrantly regulated miRNAs in CKD, we now performed genome-wide miRNA expression profiling.

Methods: Ten clinically stable hemodialysis patients and ten age- and gender-matched controls were recruited. After isolating RNA from PBMCs, high throughput miRNA expression analysis was performed by next generation sequencing. For validation of biological relevance of CKD-specific changes in miRNA expression, MACET (Massive Analysis of cDNA Ends) gene expression experiments were done.

Results: Analysis of 11,952,274 tags revealed 98 miRNAs differentially expressed (P<10^-10) between hemolysis patients and control subjects. Gene ontology analysis of potential candidate genes identified dysregulated biological processes such as “regulation of immune system process”, “immune response”, “response to external and endogenous stimulus”, “cell proliferation involved in kidney development” or “cytokine production”. Finally, annotation of candidate genes to the genetic association database identified genes which are associated with renal (e.g. DUSP6, DUSP1, TLR1, CAT) and immune disease (e.g. HSPA1A, IL1B, DUSP1, MYD88).

Conclusions: miRNA expression is significantly dysregulated in CKD and may thus account for differential gene expression, contributing to the proinflammatory milieu of CKD patients. Since miRNAs are remarkably stable in blood and urine, their analysis may become a clinically valuable tool for diagnostic and monitoring purposes in nephrology.

**HEMOLYSIS: A FATAL COMPLICATION OF ALKAPTONURIA IN SEVERE RENAL FAILURE PATIENTS**

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Introduction and Aims: Alkaptonuria (AKU) is a rare autosomal recessive disorder. The gene involved in alkaptonuria is HGD, coding for homogentisic acide oxidase. In alkaptonuria patients, deficiency of this enzyme leads to the accumulation of homogentisic acid (HGA) in tissues called ochronosis. Ochronosis is induced by the impossibility to convert HGA into maleylacetoacetic acid in the tyrosine catabolic pathway. Clinical symptoms include massive urinary excretion of HGA, kidney stone formation, arthritis and joint destruction, pigmentation of cartilage and connective tissue, and cardiac valve deterioration. Rarely, kidney stones caused by urinary HGA excretion or interstitial nephropathy with pigment deposition may cause chronic renal failure.

Methods: An unusual case of rapidly progressive ochronosis with severe decreased kidney function associated with uncontrollable fatal hemolysis was recently described. We report on the second case of acute hemolysis and multorgan failure leading to death in a patient with severe renal impairment and alkaptonuria.

Results: A 27-year-old man was admitted to the hospital for anemia one month after dialysis was initiated for previous renal transplantation failure following alkaptonuria nephropathy. Molecular studies of the patient’s DNA had detected a heterozygous insertion substitution (c.198GC>ATT) of the HGD gene responsible for a frameshift (p.F10fs). The second mutation was unknown, but parents were both originating from the Venetian region. At admission, hemoglobin was 30g/L thrombopenia 130G/L. He showed hemolysis with haptoglobin <0.1g/L and inefficient blood transfusions, but no schistocytes. At this time, his skin was colored green-blue all over the body. Patient died of unexplained multorgan failure before other analysis could be performed, but autopsy revealed HGA-melanin pigments deposits in atrophic native kidneys and transplant, principally in distal and collecting ducts as well as in glomeruli and in macrophages. They were also found in coronary arteries, on the aortic valve, lung and liver.

Conclusions: We report on the second case of unexplained hemolysis leading to death in a 27 year old ESRD patient with alkaptonuria. It may be hypothesised that hemolysis is induced by high HGA plasma level and from the formation of plasma soluble melanins caused by HGA oxidation. In vitro HGA was found to spontaneously
form plasma soluble melamins after the incubation in human blood or plasma at 37°C. Oxidation and polymerization of HGA in the blood was accompanied by hemolysis. Thus, AKU is a very dangerous state in patients with renal failure because HGA accumulation and oxidation might induce acute hemolysis. We recommend early renal transplantation in AKU patients with renal failure.

**MP064**  
**STUDY OF THE COL4A4 GENE AND DESCRIPTION OF NEW MUTATIONS RESPONSIBLE FOR ALPORT SYNDROME**

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**Introduction and Aims:** Autosomal forms represent 20% of all cases of Alport syndrome. They are caused by mutations in the COL4A3 and COL4A4 genes. Our objective is to find, in the patients diagnosed with autosomal Alport syndrome admitted in our hospital, mutations in the COL4A4 gene responsible for this disease.

**Methods:** We analyze 6 families with a clinical diagnosis of autosomal Alport syndrome. We carry out a search of mutations in the COL4A4 gene using direct DNA sequencing from the index patient after amplifying it with polymerase chain reaction and mutation analysis with CGSE-heteroduplex. All patients had undergone a previous study of the COL4A3 gene that did not reveal any pathogenic mutation. In order to characterize the missense mutation found we carried out a population genetic study of 100 alleles with CGSE-heteroduplex and in silico studies using Polyphen, SNPs3D and SIFT.

**Results:** From our 6 patients, 4 of them (66.6%) presented a dominant inheritance, one of them (16.7%) had a recessive inheritance, and another one (16.7%) had no previous family history of Alport syndrome. We have found two pathogenic mutations, which are not described in the literature. IVS3+1G>C is a replacement of Guanine with Cytosine in position +1 of intron 3. It is located in the splicing region, which makes that it is considered a pathogenic mutation. Mutation c.4267C>T; p.P1423S is considered as pathogenic and responsible for the disease, according to the following criteria (FIGURE 1). Both of them generate a dominant autosomal syndrome.

All other mutations found were polymorphisms. 7 of them are described for the first time in this work. They are intronic variants located away from splicing regions. (FIGURE 2).

**Conclusions:** We describe here two pathogenic mutations of the COL4A4 gene: IVS3+1G>C and c.4267C>T; p.P1423S. These mutations are responsible for a dominant autosomal Alport syndrome. We describe 7 new intronic variants. They are considered as demographic polymorphisms due to their location, away from the splicing regions. The COL4A4 gene presents many polymorphisms, both in the exons and the intronic regions, which makes it difficult to reach a genetic diagnosis with the method that we have used.

**MP065**  
**STUDY OF THE COL4A3 GENE AND DESCRIPTION OF NEW MUTATIONS RESPONSIBLE FOR AUTOSOMAL DOMINANT ALPORT SYNDROME**

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**Introduction and Aims:** Autosomal forms represent 20% of all cases of Alport syndrome (15% recessive and 5% dominant). They are caused by mutations in the COL4A3 and COL4A4 genes, which encode alpha-3 and alpha-4 collagen chains. Our objective is to find, in the patients diagnosed with autosomal Alport syndrome admitted in our hospital, mutations in the COL4A3 gene responsible for this disease.

**Methods:** We analyze 8 families with a clinical diagnosis of autosomal Alport syndrome. We carry out a search of mutations in the COL4A3 gene using direct DNA sequencing from the index patient after amplifying it with polymerase chain reaction and mutation analysis with CGSE-heteroduplex.

**Results:** 6 patients (75%) presented a dominant inheritance, one of them (12.5%) had a recessive inheritance, and another one (12.5%) had no previous family history of Alport syndrome. We have found 16 mutations, 2 of them were pathogenic and responsible for the disease: mutation c.345DelG; p.G115GFSX37 and the deletion of a Guanine in the position 345 of the COL4A3 gene, which produces a stop codon 37 codons later, which leads to the generation of a truncated protein and is responsible for the symptoms in this family.

This mutation has not been described in the literature. Mutation c.4235G>T; p.G1412V changes a Guanine with a Thymine in position 4235 of the gene, which generates a change of glycine with valine in the position 1412 of the protein, which has already been described as pathogenic. All other mutations can be classified as demographic polymorphisms.

7 of which have already been described and 7 are described in this study. They are intronic variants located far away from splicing areas, which means that they are not considered as pathogenic variants.

All of them are expressed in figure 1.

**Conclusions:** In the 8 patients of our study, a pathogenic mutation of the COL4A3 gene was only found in 2 cases (25%). The COL4A3 gene presents many polymorphisms, both in the exons and the intronic regions, which makes it difficult to reach a genetic diagnosis with the methods that we have used.

Mutation c.345 Del G; p.G115GFSX37 is a deletion that generates a truncated protein. This is a pathogenic mutation responsible for an autosomal dominant Alport syndrome, which is described for the first time in this study. We describe 7 intronic mutations classified as demographic polymorphisms because they are far away from splicing regions, which means that they have no effect on the resulting protein.
MP065

LRPS GENE SINGLE NUCLEOTIDE POLYMORPHISMS AND OSTEOPOROSIS IN CHILDREN WITH PRIMARY GLOMERULONEPHRITIS TREATED WITH GLUCOCORTICOIDS

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Introduction and Aims: The aim of our study was to analyze twelve single nucleotide polymorphisms (SNP) of gene LRPS potentially associated with osteoporosis risk in children with routine steroidotherapy in the course of the idiopathic nephrotic syndrome. Glucocorticosteroids are important risk factors for drug induced osteoporosis. Decrease in bone mineral density (BMD) and increased risk for pathological fractures are caused by direct division of steroids at the cellular level by inhibiting the replication of osteoblasts and stimulation of its apoptosis. Also proven its effects on the inhibition of type I collagen synthesis. LRPS is one of the Wnt signaling pathway proteins coreceptors involved through the RANK-RANKL system in inhibiting the replication of osteoblasts and stimulation of its apoptosis. Also proven its effects on the inhibition of type I collagen synthesis. LRPS5 is one of the Wnt signaling pathway proteins coreceptors involved through the RANK-RANKL system in inhibiting the replication of osteoblasts and stimulation of its apoptosis. Also proven its effects on the inhibition of type I collagen synthesis. LRPS is one of the Wnt signaling pathway proteins coreceptors involved through the RANK-RANKL system in inhibiting the replication of osteoblasts and stimulation of its apoptosis. Also proven its effects on the inhibition of type I collagen synthesis. LRPS5 is one of the Wnt signaling pathway proteins coreceptors involved through the RANK-RANKL system in inhibiting the replication of osteoblasts and stimulation of its apoptosis. Also proven its effects on the inhibition of type I collagen synthesis.

Methods: The study group was composed of 38 children with idiopathic nephrotic syndrome, 21 boys and 17 girls between the age of five to twelve years old , 14 with osteoporosis and 24 with normal bone mass density. Study also included the control group consists of 102 healthy individuals at the same age not treated with glucocorticoids. The analysis was carried out with polymease chain reaction (PCR) and TaqMan molecular probes for 12 single nucleotide polymorphisms (SNPs) nearby investigated mutations in LRPS gene that can be connected with osteoporosis phenotype. Odds ratio value (OR) was based on frequencies of single nucleotide polymorphisms in LRPS gene and its haplotype analysis.

Results: The results showed significant differences in OR value among the three groups. It was also found the differences in the LRPS gene structure. Based on Gabriel algorithm single nucleotide polymorphisms pairs analysis in children with osteoporosis and nephrotic syndrome we proved the correlation between selected SNPs pairs presence and decrection of bone mineral density in studied group.

Conclusions: The selected single nucleotide polymorphisms (SNPs) of gene LRPS can be useful as the additional osteoporosis risk factors in children with idiopathic nephrotic syndrome treated with glucocorticosteroids. Its presence can be responsible for bone mineral density decrease.

MP067

ASSOCIATION BETWEEN GENE POLYMORPHISM OF MANGANESE SUPEROXIDE DISMUTASE AND ACUTE KIDNEY INJURY

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Introduction and Aims: Reactive oxygen species (ROS) are important mediators of injury in acute kidney injury (AKI). Manganese superoxide dismutase (Mn-SOD) is a mitochondrial antioxidant enzyme that is induced and regulated by ROS through a signaling cascade. Genetic polymorphisms of Mn-SOD have been associated with increased intracellular oxidative stress.

Methods: The present study was performed to assess whether there is a genetic association between a functional polymorphism (Ala–Val) in the human Mn-SOD gene in hospitalized patients with established AKI (n=61) and healthy controls (n=50) using a polymerase chain reaction restriction-fragment length polymorphism analysis method.

Results: Significant differences in the genotypic distribution between patients and controls were observed. Genotypic distribution with 5 (8.2%) Ala/Ala, 43 (70.5%) Ala/Val and 13 (21.3%) Val/Val in patients with AKI was different from those of controls with 0 (0%), 31 (62%) and 19 (38%), respectively (p=0.02). The observed and expected genotype frequencies were significantly different, thereby not fulfilling the Hardy Weinberg equilibrium. There were no differences intern of age, gender, body mass index, serum creatinine levels, the presence of oliguria, contributing cause of AKI, coexisting conditions, dialysis requirement and hospital length of stay within genotype groups.

Conclusions: The polymorphism in the gene Mn-SOD may be associated with AKI in a Turkish population. Larger studies are needed to confirm these relationships.

MP068

SYNERGY BETWEEN THE PHARMACOLOGICAL CHAPERONE 1-DEOXYGALACTONOJIRIMYCIN AND AGALSIDASE ALPHA IN CULTURED FIBROBLASTS FROM PATIENTS WITH FABRY DISEASE

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Introduction and Aims: Fabry disease (FD) is an X-linked inherited disease due to alpha-galactosidase A (alpha-Gal A) deficiency. Enzyme replacement therapy (ERT) with recombinant human alpha-galactosidase A (rh-alpha-Gal A) is now available for the treatment of FD. Two recombinant rh-alpha-Gal A preparations are approved for ERT; agalsidase alpha and agalsidase beta. ERT efficacy may vary in different tissues and its long-term effects remain to be defined. As a strategy to improve the efficacy of ERT, we tested the combination of rh-alpha-Gal A with the chaperone molecule 1-deoxynojirimycin (DGI) in cultured FD fibroblasts with negligible residual enzyme activity. In our previous study, compared to the effects of rh-alpha-Gal A alone, co-administration of DGI and agalsidase beta resulted in better correction of intracellular alpha-Gal A activity, and increased amounts of the enzyme within the lysosomal compartment. The present study aimed to evaluate if agalsidase alpha has the same synergistic effects too.

Methods: Fibroblasts from 3 male FD patients and from one control patient, derived from skin biopsies, were incubated with agalsidase alpha (5 nM/mm) for 24 h, in the absence or in the presence of 20 μM/ml DGI, after a 72 h incubation with DGI alone. Alpha-Gal A activity was assayed by using the fluorogenic substrate 4-methylumbelliferyl-alpha-D-galactopyranoside. To study alpha-Gal A immunoreactive material, fibroblast extracts were subjected to western blot analysis.

Results: When the cells where co-incubated with DGI and rh-alpha-Gal A we observed a highly improved correction of intracellular activity (an increase from 15% to 20 times); none of the cell lines showed significant increases in baseline activity when incubated with the rh-alpha-Gal A alone. A western blot analysis showed a large increase in alpha-Gal A protein in cells treated with rh-alpha-Gal A and DGI, compared to the cells treated with rh-alpha-Gal A alone.

Conclusions: In conclusion, this study provides additional evidence for a synergistic effect between ERT and DGI and supports the idea that the efficacy of combination protocols may be superior to ERT alone. Although these studies were done in vitro and require further confirmation in vivo, our results hold promise for the treatment of FD.
patients and suggest that this approach can be extended to any other lysosomal storage disease for which ERT and chaperones are available. The efficacy of combination of ERT and DGJ on renal tissue remain to be defined.

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**MP069**

**ANGIOTENSIN RECEPTOR BLOCKERS AND ANGIOTENSIN CONVERING ENZYME INHIBITORS (ARB/ACE) SLOW THE PROGRESSION OF NEPHROPATHY IN MALES WITH FABRY DISEASE**

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1 Beccole Hospital Viterbo Italy, 2 Shire HGT Eysins Switzerland, 3 Dalhousie University Halifax NS Canada, 4 Royal Melbourne Hospital & University of Melbourne Victoria Australia, 5 Medical University Vienna Austria, 6 Hospital of Bellvitge IDIBELL Barcelona Spain, 7 FGM, Center of Internal Medicine Mullheim Germany

**Introduction and Aims:** Enzyme replacement therapy (ERT) can slow or stabilize Fabry nephropathy (FN) progression. However, patients (pts) with significant proteinuria and arterial hypertension show faster renal progression. Angiotensin receptor blockers and/or angiotensin converting enzyme inhibitors (ARB/ACE) can reduce proteinuria, control blood pressure (BP) and slow nephropathy progression, but few data exist on ARB/ACE treatment in FN. We aimed to evaluate potential ARB/ACE beneficial effects on FN progression.

**Methods:** Retrospective data were collected by the Fabry Outcome Survey (FOS, Shire HGT). Male patients included had >5y of ERT, and data on annual estimated glomerular filtration rate (eGFR), CKD-EPI formula, proteinuria/24h, arterial BP and therapies aside ERT. **Results:** 164 of 725 males on ERT fit the criteria (60 hypertensive; 104 normal BP). The annual change between the 3 groups was statistically significant (eGFR p=0.08; total protein p=0.07; Table). In ARB/ACE-treated hypertensive patients, the yearly eGFR slope was less than in hypertensive pts with other anti-hypertensive drugs) and greater than in normotensive pts. Moreover, baseline (BL) eGFR was worse in ARB/ACE-treated pts than in the other 2 groups. A greater proteinuria reduction was found in ARB/ACE-treated pts versus pts without ARB/ACE. The differences between hypertensive pts with or without ARB/ACE were not statistically significant (yearly eGFR slope reduction p=0.75; proteinuria reduction p=0.86 - possibly due to wide standard deviation). In ARB/ACE-treated pts, BP values (mmHg) were systolic BP (SBP) of 139.5±17.1 (BL) and 137.8±8.5 (5y) and diastolic (DBP) of 87.3±11.5 (BL) and 76.7±11.4 (5y); in patients without ARB/ACE, SBP was 126.7±15 (BL) and 120.5±12.7 (5y) and DBP was 74.8±11.1 (BL) and 72.9±8.3 (5y).

**Conclusions:** ARB/ACE treatment in hypertensive FN pts on ERT is associated with proteinuria reduction, better BP control and, notably, an eGFR annual slope reduction approaching the value of normotensive pts.

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**MP070**

**A NOVEL GLA MUTATION IN A SARDINIAN PATIENT WITH FABRY DISEASE: LONG TERM PROGNOSIS**

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**Introduction and Aims:** Anderson Fabry Disease (AFD) is a lysosomal disease which is involved in sphingolipid catabolism. It is characterized by a lack of α-galactosidase (GLA) that results in multiorgan dysfunction including progressive kidney and heart disease and over 600 mutations have been described. We report the clinical/genetic analysis of an AFD family member who is a carrier of the renal variant of the disease.

**Methods:** A 33 year-old male with normal renal function was referred to us due to nephrotic range proteinuria (4.4 g/24h) and hypertension. At the age of 13 he had been diagnosed with mild proteinuria and hypertension. His maternal grandfather died at the age of 38 of an unspecified renal disease. His mother suffered from non nephrotic-range proteinuria (<1 g/24h). Renal biopsy was performed: light microscopy and ultrastructural analysis showed the typical pattern of AFD. Skin evaluation, blood tests, immunology, ophthalmological study, echocardiography and ECG were all normal. GLA activity was compromised (0.77 nmol/mL/hour). Genetic tests showed the substitution of a cytosine for a guanine in codon 53 of Exon 1 of the GLA, resulting in a change of the asparagine (N) aminoacid for a lysine (K) in the binding site of the enzyme. This mutation, N53K, was also detected in hemizygosis in the patient’s mother. The pedigree is shown in Figure 1. Therapy with agalsidase β was administered for 7 years then switched to agalsidase α.

**Results:** The N53K mutation has never been reported in the Fabry mutation databases (HGMD; FABRY-DATABASE.ORG), thus we assume it is a novel mutation. Moreover, the genotype did not show clinical or instrumental signs of progression in heart and renal failure, and the patient does not report any significant limitations in his daily activities. Enzyme replacement therapy with agalsidase β and α may have had a potential role in this favorable outcome. However, the recent change from agalsidase β to α resulted in a considerable increase in proteinuria levels.

**Conclusions:** In conclusion, we have contributed to the Fabry mutation databases by identifying a new mutation (p.N53K) that is correlated to the renal variant of the disease, and that seems to be related to good long-term prognosis. Moreover, we provide further evidence of the remarkable genetic and clinical variability of AFD.

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Introduction and Aims: Patients with Fabry nephropathy lose kidney function despite treatment with enzyme replacement therapy (ERT). The FACET study (NCT00448662) examined control of urine protein/creatinine ratio (UPCR) with antiproteinuric therapy in patients receiving agalsidase beta (1 mg/kg every two weeks). Ten international study sites participated. The current analysis focuses on the reasons why individual patients did not achieve the titration goal of UPCR <=0.5 g/g.

Methods: Adults with confirmed Fabry disease, treated with agalsidase beta at 1 mg/kg every two weeks were included if baseline estimated GFR (eGFR) was <60 ml/min/1.73 m² and UPCR >0.5 g/day, or baseline eGFR <125 ml/min/1.73 m² and UPCR >1 g/day. ACE inhibitor or ARB therapy was titrated during 3 monthly visits to a UPCR ≤0.5 g/g, and the patients were then followed with visit every 3 months for the next 18 months. The primary objective was reduction of first morning UPCR to <0.5 gram/day. The primary outcome measure was the regression slope of estimated GFR with time in years.

Results: Twenty four patients (9 females/15 males) completed the protocol. Average age was 44.9±9 years, with 1:1.8:1 ratio of males. Thirteen achieved target UPCR ≤0.5 g/g/day, and 11 had averaged UPCR >0.5 during the active treatment period. Those who did not maintain average UPCR ≤0.5 g/g throughout the active treatment period were more likely to be male, had higher baseline UPCR, and had not received previous RAS blockade. Obstacles to achieving targeted UPCR included dietary salt excess, hypotension, and in a lesser extent hyperkalemia. Hypotension was often associated with the use of longer acting RAS blockade agents, and other concomitant medications (e.g., diuretics, beta blockers).

Conclusions: The eGFR slope was associated with achieved UPCR in adult patients with Fabry nephropathy treated with ERT and antiproteinuric therapy. The majority of patients could be titrated to UPCR ≤0.5 g/g, and had eGFR slopes not different from zero. Effective antiproteinuric therapy is an important adjunct to ERT in treating patients with Fabry nephropathy, and those who respond to RAS blockade have stable eGFR.

### CARDIAC VARIANT OF FABRY DISEASE RESPONDING TO DOUBLE DOSE OF AGALSIDASE ALFA

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Introduction and Aims: A 41-year old male (M) was presented in the nephrological outpatient clinic with proteinuria. He underwent a renal biopsy which revealed Fabry disease and in the subsequent genetic and enzymatic investigation both he and his mother, a 70-year old female (F), were diagnosed with the cardiac variant (pN215S mutation, 10135A>G). They were referred for antiproteinuric therapy as they were still on hemodialysis.

Methods: Thus the patients initiated on enzyme replacement therapy with agalsidase alfa (Replagal®, inj 0,2 mg/kg/d every 2 weeks, iv). Monitoring of the patients, performed twice a year, included biochemical exams of renal function, proteinuria, cardiac ultrasound, pro-BNP levels, plasmatic and urinary Gb3 as well as the titer of the anti-agalsidase antibodies and MRI scan every other year.

Results: For the following 20 months both renal and cardiac indexes remained stable or slightly improved in both patients. At that point in patient M a steep increase of proteinuria (from 56 to 2536 mg/d) was noted. Moreover, in the cardiological follow-up a progressive reduction of proteinuria (from 560 to 2536 mg/d) was noted. Moreover, in the cardiological follow-up a reduced proteinuria (from 2536 to 754 mg/d) was noted. Consequently we decided to continue with the double of the conventional dose of agalsidase and today, 24 months later, the patient presents albuminuria 1053 mg/d and stable cardiac function and LV mass (414±148.5 gr, x-BNP=166±59/μl).

Conclusions: Substitution therapy in conventional dose usually controls the progression of Fabry disease. Nonetheless the administration of enzyme’s replacement in higher dose may be helpful in select cases.
**HORMONES**

**MP074 ENDOSTRENO OUAABIN AND BLOOD PRESSURE VARIABILITY EVOKED BY LOW SALT INTAKE IN ESSENTIAL HYPERTENSION**

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**Introduction and Aims:** A series of experimental and clinical data supports the notion that Endogenous Oubain (EO) may affect blood pressure (BP), plasma sodium concentration, and renal Na excretion. The plasma sodium concentration directly affects BP but the pressor mechanism for elevated BP following an increased salt intake is unclear. A direct relation between plasma EO and plasma Na has been reported. Further, the BP response to a low salt intake is heterogeneous, with BP rising in some patients.

**Methods:** Here we investigated the response of EO, plasma Na and BP to a low salt intake (<100 mEq/day, 15 days) in a cohort of 79 naive hypertensive patients (EH).

**Results:** The BP response to the low salt intake showed high systolic and diastolic BP variability (range -62.4 to +40 mmHg, respectively). The changes in mean diastolic BP were directly related to changes in plasma EO (r=0.27, p=0.02). Patients were then segregated into quartile sub-groups according to DBP changes. Those with the greatest variability (range -62.4 to +40 mmHg, respectively). The changes in mean diastolic BP were inversely related to plasma Na (r=-0.316, p=0.005, n=78). Neither plasma aldosterone nor renin were related to OSS.

**Conclusions:** Our findings show that in EH: 1) a low salt diet lowers BP in the vast majority of patients while raising plasma EO and BP primarily in RSS patients. 2) While EO upregulates renal Na-K ATPase activity, and might be a useful mechanism minimizing sodium loss, the elevation of EO in RSS patients suggests it may account for the paradox that reduced salt intake may increase the risk for cardiovascular and renal disease in some individuals.

**MP075 ADIPONECTIN IS EXPRESSED AND SECRETED BY TUBULAR EPITHELIAL REINAL CELLS**

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**Introduction and Aims:** Adiponectin (ADPN) is an adipokine with anti-atherogenic, anti-inflammatory and insulin-sensitizing properties. To-date is not reported that the adipoocyte is the predominant cell type responsible for secretion of ADPN and that the chronic inflammatory status characterizing obese patients is responsible for a reduction of ADPN circulating levels. In vivo studies demonstrated that the hypoadiponectinemia induced by direct podocytes dysfunction. However clinical studies demonstrated that patients with overt proteinuria had higher circulating ADPN levels compared to normalbuminuric controls. Unexpectedly, similar ADPN levels were observed in obese proteinuric patients. To-date, despite all these evidences, the mechanisms linking overt proteinuria and hyperadiponectinemia are not yet clarified.

The aim of our study was to investigate whether epithelial tubular renal cells express and secrete adiponectin and, principally, whether renal cells in basal conditions and upon an inflammatory stimulus secrete this adipokine contributing to ADPN circulating levels.

**Methods:** In human proximal tubular epithelial cells, HK-2, ADPN mRNA was evaluated by real time PCR assay while protein expression levels by Western blot analysis and immunofluorescence assay. Moreover, renal ADPN distribution was assessed by immunohistochemical analysis of kidney biopsies from healthy subject and from two patients affected by rapidly progressive and membranous glomerulonephritis respectively. Finally, by ELISA assay, we measured ADPN concentrations in culture media of HK-2 cells treated with lipopolysaccharide (LPS) 10 μg/ml.

**Results:** Our analyses revealed that HK-2 cells express ADPN both in terms of mRNA and protein. These results were confirmed by the observed cytoplasmatic HK-2 intense immunoreactivity for ADPN antibody and by immunohistochemical analysis showing a diffuse ADPN distribution in normal kidney tissue. We also confirmed that HK-2 cells express both pro-inflammatory cytokines and receptors for ADPN, adipon1 and adipon2, although, the results revealed that adipon1 is the predominant isoform.

Furthermore we observed that tubular cells secrete ADPN in basal condition and, more interestingly, this secretion significantly increases (p < 0.05) upon LPS treatment in a time dependent manner. Finally, immunohistochemical analysis of kidney biopsies obtained from patients affected by membranous and rapidly progressive glomerulonephritis showed a similar pattern of ADPN staining observed in healthy control.

**Conclusions:** Our study demonstrates, for the first time, that tubular renal cells express and secret ADPN, which concentration increases upon inflammatory stimulus. These results suggest that in renal inflammatory diseases, tubular cells may contribute to the increasing ADPN circulating levels, triggering a feedback response in order to self-mitigate the inflammatory process.

**MP076 ANTIDIURETIC EFFECTIVENESS OF DESMOPRESSIN ENCAPSULATED IN NEWLY DESIGNED LIPOSOMAL CARRIERS**

Olga Gawrys1, Katarzyna Gawarecka2, Ewa Swiezezwska2, Marek Masnyk3, Marek Chmielewski4 and Ewizaek Armanska-Jezierska1

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**Introduction and Aims:** Recently liposomal formulation lies within the interest of many researchers. Drug carriers based on liposomes are considered to be efficient and convenient enabling pharmacologically active substances better penetration through biological membranes. Augmenting carrier properties by using new components seems to be a very profitable strategy to improve therapy. Previous studies on amino-prezios, new derivatives of polyisoprenoid alcohols, proved their lipofecting properties and showed their lack of toxicity in rats. In this study we investigate how they affect the bioavailability of desmopressin (dDAVP). This agonist of vasopressin acts selectively on V1 receptors, responsible for the antidiuretic effect and is deprived of its vasoconstrictory action. Antiuretic effectiveness of dDAVP encapsulated in new liposomes built of diethyl phosphatidylethanolamine and amino-prezios (dDAVP + LP, 60μg/kg of dDAVP in 7.5 μg/kg of lipids) was compared to dDAVP (60μg/kg) given in classical solution (water). Two control groups received: liposomes without dDAVP (LP, 7.5μg/kg of lipids) and solvent for classical dDAVP (W).

**Methods:** In acute experiments anaesthetized and surgically prepared male Sprague-Dawley rats received intravenous infusion of 2.5% glucose solution (36 ml/kg) to induce water diuresis. After 30 minutes the corresponding solution (dDAVP+LP, LP or W) was given intravenously as a bolus (0.5 ml for 1 min). In the clearance experiment diuresis (V), plasma osmolality and solute excretion were measured.

**Results:** Different kinetics of inhibition of diuresis caused by dDAVP encapsulated in liposomes and for dDAVP given in water was observed. After administration of dDAVP in water decrease in diuresis was visible after 0.5 h, however after 1.5h diuresis slightly started to increase again. dDAVP+LP inhibited diuresis after 1h and after 2h the decrease was still observed. This was probably caused by slower release of...
Low Triiodothyronine Syndrome in Dialysis: Does the Vascular Access Plays Any Role?

Francesca Apponi1, Valentina Sinibaldi1, Anna Giuliani1, Matteo Baldinelli1, Rebeca Pizzuti4, Remo Luciani3, Franco Giordano4, Giancarlo Panzieri4, Giorgio Punzo1, Eva Malirova3, Blanka Dlabalova3, Michaela Kubisova1 and Pavel Zak2

Introduction and Aims: Low triiodothyronine (FT3) syndrome has been reported with a high prevalence in chronic kidney disease (CKD) and has been considered an independent predictor of mortality in both hemodialysis (HD) and peritoneal dialysis (PD) patients. Several factors, such as malnutrition, inflammation, acute disease, are reported to cause this syndrome in ESRD patients. Our aim was to evaluate whether the incidence of low FT3 syndrome in a dialysis patients group was influenced by the vascular access in use: autogenous arteriovenous fistula (AVF) compared to arteriovenous graft and central venous catheter (AVG-CVC).

Methods: We studied 43 stable chronic hemodialysis patients (mean age, 60 years; M 30, F 13), divided in group A (AVF, n=21) and group B (AVG-CVC, n=22). The following parameters were measured in every patient: TSH, fT4, fT3, biochemical data related to nutritional status (serum albumin) and markers of inflammation (C-reactive protein, CRP, fibrinogen). We excluded from this study any patients with intercurrent illnesses (infectious diseases, cancer, and hospitalization within the previous 60 days) and those treated with drugs known to affect the plasma concentration of thyroid hormones (beta-blockers, amiodarone, levothyroxine).

Results: Group B (AVG-CVC) showed lower mean value of fT3 than Group A (1,91 pg/ml ± 0.56) compared to Group A (2,34 pg/ml ± 0.31) (p<0.004). No significant difference was observed between AVG and CVC patients in group B. TSH did not differ between two groups (Group A: 1,19 uIU/ml ± 0,66, Group B: 1,29 uIU/ml ± 1,11), whereas Group B showed higher fT4 (0,91 ng/dl ± 0,28) compared to Group A (0,74 ng/dl ± 0,12) (p< 0.008). C-reactive protein (CRP) and fibrinogen were higher in Group B (CRP 8,45 mg/dl ± 8,6, fibrinogen 391 mg/dl ± 111) than Group A (CRP 0,70 mg/dl ± 0,53, fibrinogen 302 mg/dl ± 61,4) (p< 0.004 and p< 0.003 respectively), but no significant correlation was found with FT3 levels. Nutritional status (serum albumin) did not differ between groups, nor any correlation with FT3 levels was found.

Conclusions: Our results would suggest that type of vascular access could influence the incidence of low FT3 syndrome in stable hemodialysis patients, independently from inflammatory parameters. Autogenous accesses (AVF) seems protective, by a mechanism that need to be clarified.

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Conclusions: Our results would suggest that type of vascular access could influence the incidence of low FT3 syndrome in stable hemodialysis patients, independently from inflammatory parameters. Autogenous accesses (AVF) seems protective, by a mechanism that need to be clarified.

Hemodialysis-Induced Changes in Thyroid Hormone Concentrations

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Introduction and Aims: Thyroid function tests are often abnormal in end-stage renal disease patients on maintenance hemodialysis. However, the effect of single hemodialysis (HD) procedure on thyroid hormone serum concentrations is not known.

Methods: Hemodialysis patients (n=110, 71 M, median age 65 years) were studied during conventional low-flux HD procedure (spKt/V 1.52, 1.32-1.72). Pre- and post-HD serum concentrations of total and free thyroxine (T4 and fT4), total and free triiodothyronine (T3 and fT3), reverse triiodothyronine (rT3) and thyrotropin (TSH) levels were measured using radioisotope assays. Data are given as median; interquartile range.

Results: All thyroid hormones increased significantly during HD (P<0.001, Wilcoxon test); T4 by 18.1%, fT4 by 45.5%, T3 by 14.6%, fT3 by 8.7%, and TSH by 15.7%. The ratio free/total T3 did not change during HD. On the contrary, the ratio free/total T4 increased significantly from 1.658 ± 1.973 (P<0.0001). Conversely to peripheral thyroid hormones, TSH levels significantly decreased during HD from 1.80 to 1.60 mIU/l. Data are shown in the table.

Conclusions: HD procedure induces profound changes in serum thyroid hormones concentration. The concordant increase in all thyroid peripheral hormones (maximum in fT4) suggests an increased release of the hormones from thyroid gland into peripheral circulation and is probably responsible for observed decrease in TSH. We can only hypothesize that removal of an excess of isode from during HD might be responsible for observed changes in TSH (Wolf-Chahkoft effect). Removal of other non-specific uremic toxins may also be involved, as well as correction of metabolic acidosis. Finally, the timing of blood sampling (before vs. after HD) is important for proper interpretation of thyroid function tests in HD patients.

Prolactin Effect on Water-Solute Balance in the Rat Model of Cholestasis of Pregnancy is Renal Aquaporin Independent

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Introduction and Aims: Prolactin regulates lactation in mammals, but in fishes and lower vertebrates it controls water-solute balance. Level of this hormone elevates during pregnancy and additionally elevates under condition of cholestasis of pregnancy. Our goal was to determine whether prolactin has any effect on water-solute homeostasis in female rats in the model of cholestasis of pregnancy.

Methods: For the modeling of pregnancy’s prolactin level hyperprolactinemia was induced by donor pituitary transplantation under renal capsule of female rat recipient, for the modeling of cholestasis of pregnancy the combination of induced hyperprolactinemia and bile duct ligation was used. Hyperprolactinemia was confirmed by measure of rat serum prolactin concentration. Surgical procedures were conducted under diethyl ether anesthesia. In these models diurnal diuresis, glomerular filtration rate (GFR) and diurnal sodium excretion were estimated. Aquaaporin 1-4 mRNA expression in the renal inner medulla was tested by real-time PCR using 3 housekeeping genes and normalized on GAPDH expression.

Results: Persistent hyperprolactinemia combined with obstructive cholestasis led to sharp 2-fold elevation of diurnal diuresis and compensatory water consumption as compared with the control. In spite of this aquaporin 1-4 mRNA expression in the renal inner medulla and glomerular filtration rate were not changed in this model of cholestasis of pregnancy. In this model sufficient elevation of diurnal sodium excretion as compared with control groups was revealed. Alone bile duct obstruction or hyperprolactinemia had no marked influence on these parameters.

Conclusions: The data on diuretic and natriuretic effects of prolactin in the model of cholestasis of pregnancy together with the lack of prolactin influence on GFR and aquaporin 1-4 mRNA expression in renal medulla let us to suggest primary prolactin influence on the sodium transporters in the kidney without substantial modulation of aquaporin expression and vasopressin action. Supported by RFBR (grant 11-04-00009-a).

Effects of a Resistance Exercise Training Program on Acyl- Ghrelin and Obestatin Levels in Hemodialysis Patients

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Introduction and Aims: Appetite hormones peptides are altered by exercises in general population; however, no study has evaluated the effects of exercise on these hormones in chronic kidney disease (CKD) patients. The purpose of this study was to assess the effects of an intradialytic resistance exercise training program (RETP) on plasma levels of gut peptides (acyl-ghrelin and obestatin) in hemodialysis (HD) patients.
Methods: The study enrolled 37 hemodialysis (HD) patients (61.5% men, 45.9±14.1 yrs, 23.5±3.9 kg/m²). Acyl-ghrelin and obestatin plasma levels (measured using the enzyme immunoassay) were performed in the fasted state at baseline and after 6 months of RETP (supervised, 3 days/week, total 72 sessions). Anthropometric measurement and food intake were assessed. Statistical analyses were performed using SPSS 17.0.

Results: After 6 months RETP, there was increase in men fat free mass (from 51.3±10 to 53.2±10 kg, p<0.05) and arm muscle area in all patients. The energy and protein intakes were similar before and after exercises; however, there were significant reduction in the anorexigenic hormone levels (obestatin) from 3.0 (2.3–3.4) ng/mL to 1.9 (0.6–3.4 ng/mL) and increase in the orexigenic (acyl-ghrelin) from 21.5 (1.3–77.7) ng/mL to 37.2 (16.7–94.1) ng/mL.

Conclusions: In conclusion, the resistance exercise during 6 months in HD patients led to significant changes in appetite hormones and it seems a good intervention to modulate appetite in HD patients.

**MP081**

**SEVERM DEHYDROEPIANDROSTERONE SULFATE IS ASSOCIATED WITH SKELETAL MUSCLE MASS, ARTERIAL STIFFNESS, AND DEPRESSIVE MOOD IN JAPANESE MALE HEMODIALYSIS PATIENTS**

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Introduction and Aims: The dialysis population is aging. There is a clear age-related decline in dehydroepiandrosterone sulfate (DHEAs) and this has suggested that a relative deficiency in this steroid may be causally related to the development of a series of diseases associated with aging including cardiovascular diseases, osteoporosis, and depressive mood. The aim of this study was to examine the effect of serum DHEAs on body composition and aging-associated diseases in hemodialysis patients.

Methods: Cross sectional observational study comprising 61 hemodialysis patients (39 men, mean age 65.2±1.2 years). Serum DHEAs levels were measured by radioimmunoassay. The Inbody 500 Body Composition Analyzer was used for bioelectrical impedance analysis. Brachial-ankle pulse wave velocity (baPWV) and quantitative ultrasound of the calcaneus were measured. Depressive symptoms were ascertained with the Patient Health Questionnaire (PHQ-9).

Results: The mean DHEAs levels of the male versus the female were 1059 versus 739 ng/mL. DHEAs correlated negatively with age (p<0.001) and baPWV (p<0.005), and positively with skeletal muscle mass (p<0.01) in men, but not in women. In patients with higher scores on the PHQ-9, the levels of DHEAs were significantly lower (640 ng/mL) than the levels in other patients (1197 ng/mL). There were no significant associations between DHEAs and the values of calcaneal speed of sound, which is an index of bone density.

Conclusions: In male dialysis patients, the lower levels of DHEAs were associated with aging process, such as decreased skeletal muscle mass, increased arterial stiffness, and depressive mood. Large prospective trials and intervention studies are needed to better assess these benefits of DHEAs in male dialysis patients.

**MP082**

**EXERCISE TRAINING DOES NOT AFFECT THE PLASMA IRISIN CONCENTRATION IN HEMODIALYSIS PATIENTS**

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Introduction and Aims: Irisin, a recently discovered hormone secreted by myocytes induced in exercise, acts as a muscle-derived energy-expenditure signal that binds to undetermined receptors on the white adipose tissue surface, stimulating its browning and uncoupling protein 1 (UCP1) expression. The purposes of this study were to assess the effect of an intradialytic resistance exercise training program (ETP) on circulating concentrations of irisin in hemodialysis (HD) patients and compare irisin plasma levels in these patients and healthy individuals.

Methods: This longitudinal study enrolled 26 chronic kidney disease patients (CKD) (50% men, 44.7±14.1 yrs, 23.5±3.3 kg/m²). The healthy individuals group consisted of 11 women and 7 men with mean age of 50.9 ± 6.1 yrs and BMI, 24.2 ± 2.7 kg/m². Anthropometric and biochemistry parameters (irisin by Enzyme-Linked Immunosorbent Assay) were measured at the baseline and after 6 months of strength ETP (in both lower limbs) that was performed during the first 3 hours of hemodialysis, three times a week for 72 sessions.

Results: There was no difference regarding gender, age and body mass index (BMI) between HD patients and healthy individuals. Baseline plasma levels of irisin in HD patients were significantly lower than in healthy individuals (71.0±41.6 vs 101.3 ± 12.5 ng/mL, p<0.05). There was no significant difference in irisin plasma levels between women and men (77.5 ± 44.6 vs 64.6 ± 39.4 ng/mL). Although the muscle mass has increased in consequence of exercise (27.9 cm²), irisin plasma levels did not differ significantly before and after ETP (71.0 ± 41.6 vs 73.3 ± 36.0 ng/mL).

Conclusions: HD patients seem to have lower irisin levels when compared to healthy individuals. Moreover, a resistance exercise training program was unable to augment irisin levels despite increasing muscle mass.

**MP083**

**ENDOGENOUS ANABOLIC HORMONES AND HIGH LOAD STRENGTH TRAINING IN MALE PATIENTS UNDERGOING DIALYSIS**

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Introduction and Aims: Sufficient anabolic hormone levels and functions are important to avoid muscle atrophy and to induce muscle hypertrophy in relation with resistance training. In male patients undergoing dialysis testosterone levels are in general lower than in healthy persons. IGF-1 expressions may also be impaired. The aim of this study was to investigate circulating testosterone and IGF-1 in a controlled design before and after 16 weeks of high load strength training in male patients undergoing dialysis and to investigate if hormone plasma levels were associated with muscle morphology.

Methods: Thirty-three male patients aged 56 ± 4 (mean ± SEM) years were tested before and after a 16 weeks control period and before and after 16 weeks of high load resistance training three times a week. The training comprised leg press, knee extension, and knee flexion. Samples of plasma were obtained after an overnight fast to analyse testosterone, IGF-1, and LH. Hormone values from the male general population was delivered by the University Department of Growth and Reproduction, Rigshospitalet, Copenhagen University Hospital, Denmark. Muscle fibre size and percentage number were analysed in muscle biopsies from the vastus lateralis muscle.

Results: Total testosterone (24.6 ± 3.4 nmol/l), free testosterone (520 ± 73 pmol/l), IGF-1 (262.8 ± 38.5 ng/ml), and IGF-BP3 (5452 ± 485 ng/ml) remained stable during the control and training period and was within normal ranges. All participants (34.1 ± 13.9 cm²), irisin plasma levels did not differ significantly before and after ETP (71.0 ± 41.6 vs 73.3 ± 36.0 ng/mL).

Conclusions: HD patients seem to have lower irisin levels when compared to healthy individuals. Moreover, a resistance exercise training program was unable to augment irisin levels despite increasing muscle mass.
HYPERTENSION - EXPERIMENTAL MODELS

**MP084 GONADECTOMY PREVENTS THE INCREASE IN BLOOD PRESSURE AND SERUM ACE ACTIVITY IN ACE2 KNOCKOUT DIABETIC MALE MICE**

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Introduction and Aims: Whereas ACE2 deletion worsens kidney injury; its amplification ameliorates diabetic nephropathy. We previously showed that circulating ACE2 activity is increased in male diabetic NOD mice. The effect of gonadectomy in diabetic ACE2 knockout (ACE2KO) male mice has not been previously studied.

Methods: We study the effect of ACE2 deletion on systolic blood pressure (SBP), urinary albumin excretion (UAE), kidney to body weight ratio (KW/BW) and serum (s) and kidney (k) ACE enzymatic activity in C57BL/6 streptozotocin (STZ)-induced male mice and their respective controls. We also evaluated the effect of gonadectomy in diabetic ACE2KO mice. Mice were followed-up for 19 weeks after induction of diabetes with STZ injection. Citrate was administered as a vehicle (cont). Study groups: ACE2KO-cont, ACE2KO-STZ, gonadectomy before diabetes induction GDX-ACE2KO-STZ.

Results: Hyperglycemia was observed in all groups given STZ. KW/BW and UAE were increased in both diabetic wildtype (WT) (UAE 12-fold) and ACE2KO mice (UAE 27-fold). ACE2KO diabetic mice had increased SBP compared to diabetic WT. In addition, gonadotomized diabetic ACE2KO showed significantly lower values of blood glucose, SBP, UAE, KW/BW compared to non-gonadotomized diabetic ACE2KO.

Circulating ACE activity positively correlated with SBP (r=0.28; p=0.04) and was significantly increased in WT diabetic mice compared with WT-cont. Circulating ACE activity was increased in ACE2KO control mice as compared to WT control mice. Gonadectomy significantly decreased circulating ACE activity in diabetic ACE2KO mice. In contrast, renal ACE activity was significantly reduced in diabetic ACE2KO and WT animals.

Conclusions: In ACE2KO mice circulating ACE activity was increased as compared to WT mice. In addition, diabetic ACE2KO mice SBP was increased compared to diabetic WT mice. Gonadectomy reduced blood glucose, UAE, renal hypertrophy, blood pressure and circulating ACE activity.

**MP085 MYOCARDIAL AND RENAL REMODELING IN MALE WISTAR RATS RECEIVING HIGH SALT DIET**

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Introduction and Aims: Myocardium, kidney and vasculature, in particular, reacts to changes in dietary NaCl intake through a complex series of events that are independent of blood pressure. The aim of this study was to compare the effect of normal and high NaCl content in the diet on the remodeling of the heart and kidney, and the NFκB expression in the myocardium in rats.

Methods: The study was performed in male Wistar rats. Control group (C) of animals (n=8) received normal NaCl intake (0.34%), experimental (E; n=8) – high (8%). Experimental period was 8 weeks. Mean BP was measured in awake rats by tail cuff method. Serum urea (Ur), creatinine (Cr), total calcium and sodium levels were determined. Daily volume of urine and concentration of sodium in the urine was also determined. The degree of left ventricular hypertrophy was estimated as a ratio of left ventricular mass/body mass (LVH; mg/g). The degree of left (LKH) and right (RKH) kidneys hypertrophy was estimated as a ratio: kidney mass/body mass, mg/g).

Determination of NFκB expression relative level in myocardium was performed with the semi-quantitative protocol. The obtained results were normalized by the expression level of reference gene GAPDH and compared between control and experimental myocardium with the use of 2-ΔΔCt method.

Results: High salt intake does not lead significant rise (mean±SE) of BP (135±5 mmHg) compared with C (130±5 mmHg). There are no difference in concentrations of Ur (6.2±0.5 mmol/l in C vs. 5±1±0.8 mmol/l in E), Cr (0.044±0.01 mmol/l in C vs 0.038±0.02 mmol/l in E), calcium and sodium in the blood serum between groups. High intake of NaCl produced a significant increase in urinary excretion of sodium (434±167.4 mmol/l in C vs 89±14.3±0.3 mmol/l – in C, p<0.001) in the absence of significant distinction of daily volume of urine between groups. Consumption of a diet with the high intake of NaCl was accompanied by increase of weight of left and right kidneys: the LKH was 3.5±1.07 mg/g (vs 2.7±0.88 mg/g – in C, p<0.01), the RKH – 3.65±0.05 mg/g (vs 3.05±0.07 mg/g – in C, p<0.01). No significant differences in LVH could be detected among the groups (3.1±0.12 mg/g in C vs 3.0±0.10 mg/g in E). On the other hand high NaCl diet was accompanied by increase activity of the NFκB. Relative level of NFκB gene expression in E was in 3.4 times higher than in C.

Conclusions: Consumption during the 2 months of a diet high in NaCl, without causing a rise in BP in Wistar rats leads to an increase in mass of the kidneys and the activation of NFκB in the myocardium, which may be one of the ways of myocardial remodeling and fibrosis.

**MP086 EFFECTS OF CHYMOSTATIN, A CHYMASE INHIBITOR, ON BLOOD PRESSURE AND KIDNEY HAEMODYNAMICS IN DIFFERENT MODELS OF HYPERTENSION IN THE RAT**

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Introduction and Aims: Chymase is known to form angiotensin II in cardiovascular and renal tissues independent ofangiotensin-converting enzyme (ACE), and its expression is increased in pathological conditions. It was proposed that chymase inhibitors could be applied to inhibit the local renin-angiotensin systems (RAS) and possibly prevent the development of cardiovascular diseases. In this study we examined how blockade of chymase activity would affect blood pressure and renal haemodynamic parameters in different models of experimental hypertension.

Methods: Male spontaneously hypertensive rats (SHR) in the development (age:7 weeks) and established stage of hypertension (16 weeks), male Sprague-Dawley rats with hypertension induced by stenosis of the renal artery performed 28 days before acute experiments (LKH), and Sprague-Dawley rats with hypertension induced by unilateral nephrectomy followed by exposure to high sodium diet (4% Na w/w) for two weeks, were used. In acute experiments rats of all groups were anaesthetised with sodium thiopental, 100 mg/kg i.p. Mean arterial pressure (MAP) was recorded throughout experiments. Effects of chymostatin on haemodynamic parameters (laser-Doppler fluxes) of the left kidney were measured, including cortical blood flow (CBF) as well as outer- and inner medullary blood flow (OMBF, IMBF). Perfusion of the whole kidney and of the hind limb was measured using non-cannulating probes (Transonic system) placed on the left renal and the right iliac artery, respectively. Chymostatin (dissolved in 0.05% DMSO in a saline and PBS) or its solvent was infused intravenously during one hour at a rate of 2 mg/kg.

Results: After chymostatin infusion there was a slight decrease in MAP in each model of experimental hypertension. However, only the 16-week SHR rats responded to chymase blockade with a significant decrease in blood pressure (145±7 vs154±7 mmHg

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in control period) and in RBF (4.8±0.9 vs 6.5±1.0 μl/min in control period). Chymase inhibition caused a significant decrease in OMBF in all groups with one exception. In unilaterally nephrectomised rats on high sodium diet OMBF remained unchanged but there was a significant decrease in IMBF (139±3 vs 97±3 μl/min in control period). Effects of chymostatin infusion persisted or were even enhanced after discontinuation of the infusion.

Conclusions: The degree of MAP reduction after chymostatin was found to depend on the model of hypertension. The greatest decrease was observed in SHR rats aged 16 weeks, which suggests an important functional role of the alternative, ACE-independent pathway of the tissue renin-angiotensin system is distinctly active only in the stage of established hypertension. Probably, the ACE-independent pathway of angiotensin II synthesis is known to be active in pathological conditions, chymase inhibitors could be useful in prevention of cardiovascular diseases. To explore this possibility, we examined effects of chymostatin, a commercially available chymase blocker, in different forms of experimental hypertension: dependent on renal artery stenosis, genetically determined and sodium-dependent.

Methods: Male spontaneously hypertensive rats (SHR)in the early (age: 7-weeks) and established stage of hypertension (16 weeks), male Sprague-Dawley rats with hypertension induced by renal artery stenosis (two- kidney, one-clip model, 2K,1C), and Sprague-Dawley rats with hypertension induced by unilateral nephrectomy followed by two-weeks high sodium diet (4% Na w/w) were used. In acute experiments all rats were anaesthetised with sodium thiopental, 100 mg/kg i.p. Chymostatin (dissolved in 0.05% DMSO) or its solvent were infused intravenously at 2 mg/kg/h, for one hour. Timed urine collections were made and blood was sampled to determine renal excretion, glomerular filtration rate (GFR, inulin clearance), and plasma osmolality (Posm), plasma sodium (P Na) and potassium (P K) concentration. Urine volume was determined gravimetrically. To correct for major inter-group differences in kidney size, the values of diuresis and sodium excretion were expressed per g kidney weight (V/g, UNaV/g).

Results: After administration of chymostatin, the diuresis and sodium excretion slightly decreased in all groups. Only in 16-week SHR there was a significant (17%) decrease in V/g (1.82±0.3 vs 0.42±0.04 μl/min/g in control period; p<0.05) and a 76% drop in UNaV/g (0.21±0.03 vs 0.02±0.04 μmol/min/g in control period; p<0.05). In 16-week-old SHR there was also significant decrease in GFR (0.41±0.06 vs 1.60±0.9 μl/min in control period; p<0.05). In the other groups chymostatin caused only a slight decrease in GFR. Chymostatin significantly increased P Na in 7-week-old SHR (144±3 vs 139±2 mmHg in control period; p<0.05).

Conclusions: Remarkably, chymase blocking effects were increasing progressively over the one-hour infusion time and remained elevated for 0.5-1 h after discontinuation of drug administration. The most pronounced chymase impact on renal excretoriness was observed in the 16-week SHR group. Probably, the ACE-independent pathway of the tissue renin-angiotensin system is distinctly active only in the stage of established hypertension in SHR group. In the early stage of hypertension development a 7-week-old SHR chymase blockade did not affect renal excretion but resulted in an elevation of P Na. Considering the relatively slow onset of chymostatin action, experimental protocols involving chronic administration of the drug are recommended.

Effects of Adenosine Diphosphate, a Purinoreceptor Agonist, on Blood Pressure and Renal Function in the Rat

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Introduction and Aims: P2 purinergic receptors (P2R) are expressed in kidney vessels and tubules, however, the functional role of P2R-Y, one of two P2R families, in physiological and pathological states, remains unclear. The available information on the impact of P2R-Y on renal functions based mainly on studies of isolated preparations. The present whole-kidney study explored renal haemodynamics and excretion as affected by adenosine diphosphate (ADP), a non-selective agonist of P2R-Y.

Methods: In adult male Sprague-Dawley rats anaesthetized with sodium thiopental, 100 mg/kg i.p. Effects of ADP or its solvent on mean arterial pressure (MAP), heart rate (HR), renal haemodynamics and excretion were measured simultaneously. After control period (CP), three subsequent doses of ADP (2, 4, 8 mg/kg) were infused iv., followed by recovery period. The whole-kidney blood flow (BBF) was determined using laser Doppler perfusion imaging. Intrarenal blood flow was determined using laser-Doppler probes placed on the kidney surface (superficial cortex, CBF) or inserted into the outer-(OMBF) and inner-medulla (IMBF). Urine flow (V), sodium and potassium excretion (U NaV, UKV), and total solute excretion (U Na+K V) were measured and expressed per g kidney.

Results: In time control group no significant changes were shown. ADP induced a dose-dependent decrease of MAP, to 95±3 with the 3rd dose vs 111±1 mmHg in CP (p<0.001) and a concurrent increase of HR (394±8 vs 345±9 beats/min in CP; p<0.05). BBF increased with the lowest dose and remained elevated throughout ADP infusion (9.3±0.8 with the 3rd dose vs 8.3±0.6 ml/min in CP; p<0.02). After cessation of drug infusion MAP and BBF returned rapidly to the control value. CBF increased 10% with the lowest dose of ADP (p<0.04) and declined slightly after the second dose, down to the value not different from control. OMBF was not affected by ADP but in recovery period it decreased 10% (p<0.01), whereas IMBF remained stable throughout the experiment, similarly as in the control group. A small but persistent drop in V was induced by the highest dose of ADP (5.4±0.6 vs 7.6±1.7 μl/min in CP; p<0.02). This was followed by a return to control values after ADP administration.

Conclusions: In conclusion, P2R-Y play an important role in modulation of blood pressure of the deep cortex (measured as BBF). Within the medulla, their activity could help stabilize blood perfusion of the outer-zone despite changes in arterial blood pressure. In the tubules they might stimulate water and solute transport independent of renal haemodynamics.
DELETION OF HYPERTENSION CANDIDATE GENE ATP2B1 IN VASCULAR SMOOTH MUSCLE CELLS PRODUCES INCREASED VASCULAR CONTRACTILE RESPONSE AND BLOOD PRESSURE ELEVATION WITH SALT SENSITIVITY IN MICE

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Introduction and Aims: We previously reported that ATP2B1 was one of the genes for hypertension receptivity in a large-scale Japanese population, which has been confirmed recently in Europeans, Koreans and Japanese. ATP2B1 encodes the plasma membrane calcium ATPase isoform 1, which plays a critical role in intracellular calcium homeostasis. In addition, it is suggested that ATP2B1 plays a major role in vascular smooth muscle contraction. Furthermore, it is suggested that ATP2B1 is associated with salt sensitivity. Since the ATP2B1 knockout mouse is embryo-lethal, we generated mice with vascular smooth muscle cell specific knockout of ATP2B1 using the Cre-loxP system, in order to identify the relationship among ATP2B1 and hypertension and salt sensitivity.

Methods: To generate conditional ATP2B1 knockout mice, we utilized the Cre-loxP and FLIP: FRT recombination system. Blood pressure of ATP2B1 knockout mice were measured by tail-cuff method and radiometriometry system under normal salt diet and high salt diet. Vascular smooth muscle cells of ATP2B1 knockout mice were isolated from aorta and cultured for calcium imaging assay and real-time quantitative RT-PCR. We measured isometric tension of femoral artery vascular rings from each mice.

Results: The knockout mice expressed significantly lower levels of ATP2B1 mRNA and protein in the aorta compared to control mice. Knockout mice showed significantly higher systolic blood pressure as measured by tail method and radiometriometry methods measuring for 24 hours. Moreover, femoral artery isolated from knockout mice showed significant elevated contractile response to phenylephrine. Similarly, primary cultured vascular smooth muscle cells isolated from the aorta of knockout mice showed significant higher phenotype mediated increase in intracellular calcium concentration. This finding was associated with the decreased expressions of Na+/Ca2+ exchanger isoform 1 in the cultured cell. On the other hand, the knockout cells showed up-regulation of ATP2B4, while neuronal nitric oxide synthase showed down-regulation. Moreover, knockout mice showed significant blood pressure elevation with hypercalcemia while high salt loading.

Conclusions: These results suggest that ATP2B1 plays important roles in the regulation of blood pressure through alteration of vasoconstriction and calcium handling in vascular smooth muscle cells. Moreover, salt sensitivity and hypercalcemia seen in knockout mice while high salt loading may suggest that there are important relationship among calcium metabolism and salt sensitivity.

MESENCHYMAL STEM CELLS ATTENUATE RENAL INFLAMMATION, MICROVASCULAR RAREFACTION AND FIBROSIS IN A MODEL OF RENOVASCULAR HYPERTENSION

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Introduction and Aims: Renovascular hypertension induced by 2 Kidney-1 clip (2K-1C) results in chronic hypoxia in the clipped kidney with significant renal functional deterioration in consequence of inflammation, microvascular rarefaction and fibrosis. It was investigated the beneficial effects of mesenchymal stem cells (MSC) in 2K-1C rats.

Methods: MSCs obtained from the tibias and femurs of male Wistar rats were expanded during 7–15 days under appropriated conditions and characterized by differentiation into osteocytes/osteocytes and immunopositive CD90, CD105, CD73 and negative for CD34 and CD45. Three weeks after renal artery occlusion, fluorescently tagged MSC (2x10⁶ cells/animal) were weekly injected into the tail vein. Rats were divided in groups control (n=5), control treated with MSC (n=2), 2K-1C (n=8) and 2K-1C treated with MSC (n=7).

Results: Tracking assay by flow cytometry showed that labeled MSC were present in the cortex and medulla of the clipped kidney. MSC prevented further increase in the arterial pressure in 2K-1C rats, improved the morphology and decreased fibrosis in the clipped kidney. Renal inflammatory cytokines IL-1β, IL-6 and TNF-α mRNA expression levels were significantly decreased after MSC treatment, while the anti-inflammatory IL-10 expression was increased. MSC improved the renal microvascular architecture in the clipped kidney and reduced the proteinuria.

Conclusions: The present study showed that MSC improved the morphology and attenuated inflammation, microvascular rarefaction, fibrosis and proteinuria in the clipped kidney, suggesting a therapeutic potential of MSC in kidney exposed to chronic hypoxia induced by renal artery stenosis.

PARICALCITOL IMPROVES RENAL INFLAMMATION AND HYPERTENSION RESULTING FROM A HIGH SALT DIET ADMINISTERED FOLLOWING INHIBITION OF NITRIC OXIDE SYNTHASE

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Introduction and Aims: Renal inflammation and its constant companions, oxidative stress and angiotsenin system are associated with salt sensitive hypertension (SHTN). Since paricalcitol (vitamin D analog) suppresses the activation of the renin-angiotensin system by attenuating inflammation and reduces the progression of chronic renal disease (Kidney Int. 2007; 75:1394-1402) we studied its effects in the SHTN induced by transient inhibition of nitric oxide synthase.

Methods: Male SD rats (280-340g) pre-conditioned to tail plethysmography were randomly assigned to 4 groups: L) NAME (n=10) given LNAME in the drinking water (70 mg/ml/100mL) for 3 weeks followed by 8 weeks of a high salt (4% NaCl) diet. 2) L-NAME/PAR group (n=10) that received in addition paricalcitol by intraperitoneal injection (0.1 mg / kg) three times a week during the 6 weeks of a high salt diet. 3) C-PAR group (n=10) received only paricalcitol and 4) Control (C) group (n=10) untreated.

Systolic blood pressure (SBP), plasma creatinine and proteinuria were evaluated weekly and kidneys were obtained at the end of the experiment to study infiltration of macrophages(CD68+cells) and lymphocytes (CD5+ cells), apoptosis (TUNEL), nuclear factor NFκB p65 (IκBαB) and nitrotyrosine (positive area by image analysis).

Results: Table. 1. Results (mean ± SD)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control (C)</th>
<th>3) C-PAR</th>
<th>L-NAME/PAR</th>
<th>L) NAME</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mmHg)</td>
<td>130 ± 10</td>
<td>125 ± 10</td>
<td>115 ± 10</td>
<td>110 ± 10</td>
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<tr>
<td>Creatinine (mg/dL)</td>
<td>2.0 ± 0.5</td>
<td>2.5 ± 0.5</td>
<td>3.0 ± 0.5</td>
<td>2.5 ± 0.5</td>
</tr>
<tr>
<td>Proteinuria (mg/mg)</td>
<td>30 ± 10</td>
<td>20 ± 10</td>
<td>15 ± 10</td>
<td>10 ± 5</td>
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</tbody>
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Nitrotyrosine positive extension evaluated by computerized image analysis. Statistical differences among groups were evaluated by multigroup analysis of variance (ANOVA) and post hoc analysis.
and Tukey post test. **P<0.001.

Conclusions: paricalcitol lowers blood pressure increase driven by a high salt diet in this experimental model in association with reduced inflammation and oxidative stress.

**MP094**

ALTERATIONS OF RENAL SODIUM TRANSPORTERS IN THE ERYTHROPOIETIN-TREATED CHRONIC RENAL FAILURE RAT

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Introduction and Aims: Erythropoietin (EPO) administration in uremic rats leads to an increase in blood pressure. The present study was designed to investigate the change of sodium balance and alteration of major renal sodium transporters in EPO-treated chronic renal failure rats. 

Methods: Renal failure was induced by a two-stage 5/6 nephrectomy in 30 Sprague-Dawley rats. Uremic rats were divided into two groups and received vehicle or EPO (150 U/kg, intraperitoneal injection, x2/week) for 4 weeks. Half of the rats were sacrificed after 1 week of treatment, and the rest after 4 weeks.

Results: Serum creatinine and sodium level, hematocrit, body weight, and systolic blood pressure were similar in both groups before treatment. After 1 week of treatment, hematocrit increased in the EPO group (48.9 ± 0.8 vs. 38.4 ± 1.0%, P = 0.001). Systolic blood pressure (SBP) was 153.5 ± 6.8 mmHg in the EPO group and 147.3 ± 4.7 mmHg in control group (P = 0.793) after 1 week. After 4 weeks treatment, SBP increased significantly (159.5 ± 3.3 vs. 146.4 ± 2.3 mmHg, P = 0.007). Urinary sodium excretion and daily sodium balance did not show significant difference between groups throughout the experiment period. Expression of ENaC α decreased significantly (58.6 ± 5.1% of the control, P = 0.001) after 1 week of EPO treatment on immunoblot analysis. After 4 weeks of treatment, the renal abundances of ENaC α, γ, and NHE3 significantly decreased (56.1 ± 6.1%, 49.4 ± 9.7%, and 38.6 ± 9.4% of the control, P = 0.011, 0.026, and 0.007, respectively) in the EPO group. Renal medullary endothelin levels of EPO-treated group increased significantly (10.2 ± 2.9 pg/mg vs. 5.2 ± 0.8 pg/mg, P = 0.028, at the 1st week; 3.6 ± 0.8 pg/mg vs. 1.5 ± 0.4 pg/mg, P = 0.035, at the 4th week) than that of control group. Plasma renin and serum aldosterone levels were not different between groups.

Conclusions: EPO increases renal medullary endothelin-1, and inhibits renal ENaC α and NHE3 expression. Increased production of renal medullary endothelin-1 and decreased expression of renal sodium transporters might work as compensatory mechanisms in EPO-treated hypertensive chronic renal failure model.

**MP095**

EFFECT OF LISINOPRIL AND A COMBINATION OF LISINOPRIL WITH THE DIURETIC HYDROCHLOROTHIAZIDE ON KIDNEY FUNCTION AFTER UNILATERAL NEPHRECTOMY IN DAHL SALT RATS WITH ESTABLISHED HYPERTENSION

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Introduction and Aims: Dahl Salt Sensitive Rats develop hypertension and renal injury under high salt diet. Aim of the present study was to investigate the effect of unilateral nephrectomy (UNx) in Dahl SS rats pre-fed for 2 weeks with 8% NaCl diet on the progression of kidney disease with established hypertension and the effect of Lisinopril and the combination with hydrochlorothiazide (HCTZ).

Methods: Kidney function was assessed by GFR, creatinine (CREA) clearance and plasma Cystatin C. GFR was measured using plasma clearance kinetics of fluorescein isothiocyanate insulin following a single bolus iv injection. Cystatin C was analyzed by Luminex Millipore assay. Albumin was measured by ELISA and CRE was quantified by COBAS System. Blood pressure measurement was done by tail cuff method (Kent CODA System). Kidney morphology was evaluated from Hematoxylin and Eosin and Periodic Acid Schiff stained formalin-fixed and paraffin-embedded tissue sections.

Results: UNx rats had increased albuminuria compared to sham rats (148±35 to 375±53 mg/day). CREA clearance and GFR worsened in the UNx rats (1.35±0.24 to 0.66±0.05 ml/min/g kidney to 0.72±0.05 and 0.44±0.03 ml/min/g kidney). In parallel Cystatin C rose after UNx. There was no change in mean arterial blood pressure after UNx (143±9 and 148±11 mm Hg, respectively). Both glomerular (mesangial expansion and glomerulosclerosis) and tubulo-interstitial (tubular degeneration/ regeneration, tubular dilation, arterial thickening/necrosis, inflammatory infiltrates and interstitial fibrosis) histopathologic lesions were significantly increased in UNx rats compared to sham rats. 4 week treatment of UNx rats with Lisinopril 100µg/kg/d as oral gavage did not lower albuminuria. Lisinopril 100 µg/kg/d + HCTZ 15µg/kg/d as oral gavage significantly reduced renal histological lesions compared to UNx controls (P = 0.038).

Conclusions: Lisinopril alone did not improve Crea clearance nor GFR, whereas the Lisinopril/HCTZ combination significantly preserved both (1.22±0.09 and 0.56±0.04 ml/min/g kidney). Only Lisinopril/HCTZ treatment decreased Cystatin C significantly compared to UNx controls. Lisinopril had no effect on mean blood pressure (150.5±7 to 171±4 mm Hg), whereas Lisinopril/HCTZ significantly reduced blood pressure (117±4 mm Hg). Lisinopril alone was not able to decrease kidney tissue damage. The combination of Lisinopril/HCTZ was able to prevent both glomerular and tubule-interstitial histopathological lesions significantly.

**MP096**

THE DISTURBED CIRCADIAN RHYTHM AND SALT SENSITIVITY OF BLOOD PRESSURE IN ADRIAMYCIN NEPHROPATHY RATS

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Introduction and Aims: The prevalence of the disturbed BP circadian rhythm is striking in CKD patients. The circadian rhythm is a key peripheral oscillator involved in the regulation of renal and cardiovascular rhythmic functions. Disturbed BP circadian rhythm is an independent prognostic factor for cardiovascular morbidity and relatives with the accelerated progression of kidney injury. Resetting the abnormal BP rhythm would be helpful. The solution of the problem required for getting a suitable animal model for CKD patients with disturbed BP rhythm. Adriamycin Nephropathy Rats (ADRs) represent a useful mouse model to study nephritic syndrome. In this present study we found ADRs lost the normal BP circadian rhythm and showed sodium sensitivity.

Methods: In the present study the circadian characteristics of MAP, SBP, DBP, heart rate (HR), pulse pressure (PP) and locomotor activity were measured in conscious and unrestrained 12-week old ADRs and age-matched SD control rats by the radiotransmission system. After baseline studies were obtained, the rats were were provided a high salt diet (8.0%) for a 1 wk period prior to the 7 day telemetry study.

Results: 1. Adriamycin Nephropathy rats presented with the reversed circadian rhythms of the MAP, SBP, DBP, and PP compared with SD control rats respectively. However, there was no significant difference in 24-h mean value of BP. 2. In the ADRs the circadian rhythm of the urine sodium excretion was disturbed, the RUNa in Dark period was significantly lower than that in the Light period of the same group([14.69±3.65]μmol/h vs [27.66±5.84]μmol/h, P=0.001) and also significantly lower than that in the Dark period of the control group([14.49±3.65]μmol/h vs [39.49±22.44]μmol/h, P=0.023). 3. In the ADRs, the FENA in Dark period was significantly lower than that in the Light period of the same group(0.15±0.06 vs 0.29±0.06, P=0.008) and also significantly lower than that in Dark period of the control group(0.15±0.06 vs 0.31±0.19, P=0.050). 4. Under high salt diet, SBP and MAP in Dark period increased significantly by 19.8mmHg and 18.5mmHg respectively than those before high salt diet (P=0.001) in ADRs. In the control group, the SBP and MAP in Dark period increased significantly by 8.4mmHg and 6.2mmHg respectively than those before high salt diet (P=0.01). In the ADRs, the SBP and MAP in Light period increased significantly by 20.1mmHg and 17.7mmHg respectively than those before high salt diet (P=0.001). In the control group, the SBP and MAP in Light period increased by 7.2mmHg and 3.0mmHg respectively than those before high salt diet, but both differences were not significant. After the high salt diet, the control rats maintained the normal BP rhythm while the ADRs still presented disturbed BP rhythm.

Conclusions: We concluded that the circadian patterns of blood pressure were dramatically altered in ADR nephropathy rats with the disturbed circadian rhythm of the urine sodium excretion and FENA. And the ADR nephropathy rats showed a
striking salt sensitive of blood pressure. The ADR nephropathy rat was a suitable CKD animal model with disturbed circadian BP rhythm and sodium sensitivity.

**Introduction and Aims:** Endothelin-1 is considered as a pathogenic factor in hypertension and kidney disease development. However, it also demonstrates natriuretic and diuretic properties in the kidney. Previously we showed that chronic ET-1 synthesis inhibition aggravates 1kidney-1clip hypertension in adult male rats. It is well known that androgens are prohypertensive and may alter renal function, but the influence of androgens on renovascular hypertension and ET-1 renal excretion has not been studied before. The aim of this study was to determine the effect of chronic ET-1 synthesis inhibition on 1kidney-1clip hypertension development and renal function in gonadectomised male rats.

**Methods:** Male Wistar rats were divided into 8 groups. Among them 4 groups were treated with an endothelin-converting enzyme inhibitor (PP36) for 1week after the operation. The groups iH, iH-PP with intact testicles, and castrated ch and ch-PP groups were subjected to right nephrectomy and a clip on left renal artery. Other four groups were sham-operated (Sham-p, chsham, csham-P, chsham). Blood pressure (BP) was controlled with the tail-cuff method. To evaluate creatinine clearance and water balance rats underwent 24h urine collection.Creatinine and urea in serum and urine were analysed by spectrophotometry. Urine osmolality was analysed by cryoscopy.

**Results:** Hypertension was less pronounced in castrated males. BP rise in group iH-PP was significantly higher than in iH (67±16 vs 52±5 mmHg, p<0.05), but BP rise in group ch-P was similar to ch (55±6 vs 56±5 mmHg). Hypertension development resulted in ET-1 excretion rise in group iH by 74% and in group ch by 135% compared to sham-groups. PP36 treatment resulted in plasma ET-1 reduction by 28% in group iSham-PP. Urinary ET-1 excretion was reduced by 43% in group iH-PP compared to iH, but PP36 did not alter ET-1 excretion in castrated rats. The iH-PP group demonstrated elevated urine osmolality (799±200 vs 447±61 mOsm/kg p<0.05) and reduced free water clearance (-22±4.5 vs -16±4 ml/24h) compared to iH. However, urine osmolality and free water clearance (-15±5 vs -16±4 ml/24h) were not altered in ch-PP group. Serum creatinine and urea were significantly enhanced in hypertensive rats. Creatinine clearance (Ccr) was reduced by 37% in iH-PP rats compared to cH (0.78±0.1 vs 1.24±0.2 ml/min/1.73m²). However, ch-PP demonstrated elevated Ccr compared to ch (0.88±0.05 vs 0.79±0.06 ml/min/1.73m²), but it was 16% lower than in group csham.

**Conclusions:** We suppose that ET-1 excretion reduction by PP36 contributed to free water clearance reduction in adult male hypertensive rats, which might have potentiated hypertension development. Our results indicate that androgens interact with ET-1 system and probably have a role in inhibiting renal ET-1 synthesis, which may influence renal function.
Introduction and Aims: The Chronic Kidney Disease Japan Cohort (CKD-JAC) study started in Sep 2007, and 2,977 subjects were enrolled from 17 facilities. CKD and hypertension (HTN) are closely related; HTN causes and exacerbates CKD, and vice versa. Exploring this relation, the Ambulatory Blood Pressure Monitoring (ABPM) sub-study was conducted. In this presentation, we suggest a new indicator calculated from ABPM which reflects blood pressure (BP) load, and evaluate an actual condition of antihypertensive prescribing using this indicator.

Methods: ABP was measured every 30 minutes for 24 hours with TM-2421 device. A simple questionnaire was completed by each patient, and it collected the information such as bedtime, awakening time, the frequency of using lavatory at night and how the monitoring affected sleep. Data on medical history, medications, office BP and renal function were used from the registration data. The following indicators were calculated; 24hr mean BP, daytime and nocturnal mean BP and hyperbaric area index (HBI). HBI is an area encircled by ABPM polygonal line, 135/85mmHg line (daytime), and 120/70mmHg line (nighttime). The criterion for HTN was 140/90 mmHg for the office BP and 130/80 mmHg for the 24-hr mean BP. Total HBI is the sum of systolic and diastolic HBI.

Results: The data of 1,075 subjects (393 female, age 58.5±12.3; 682 male, age 62.0±10.6) was analyzed. Mean office BPs were 129.8/76.3mmHg (female) and 132.1/77.6mmHg (male). Based on the 24-hr mean BP and office BP, 37.5% were classified as normal BP. Only 100 subjects were prescribed no antihypertensives, while 374 subjects were prescribed more than 3 antihypertensives. Total HBI [mmHg×hour] was greater with male (+74.3 vs. female), low eGFR (+23.5 per 10ml/min/1.73m2), diabetes (+90.8), proteinuria (+119.8), nocturia (+67.2) and in winter (+77.3 vs. summer). The number of antihypertensives remained significant after adjustment for these factors (+29.6 for each additional one medicine, P=0.005).

Conclusions: HBI was a very sensitive indicator reflected various factors relevant to progression of CKD. It also reflected factors which had effects on ABP measurements such as nocturia and season. The more a patient’s BP control worsens, the more a doctor increases antihypertensives hoping for good BP control. However, even if adjusted by various background factors, HBI increased significantly with increasing antihypertensives. This shows actual condition of antihypertensive prescribing, where BP control of the CKD patients is quite difficult. More detailed BP control can be carried out using HBI.
AKI - HUMAN STUDIES

MP101 OPTIMAL TREATMENT IN CRITICALLY ILL PATIENTS WITH ACUTE KIDNEY INJURY: COMPARISON OF INTERMITTENT HEMOFILTRATION AND HEMODIALYSIS IN A RANDOMIZED CONTROLLED TRIAL

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Introduction and Aims: Almost one-third of critically ill patients in intensive care units have acute kidney injury (AKI), predominantly due to acute tubular necrosis and as part of multiple organ failure. The optimal dialysis in these patients is still unclear. The purpose of the study is to compare clinical outcomes between intermittent hemofiltration and standard hemodialysis in this specific population.

Methods: The purpose of this prospective randomized controlled single centre clinical study was to compare mortality and recovery of kidney function between intermittent hemofiltration (HF) and hemodialysis (HD) in critically ill patients with AKI. From 2010 to 2012 we randomly assigned 86 patients with AKI to intermittent HF or HD. Death from any cause within 30 and 60 days were primary study outcomes. In subgroup of patients with in hospital recovery of kidney function time to kidney function recovery and the number of required dialysis procedures were analyzed.

Results: Forty-four patients were given intermittent HF and 42 were given HD. The mean age (±SD) was 61.8±8.8 years. 72.5% of patients were male, 52.1% were oligouric and 60.2% required mechanical ventilation. The most attributed conditions in AKI were sepsis and ischaemia. The two groups had similar baseline characteristics and received treatment for an average of 10.2 days (HF) and 9.8 days (HD). Total all cause mortality by day 60 was 74.8% and was similar between the HF and the HD study groups. There were no significant differences between the groups in number of deaths at 30 and 60 days. Kidney function has recovered during hospitalization in 86 (39.8%) patients. In survivors at day 60 the two groups were similar for renal outcome.

Conclusions: In this randomized, controlled clinical study, intermittent HF in critically ill patients with AKI does not improve survival or recovery of kidney function compared to standard intermittent HD. The optimal treatment modality in AKI in critically ill patients remains unclear and needs further studies.

MP102 SHOULD WE NEED FLUID OVERLOAD IN THE CRITICALLY ILL PATIENTS?

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Introduction and Aims: Acute kidney injury is common in critically ill patients and is linked to increased morbidity and mortality. Fluid therapy is key in the management of these patients. Emerging data increasingly suggest that fluid overload in these patients may be associated with adverse outcomes.

Methods: We conducted a prospective single center observational study in an ICU. All patients over 18 years old were included. Demographic data, fluid balance, SOFA score, serum creatinine, and diuretic therapy from day 1 to day 5 were recorded. Statistical significance was considered when p<0.05, with a confidence interval of 95%.

Results: Out of a total of 81 patients, 84 were excluded because they needed renal replacement therapy. Seventy three patients (60.3% male, age 66.7±16.6 years, weight 73.7±20.6 Kg, length of stay in ICU 10.7±5.9 days) were enrolled. Mortality rate was 15.1% (n=11). Patients were stratified into 2 groups: survival (n = 62, 59.7% male, 66.5 ±16.7 years, weight: 72.7±18.4 Kg, length of stay in ICU 10.5±5.8 days) and deceased (n=11, 63.6% male, 67.7±16.3 years, weight 79.6±30.7 Kg, length of stay in ICU 11.3±6.8 days). There were no statistically significant differences between the two groups. Changes in serum creatinine and urea showed a positive correlation between groups (p =0.001) during the first 5 days of hospitalization. Mean SOFA score in the first three days showed a positive correlation between groups (p =0.026).Mean fluids administration on the first day of hospitalization showed significant differences between groups: survival 2989±1204 mL vs deceased 4090±3595 mL (p =0.042). Similarly, mean fluid balance on the first day showed significant differences: survival 621.4 ±1430 mL vs deceased 2609±3286 mL. Cumulative fluid balance and diuresis at third and fifth days of hospitalization did not show this relationship.

Conclusions: Our results emphasize the current concern existing in our ICU in obtaining early negative fluid balance. This finding further supports the current opinion that fluid accumulation is not innocuous but potentially harmful and influences patient outcomes. To further clarify the relationship between fluid overload and outcomes in the critically ill patients additional studies are necessary.

MP103 PREDICTORS ASSOCIATED WITH SHORT AND MEDIAN-TERM OUTCOME OF PATIENTS ADMITTED TO ICU WITH SEPSIS

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Introduction and Aims: Data on short and median term outcome of patients admitted with sepsis to ICU are scarce. We explored in a cohort of sepsis patients factors potentially associated with mortality at 3 months (early mortality) and also with 1 and 2 year mortality in those who survived ICU (median term mortality).

Methods: In this prospective cohort of 107 consecutive patients admitted to ICU with sepsis, 3 month, 1 and 2 year mortality data were registered. Acute kidney Injury (AKI) was defined according to RIFLE during the first 5 days of admission. Logistic and Cox regression were performed in forward and backward mode, presenting age, gender, APACHE II score, need for ventilation, Chronic Kidney Disease, AKI vs no AKI, and serum creatinine at day 1 as parameters to the model.

Results: In this cohort, 27 patients (25.2%) died in the ICU, and cumulative mortality rates were 32.7, 44.9 and 53.3% at 3 months, 1 and 2 years respectively. Mortality rate at 3 months was 26.3% in those with no AKI versus 31.8, 32.4 and 53.8% in RIFLE R, I and F respectively (p=0.34). In a logistic regression model adjusted for age and gender, APACHE II score, need for ventilation, Chronic Kidney Disease, AKI vs no AKI, and low serum creatinine at day 1 (OR=0.33; 95%CI 0.10-1.05) were independent predictors for mortality at three months. In the group that survived ICU (N=88), 61 (74.3%) had AKI during their stay at ICU, and 21 died during the first 26.2±26.3%, p=NS in AKI vs no AKI), and an additional 9 during the second year after ICU admission (so in total 39.3 vs 31.6% in AKI vs no AKI, p=0.54). In a multivariate model, age (RR=1.05; 95%CI 1.05-1.09) and low serum creatinine at day 1 (RR=0.33; 95%CI 0.10-1.05) were independent predictors for mortality (when censored at 1 year), whereas age (RR=1.03, 95%CI 1.004-1.06), low serum creatinine at day 1 (RR=0.24, 95%CI 0.08-0.70) were independent predictors when censored at 2 years.

Conclusions: Mortality after ICU admission for sepsis is high, not only during the stay on the ICU, but also in the following months and the first year. Although septic patients classified as RIFLE ‘F’ have higher mortality rates at 3 months than those having ‘no-AKI’, ‘R’ or ‘T’, only APACHE II score and need for ventilation are independent predictors for early mortality. In contrast to post-cardiac surgery ICU patients, AKI does not predict long term outcome in septic patients who survive ICU. A higher serum creatinine at day 1 was a positive prognostic marker in ICU survivors, probably because this reflects a better nutritional status. Our data suggest that severity of acute illness and underlying general condition predict short and medium term outcomes of patients admitted to ICU with sepsis, and that AKI as defined by RIFLE is a reflection of rather than a contributor to severity of disease.
Introduction and Aims: Acute kidney injury (AKI) is a serious complication that occurs frequently in critically ill patients, and is associated with worse outcomes. We investigated clinical features of patients who developed AKI according to the time of AKI development in ICU.

Methods: We retrospectively collected the data of adult patients with AKI (n = 206) admitted to ICUs between December 2011 and June 2012. AKI diagnosis was defined according to the AKIN criteria. Of 206 patients, 140 (68%) had AKI within 48 hours of ICU admission (early AKI group) while 66 developed AKI later during their stay at the ICU (late AKI group).

Results: The patients with late AKI were older, had greater changes in serum urea from the baseline, were more likely to have a sepsis, and had higher mortality rate than those with early AKI (OR = 2.95, CI 1.5-5.3, p = 0.000). The patients with early AKI were more likely to be treated with RRT in the ICU.

Conclusions: Our study demonstrates that patients in the ICU with early AKI have some distinguishing features when compared with those with late AKI. We showed that the group with earlier occurrence of AKI had lower mortality rate than the late AKI group.

Acute kidney injury (AKI) is a common and potentially fatal complication in tropical diseases. The aim of this study is to investigate the clinical and laboratory characteristics of AKI in critically ill patients with tropical diseases.

Methods: A retrospective study was conducted with 253 consecutive patients with confirmed diagnosis of tropical diseases admitted to an intensive care unit in Fortaleza, Ceara, Brazil, from January 2003 to January 2011. AKI was defined according to the RIFLE criteria, and the severity was assessed through APACHE II score.

Results: Patients’ mean age was 46 ± 16 years, and 72% were male. The main diseases were HIV/AIDS (30.4%), tuberculosis (12.2%), leptospirosis (11%), meningitis (7.5%), visceral leishmaniasis (4.3%) and dengue (3.9%). Hemodialysis was required for 70 patients (27.6%). The time between the diagnosis of AKI and the initiation of RRT was 3.6 ± 4.7 days. Oliguria was observed in 129 cases (50.9%). Laboratory tests at ICU admission evidenced Cr 2.7 ± 1.8 mg/dL, U 105 ± 68 mg/dL, AST 346 ± 888 IU/L, ALT 172 ± 356 IU/L, Na 136 ± 10 mEq/L, K 4.4 ± 2.5 mEq/L, Ht 30 ± 7.9%, Hb 10 ± 2.6 mg/dL, white blood count 11.96 ± 10.529 × 10^9/mm^3, platelets 131488 ± 11706 × 10^9/mm^3, pH 7.29 ± 0.13, HCO3 16 ± 6.1, PaCO2 34 ±12 mmHg. The mean APACHE II score was 50.22, and it was higher among patients with HIV/AIDS (57 ± 20, p = 0.01) and dengue (68 ± 11, p = 0.01), and lower among patients with tuberculosis (33 ± 19, p = 0.001) and leptospirosis (34 ± 18, p = 0.002). Death occurred in 159 cases (62.8%). Mortality was higher in patients with HIV/AIDS (76.6%, p = 0.02) and lower in patients with leptospirosis (28.5%, p = 0.0009). Risk factors for death were use of vasopressors (OR = 6.7, IC 95% = 3.7-11.9, p = 0.0001), metabolic acidosis (OR = 4.9, IC 95% = 2.7-8.7, p = 0.0001), sepsis (OR = 4.3, IC 95% = 2.4-7.6, p = 0.0001), mechanical ventilation (OR = 3.7, IC 95% = 2.1-6.5, p = 0.0001), hyperkalemia (OR = 3.01, IC 95% = 1.5-6.04, p = 0.001) and hypotension (OR = 2.1, IC 95% = 1.1-4.0, p = 0.02). Dialysis was instituted in 70 cases (27%) and generally started late.

Conclusions: AKI is a frequent complication in tropical disease and presented a high mortality rate in the present study. The clinical picture is marked by oliguria in the majority of cases. Mortality was higher in patients with HIV/AIDS, which is probably due to severe opportunistic diseases.
**Abstracts**

**Introduction and Aims: Acute kidney injury (AKI) is a frequent complication of hospital admissions, especially those in intensive care units (ICU). Nevertheless, information on factors predicting AKI and influencing the survival is limited. The present study aims to elucidate the incidence and predictors of AKI and mortality in internal medicine ICU.**

**Methods:** This is a single-center retrospective study conducted in an internal medicine ICU. 414 consecutive patients hospitalized for longer than two days were screened. Patients with previous renal disease within first 48 hours of admission were excluded; remaining 304 patients were enrolled. AKI was defined based on AKIN criteria during ICU stay. Baseline characteristics, laboratory examinations at admission to ICU, Glasgow coma score in first 24 hour, APACHE II and SOFA scores were noted. Independent predictors for AKI development and ICU mortality were defined with logistic regression analysis by using backward method.

**Results:** The mean age was 61.19 years and 50.7% of the patients were male. AKI was observed in 85 (28%) patients. Patients with AKI had higher APACHE II and SOFA scores, longer length of stay in ICU, higher levels of serum phosphorus, uric acid, AST, LDH, bilirubin (total and direct) and INR at admission; but also lower Glasgow coma score and albumin level rather than patients without AKI (for all p<0.05). Multivariate analysis revealed that higher APACHE II score (OR 1.045, 95% CI 1.001-1.092, p<0.05), longer length of ICU stay (OR 1.054, 95% CI 1.023-1.087, p<0.05), need of mechanical ventilation (MV) (OR 3.7, 95% CI 0.131-0.543, p<0.05), lower albumin (OR 1.75, 95% CI 0.372-0.873, p< 0.01) and higher uric acid levels (OR 1.126, 95% CI 1.036-1.224,p< 0.05) were independent predictors of AKI development during ICU stay. Mortality in the ICU was much higher in patients with AKI than in patients without AKI (68.2 % vs 28.8%, OR 5.53, 95% CI 3.099-4.194, p<0.001). The independent risk factors for mortality were pre-existing hypertension (OR 2.02, 95% CI 1.05-3.828, p<0.05), AKI development (OR 2.05, 95% CI 1.646-2.094, p<0.05), worse APACHE II (OR 1.107, 95% CI 1.055-1.162, p<0.05) score and need of MV (OR 8.13, 95% CI 0.062-1.224, p<0.05).

**Conclusions:** One of three our patients developed AKI during ICU stay and it was significantly associated with increased mortality. It has been shown that lower serum albumin and higher uric acid levels at admission predict AKI development; while pre-existing hypertension and AKI development emerged as independent predictors of ICU mortality. APACHE II score and need of MV were found as predictors of both AKI development and ICU mortality.

**Methods:** We analyzed data from a prospective study of 128 consecutive ICU patients. AKI was classified by RIFLE criteria. Serum (Scr) and urinary creatinine (Ucr) were measured daily up to ICU discharge. Fluid balance was calculated with daily input-output fluids. GFR was estimated by Modification of Diet in Renal Disease (MDRD), Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI), and Jelliffe equations. Creatinine clearance (CrCl) was calculated according to the correspondent formulas: 

\[ \text{CrCl} = \frac{\text{Scr} \times \text{weight} \times 1.036 \times (1 - 0.002 \times \text{age})}{1.036 - \text{age}} \]

Intra-class correlations showed better agreement between calculated GFR and CrCl. There was better association between RIFLE class and severity and median values of corrected GFRs than Jelliffe or CrCl.

**Conclusions:** GFR estimated over two time intervals with the proposed equation could provide more accurate kidney function measurement in ICU-AKI patients. Our results must be validated in larger cohort of patients with a gold standard based on a more reliable biomarker than serum creatinine.
patients, 229 patients had a normal pre-admission kidney function and in 149 there was no information on kidney function prior to hospital admission. Sixty-four percent of the patients left the hospital with an eGFR < 60 ml/min/1.73m². The median follow-up was 8.5 years (range = 1-17). Six and twelve year overall survival rates were 62% and 44%, respectively. Six and twelve year renal survival rates were 83% and 74%, respectively. Multivariable Cox-regression analysis demonstrated that age, non-surgical type of ICU admission, prior existing CKD, malignancy and eGFR <15 ml/min/1.73m² (HR = 1.87, 95%-CI = 1.20-2.97) at hospital discharge were independent predictors for mortality. Renal survival was significantly affected by the degree of kidney dysfunction at hospital discharge. An eGFR 15-29 ml/min/1.73m² (HR = 26.26, 95%-CI = 5.59 – 123.4) and an eGFR <15 ml/min/1.73m² (HR = 127.28, 95%-CI = 37.73 – 786.75) were independent risk factors for initiation of chronic RRT.

Conclusions: An impaired kidney function at hospital discharge is independently associated with worse long-term overall and renal survival. Long-term nephrological follow up is necessary for patients who experience incomplete recovery of renal function especially those discharged with an eGFR <30ml/min/1.73m², to minimize the complications of chronic kidney disease.

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**Abstracts**

**MP110**

**VALUE OF PLASMATIC NGAL LEVELS IN ASSESSING SEVERITY IN ACUTE KIDNEY INJURY PATIENTS OF DIFFERENT ETIOLOGIES**

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Introduction and Aims: Acute kidney injury (AKI) is an established predictor of all-cause mortality in hospitalized patients. Mortality among ICU patients with AKI has been reported to be more than 50% and if renal replacement therapy is required, mortality may be as high as 80%. The aim of this study is to assess if plasmatic NGAL (Neutrophil Gelatinase-Associated Lipocalin) level at the time of AKI diagnosis is a good marker for identification of patients who will need renal replacement therapy or who die during an AKI event.

Methods: 134 plasma samples were collected in a tertiary hospital including different AKI-etiologies; 27 were ICU-septic patients (septic model of AKI); 51.9% with AKI vs 48% non-AKI, 50 were patients under colistin treatment (nephrotoxic model); 46% AKI vs 54% non-AKI 17 patients with multifactorial-AKI and 40 renal allograft recipients (ischemia-reperfusion model); 72.5% with AKI. We tested NGAL means to immunofluorescence assay. Results were expressed in mean ± standard error.

Results: In our overall patient population, 52% of patients had AKI diagnosis and 48% normal kidney function. Plasmatic NGAL levels were significant higher in AKI patients (582 ± 44ng/ml vs 316± 41 ng/mL; p = 0.001). NGAL levels were significantly higher in AKI patients who needed renal replacement therapy during hospitalization compared with those who did not needed such treatment (715±73 ng/ml vs 499± 48 ng/mL; p =0.014) and significant higher in AKI-patients who recovered renal function at time of discharge (258 ±84 ng/mL vs 336 ± 73 ng/mL; p=0.01).

Conclusions: Our data show that plasmatic NGAL in AKI-patients could be useful to distinguish patients who are in risk for renal replacement therapy or die during the event, and it may serve to identify those patients who will recover renal function.

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**MP111**

**ASSOCIATION OF IMPAIRED KIDNEY FUNCTION AT ICU DISCHARGE WITH LONG-TERM RENAL AND OVERALL SURVIVAL**

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Introduction and Aims: Critically ill patients with acute kidney injury (AKI) necessitating renal replacement therapy (RRT) have high in-hospital mortality and survivors are at risk for kidney dysfunction at hospital discharge. Furthermore, recent studies have shown the interplay between AKI, chronic progressive kidney disease (CKD) and mortality in the long-term. The objective of this study was to evaluate the degree of renal function at hospital discharge as an independent risk factor for long-term renal and overall survival after an episode of AKI requiring RRT.

Methods: A retrospective cohort study was performed in the intensive care unit (ICU) of a large academic hospital selecting for patients older than 18 years receiving continuous RRT in the ICU between 1994 en 2010. Patients known with RRT or a kidney transplant prior to ICU admission were excluded. Data were analyzed using Kaplan-Meier and Cox regression analyses.

Results: Of the 1220 critically ill patients recruited, 670 patients died in hospital. After exclusion of 75 patients with RRT or kidney transplant prior to hospital admission the study cohort included 475 patients. The mean age in the study population was 57 years (SD = 15). Sixty-three percent of the patients had a surgical indication for ICU admission. The largest groups of patients (25%) were admitted to the ICU after thoracic surgery followed by sepsis (17%). Pre-existing CKD was reported in 97

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**MP113**

**URINARY NGAL (NEUTROPHIL GELATINASE ASSOCIATED LIPOCALIN) EXCRETION AT BIRTH IS PREDICTIVE OF SUSCEPTIBILITY TO ACUTE KIDNEY INJURY (AKI) IN VERY LOW BIRTH WEIGHT INFANTS**

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Introduction and Aims: Preterm infants are particularly susceptible to renal damage and acute kidney injury (AKI); closure of patent ductus arteriosus (PDA) with prostaglandin inhibitors is an additional risk factor. Novel AKI biomarkers, such as urinary NGAL, are emerging but their value as predictors of renal damage in very preterm infants has not yet been assessed. Aim of the study was to evaluate in a cohort of very low birth weight (VLBW) infants the urinary excretion of NGAL as early AKI biomarker during treatment with ibuprofen for PDA.

Methods: We evaluated 50 VLBW infants (birth weight ≤1500 gr and/or gestational age ≤32 weeks) without congenital nephropathies, 19 treated with ibuprofen and 31 not treated. Renal function was assessed by serum creatinine (sCr) (IDMS method) within 24h after each dose of ibuprofen. Results: Newborns requiring treatment (19) had lower gestational age (28.37±2.79w vs. 30.61±2.17w untreated, p=0.0045), lower APGAR score (6.63±1.83 treated vs 8.16±0.97 untreated, p=0.0009) and required more ventilatory support (74% vs 16%, p <0.001). At birth sCr and uNGAL were similar in two groups (s C: 1.02±0.34 mg/dl vs
30-days mortality. The use of uNGAL might be useful for the clinician to suspect the without uNGAL increase. NGAL(+)/SCr(+) died in 30 days. There were no deaths in 30 days in patients with AKI p<0.01). All patients with AKI and NGAL(+)/SCr(-), 50% of patients with AKI and χ²(uNGAL) pre CVVHDF 1423 ± 737 IU/L. The common causes for initiation of RRT (CVVHDF). The mean age of our cohort was 66 ± 17 years, 60% were males, with distribution during renal replacement therapy (RRT) has not been reported. Additionally, the novel marker Cystatin C (Cys-C) may correlate closer with the delivery of iron into tubular cells, NGAL assist kidney tubule cell protection. NGAL infant treated with ibuprofen. Moreover uNGAL value at birth is an independent predictve factor of AKI in preterm infants, with the advantage of being not invasive and repeatable, with potential widespread use in this age group.

### Introduction and Aims

Acute decompensated heart failure (ADHF) is one of the leading causes of hospitalization worldwide. The development of acute kidney injury (AKI) is associated with poor outcomes. There is a strong need to detect AKI before the rise of serum creatinine (scr). The aim of the study was to investigate the association of urinary neutrophil gelatinase associated lipocalin (uNGAL) with changes in kidney function and outcomes.

### Methods

In 51 patients with ADHF (18 male, 70.3±9.1 years (M±SD), 92% arterial hypertension, 56% ischemic heart disease, 67% myocardial infarction, 67% atrial fibrillation, 27% diabetes mellitus (DM), known chronic kidney disease 33%) levels of scr and uNGAL were determined on admission. AKI was defined using 2012 KDIGO Guidelines criteria. Patients with AKI were classified into three groups on the basis of their levels of SCR and uNGAL. Mann-Whitney and multiple logistic regression analysis were performed. P <0.05 was considered statistically significant.

### Results

53% of patients developed AKI. Patients with AKI compared with patients without AKI had higher SCR (188.8±94.3 vs 114.5±50.2 nmol/l, p<0.001) and uNGAL (203.3±270.7 vs 114.5±50.2 nmol/l, p=0.001). Urine NGAL -184.3 ng/ml (odds ratio 3.85; 95% confidential interval 2.4-6.1) was determined to be significant and independent factor for development of AKI. Of 27 patients with AKI 48% had isolated Cr criteria of AKI [NGAL(-)/SCr(+)], 15% - isolated increase of uNGAL [NGAL(+)/SCr(-)] and 37% - both Cr criteria of AKI and increase of uNGAL [NGAL(+)/SCr(+)]. Patients with NGAL(-)/SCr(-) or NGAL(+)/SCr(+) demonstrated better short-term outcomes: the 30-days mortality 0% vs 100% (χ²=17.00, p=0.001) and 0% vs 50% (χ²=8.31, p<0.01). Patients with AKI and NGAL(+)/SCr(-) or NGAL(+)/SCr(+) compared with patients without increase of uNGAL demonstrated worse short-term outcomes (χ²=17.00, p=0.001 and χ²=8.31, p<0.01). All patients with AKI and NGAL(+)/SCr(-), 50% of patients with AKI and NGAL(+)/SCr(+) died in 30 days. There were no deaths in 30 days in patients with AKI without uNGAL increase.

### Conclusions

53% of patients admitted to the hospital with ADHF developed AKI. Level of uNGAL >184.3 ng/ml in patients with AKI is associated with higher risk of 30-days mortality. The use of uNGAL might be useful for the clinician to suspect the subgroup with high risk of poor outcomes in patient population with ADHF and AKI.

### Introduction and Aims

Neutrophil Gelatinase Associated Lipocalin and Serum Cystatin C Kinetics on Continuous Venovenous Hemofiltration

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The present study aims to evaluate the kinetics of NGAL and sCystatin C over time during CVVHDF, and to compare them between AKI and non-AKI patients.

### Methods

The study included 40 AKI patients with a mean age of 66.7±14.8 years and 18.7% females, and 40 non-AKI patients with a mean age of 67.4±13.5 years and 37.5% females. NGAL and sCystatin C were measured at five different times during the hemofiltration procedure: at the beginning of the procedure (H0), at 6 h (H6), at 12 h (H12), and at 24 h (H24).

### Results

The kinetics of NGAL and sCystatin C were significantly different between AKI and non-AKI patients at all time points except at H0. The area under the ROC curve for NGAL at H24 was 0.76 (95% CI 0.67-0.85), while for sCystatin C it was 0.64 (95% CI 0.53-0.75).

### Conclusions

These results suggest that NGAL and sCystatin C kinetics during CVVHDF can be used as biomarkers for the assessment of renal injury in AKI patients.
patients was glomerular and vascular lesions. There were more patients on steroids and immunosuppressive agents and less patients on renal replacement therapy (RRT) in A/C group. There was no difference of renal survival and mortality rate between 2 groups during follow-up, but there were more patients with stable primary diseases and lower co-morbidity rate than AKI patients without CKD. RRT was inversely correlated with mortality and ESRD. Age, serum creatinine level and co-morbidities were not associated with prognosis.

Conclusions: A/C patients were different from AKI without CKD in epidemiology, causes, clinical characteristics and prognosis. Causes of AKI patients with CKD should be stressed and early diagnosis and prevention be warranted in order to shorten the clinical course and eventually improve prognosis.

**MP120** RISK FACTORS AND PREDICTIVE SCORE OF ACUTE KIDNEY INJURY IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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Introduction and Aims: Although an acute kidney injury (AKI) commonly occurs among patients hospitalized for acute myocardial infarction (AMI), its risk factors is unknown. The article aims to develop a clinical predictive score in order to predict the AKI after AMI. The early identification of patients with risks of developing AKI can reduce its incidence.

Methods: We analyzed data on consecutive patients with AMI from January, 2010 to July, 2011 at Beijing Anzhen Hospital. All the patients were divided into two groups, AKI group and non-AKI group, with the definition of AKI by Acute Kidney Injury Network. The univariable analysis and logistic regression model were used to establish the predictive score.

Results: The total cohort consisted of 1429 patients. The derivation cohort consisted of 1033 patients and the validation cohort consisted of 396 patients. In the derivation cohort, the rate of AKI was 14.3%. Mortality was significantly higher in the AKI group (10.1% vs 6.0% in those without AKI, P<0.000). In the validation cohort, the rate of AKI was 15.7%. A lot of in-patients occur AKI within a week, patients with AKI stay longer than without AKI.Univariate analysis disclosed age, hyperension, diabetes mellitus, chronic kidney disease(KD), stroke, heartrate, lower estimated glomerular filtration rate (eGFR), anaemia, severe Killip class, extensive anterior myocardial infarction, troponin I(TNI);500ng/ml,left ventricular ejection fraction (LVEF)<50%, shock, Ventricular Fibrillation,B-blocker non-use and longer time before admission to hospital as risk factors to develop AKI. After adjusting for other factors associated with AKI, reduced GFR at presentation, severe Killip class, extensive anterior myocardial infarction, hypertension,B-blocker non-use and longer time before admission to hospital were independently associated with AKI.

Conclusions: We developed a clinical predictive score for AKI after AMI. This predictive score presented good discrimination and calibration. It would help the clinicians to make decision for preventive intervention. Further studies on interventions to minimize AKI or to more aggressively treat patients developing AKI should be tested.

**MP121** THE EFFECTIVENESS OF AN E-ALERT WARNING IN THE MANAGEMENT OF PATIENTS WITH ACUTE KIDNEY INJURY

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Introduction and Aims: The 2009 NCEPOD report “Adding Insult to Injury” highlights the importance of early recognition of Acute Kidney Injury (AKI). Acute kidney injury (AKI) is both a preventable and serious problem in hospitalised patients. If unrecognized and allowed to deteriorate, AKI will result in uremia, acidosis, hyperkalemia and ultimately death. Strategies to reduce the risk of AKI are well known and they include identifying relevant risk factors, appropriate monitoring of blood biochemistry, rapid remedial action when AKI occurs, and appropriate referral of patients to specialist services. Despite the seriousness of this condition, early recognition and treatment leads to favorable outcome. Hospital guidelines are a useful tool that guides clinicians into appropriate management of AKI. The e-alert was introduced at Aintree University Trust to detect patients who developed AKI and flag this to the patient team with a link to the trust online AKI management algorithm.

Methods: To assess management of AKI in a large teaching hospital, in comparison to data from the 2009 NCEPOD “Adding Insult to Injury” Report. To compare the outcomes measures as defined by our trust guidelines, in 2 groups of patients; ones that had e-alerts seen by patient-team and those that had not. To look at defined outcome measures including length of stay, renal recovery, complications & Nephrology referral.

Results: A total of 38 patients out of 58 were studied. Acidosis (5), pulmonary oedema (3) or hyperkalemia (3) were uncommon. We analysed whether the appropriate general measures detailed in the online guide were performed. 100% of the patients with AKIN 3 were referred to nephrology. 50% of the patients with AKIN 2 were referred to nephrology. All patients with AKI complicated with hyperkalemia and pulmonary oedema were managed with nephrology input. Online junior doctors survey on AKI management was undertaken simultaneously and the outcomes are as below which highlights the importance of on going junior doctor training and education in AKI management.

— 64% aware of Trust AKI guidelines.
— 82% do not use Trust AKI guidelines in day-to-day practice.
— 72% not aware of AKI classification system.
— 91% of juniors (FY1-CT2) very interested in learning more on AKI.

Conclusions: E-alerts and online AKI management guidelines appear to be working well, with appropriate patients being referred to nephrology. However, a third of e-alerts are not picked up by the parent team. Further education for junior doctors, is the key to maximise effectiveness of on-line tools. Overall AKI management was better than the NCEPOD report.

**MP122** MODEL OF A ROBUST ELECTRONIC ‘ACUTE KIDNEY INJURY ALERT SYSTEM’ TO IDENTIFY THE ONSET AND PROGRESSION OF ACUTE KIDNEY INJURY IN HOSPITALIZED PATIENTS

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Introduction and Aims: Acute Kidney Injury (AKI) is a common complication in hospitalized patients and the condition frequently goes undetected, thus worsening outcome for the patient. Guidelines have suggested employing serum creatinine (CR) and urine output to detect AKI and, using the former, laboratory information management systems (LIMS) may help with both the diagnosis and management of the condition.

Methods: Utilizing Kidney Disease: Improving Global Outcomes (KDIGO) criteria on definition and staging of AKI, we have developed and implemented algorithms into our LIMS software that stage and alert clinicians to the possible presence of AKI. In published literature, alert system algorithms uses either lowest or mean CR value or theoretical reference values when comparator not available. In our LIMS, alert system algorithms uses either lowest or mean CR value or the theoretical reference values when comparator not available. In our LIMS, introduced at Aintree University Trust to detect patients who developed AKI and flag this to the patient team with a link to the trust online AKI management algorithm.

Results: We tested the AKI algorithm analysis for 173 in-patients with raised admission serum CR values comparing with reference CR values identified by different methods. The analysis calculates the AKI staging by looking back 365 days and based
upon the lowest, mean, median if there are previous results; and irrespective of previous results it calculates the AKI score on the population gender dependent regressed median CR and a reverse eGFR of 75 (table 1). We compared the reverses eGFR method which is being reported in the literature.

**Table:** Examples of AKI alert: compares between different methods

**Conclusions:** Implementing a robust electronic AKI alert algorithms into a LIS system facilitates detection of AKI in hospitalized patients and may subsequently improve their management and outcome. We also demonstrated that a 'regressed system facilitates detection of AKI in hospitalized patients and may subsequently improve their management and outcome. We also demonstrated that 'regressed creatinine' reflects the true population better as it is based upon a 'real' aging population and therefore, generates more accurate AKI alerts when there is no comparator value available.

**Reference:**

Kathryn K. Stevens1, Rajan K. Patell1, Patrick B. Mark1, Christian Deelis1 and Alan G. Jardine1
1ICAMS University of Glasgow Glasgow United Kingdom

**Introduction and Aims:** Serum phosphate is linked with increased cardiovascular risk although the mechanism is unclear. The effect of sustained short term phosphate loading on endothelial function has not previously been studied. This study considers the effect of phosphate loading on endothelial function measured by flow mediated dilatation (FMD).

**Methods:** Healthy volunteers attended for a baseline and 2 subsequent visits. Blood was drawn for measures including bone biochemistry, vitamin D, FGF-23 and klotho. A caffeine urine output was performed prior to attendance and any results included urinary cGMP and FGF-23 concentrations. FMD was recorded. Volunteers were randomized to take lanthanum carbonate (LC) or Phosphate Sandoz (PS) for 2 weeks prior to the next visit. After a wash out period, volunteers took the other drug and attended for a final visit. One individual, blinded to the order of drug treatment, performed and analysed each FMD measure.

**Results:** Of 19 participants, 12 were female. At baseline, mean age was 42±14 years, eGFR 102±110 ml/min, serum phosphate 1.05±0.81 mmol/L and fractional excretion of phosphate (FeP) 14.3±5.4%. Median FMD was 8.4% (IQR 6.2-11.6%) post cuff inflation. After PS, there was a trend towards a higher serum phosphate within the normal range. FGF-23 and FeP rose significantly compared to baseline (p=0.013, p=0.001). FMD post cuff inflation reduced significantly (3.38% (IQR 2.57-5.20%), p<0.001). With LC, the highest phosphate was unchanged FeP fell (11.4±4.3, p<0.001). Post cuff inflation FMD fell (6.6% (IQR 3.4-10.3%), p=0.033). Randomization order had no effect. In a regression model, higher FeP was an independent predictor of attenuated post cuff inflation FMD (p=0.02). Urinary cGMP correlated negatively with serum phosphate (p=0.003).

**Conclusions:** This is the first study to demonstrate that sustained phosphate loading impairs endothelial function. The observed deleterious effect observed on FMD seen with PS may be explained by elevated total body phosphate with resultant elevated intra-cellular phosphate. FeP is likely a surrogate marker of total body phosphate. Urinary cGMP, as a marker of endothelial dysfunction negatively correlates with serum phosphate level. This study supports the hypothesis that phosphate increases cardiovascular risk by impairing endothelial function, possibly via the nitric oxide pathway. Sustained phosphate loading is directly detrimental to the vasculature even when serum phosphate remains within the normal range.

**Reference:**

Julia Wittfingsseder1,2, Andreas Heinze3, Paul Mayer4, Paul Perco5, Alexander Kanz1,2, Bernad Mayer1 and Rainer Oberbauer1,2
1Nephrology Medical University of Vienna Vienna Austria, 2Nephrology KH der Elisabethinen Linz Austria, 3R&D Emergentec: Biodevelopment GmbH Vienna Austria

**Introduction and Aims:** The revolution of ‘omics’ technologies allows to model a molecular process landscape characterizing acute kidney injury (AKI), from there delineating a multi-marker candidate profile for classifying the heterogeneous pathophysiology of AKI.

**Methods:** We investigated the molecular predictors of AKI by incorporating a broad range of publicly available Omics data. A systematic literature search for AKI omics studies and an automated literature mining for genes associated with AKI were also incorporated into the analysis. A hybrid molecular interaction network covering about 15,000 human proteins, and holding about 800,000 interactions were used as reference network to derive an AKI induced protein interaction network covering all molecular features being identified as associated with AKI based on Omics and literature data. This network was then segmented into distinct molecular subgraphs (processes) apparently relevant in AKI pathology, providing a molecular model of AKI.

**Results:** The systematic literature search for AKI Omics studies revealed 19 studies (4 SNPs, 3 transcriptomics, 2 metabolomics, 8 proteomics, 2 miRNA), and literature mining identified 139 genes associated with AKI. Ten AKI-specific molecular subgraphs could be identified on the basis of the given AKI-specific feature set. We interpret each such subgraph as a distinct molecular process being relevant in AKI. We further evaluated which of these processes were already being addressed by currently discussed AKI biomarker candidates. A biomarker candidate list was derived from text mining and a manual literature search provided 38 such features (7%); acute kidney injury (AKI) and CXCL10 were members of our molecular model, and established AKI markers such as NGAL, KIM1, FABP1 and CST3 were found to be distinct to the AKI-specific network. We therefore screened for further biomarker candidates better representing the AKI molecular model, and tested the principal suitability of such candidates in an independent transcriptomics data set on AKI in the transplant setting.

**Conclusions:** We integrated data from human Omics studies generating a molecular model of AKI. Such models provide a basis rationale for biomarker panel selection.

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**Conclusions:** This is the first study to demonstrate that sustained phosphate loading impairs endothelial function. The observed deleterious effect observed on FMD seen with PS may be explained by elevated total body phosphate with resultant elevated intra-cellular phosphate. FeP is likely a surrogate marker of total body phosphate. Urinary cGMP, as a marker of endothelial dysfunction negatively correlates with serum phosphate level. This study supports the hypothesis that phosphate increases cardiovascular risk by impairing endothelial function, possibly via the nitric oxide pathway. Sustained phosphate loading is directly detrimental to the vasculature even when serum phosphate remains within the normal range.

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**Conclusions:** We integrated data from human Omics studies generating a molecular model of AKI. Such models provide a basis rationale for biomarker panel selection.

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hypertension (35%). Initial abnormal laboratory values showed increased WBC (70.0%), elevation of AST (61.7%), ALT (50%), CK (26%), and LDH (98.8%). Acute renal failure (ARF) occurred in 43 patients. Infarct size was positively correlated with occurrence of ARF (p<0.003). ARF was frequently seen in patients with AFI and/or CHF (p=0.040 and 0.036, respectively). Higher ALT and LDH level was presented in patients with ARF (p<0.05). Most of all patients recovered from ARF except for 6 patients leading to persistent renal impairment. Patients with persistent renal impairment were also closely correlated with infarct size (p=0.001). Six patients were died because of combined morbidity.

Conclusions: ARF is often accompanied by acute renal failure. Although most of ARF is recovered spontaneously, we should keep it mind that renal impairment by acute renal failure can persist. Therefore, we think that in urgent care efforts of early diagnosis and intervention are needed for the prevention of renal function.

**MP127**

**STROKE VOLUME VARIATION (SVV) AND OXIGENATION INDEX (OI) ARE RISKFACTORS FOR ACUTE KIDNEY INJURY (AKI) IN ABDOMINAL AORTIC ANEURYSM (AAA) SURGERY**

Pablo Lentini1, Luca Zanolli2, Antonio Granata3, Andrea Contestabile1, Graziaella Berlingo1, Anna Basso1, Valentina Pelliccia1, Massimo de Cat1, Rudi Stramarrani2, Diego Cogno3,1 Marco Balicchi4 and Roberto Dell’Aquila1

1Nephrology S. Bassiano Hospital Bassiano Del Grappa (VI) Italy, 2Intensive Care Unit S. Bassiano Hospital Bassano Del Grappa (VI) Italy, 3University of Catania Catanisa Italy, 4Intensive Care Unit S. Giovanni Di Dio Hospital Agriento Italy, 5Nephrology S. Bartolo Hospital Vicenza Italy, 6Vascular Surgery S. Bassiano Hospital Bassano Del Grappa (VI) Italy, 7Intensive Care Unit S. Bassiano Hospital Bassano Del Grappa (VI) Italy

**Introduction and Aims:** AAA surgery patients are at high risk for AKI. Hemodynamic instability, hypovolemia, haemorrhage and reduced cardiac output may play a key role in AKI development. SVV predicts volume responsiveness in mechanically ventilated patients; elevated levels of Oxigenation Index (OI) are linked to patients leading to persistent renal impairment. Patients with wide changes of SVV or OI at clamping and declamping of the aorta are associated with high risk of AKI. SVV predicts volume responsiveness in mechanically ventilated patients; elevated levels of Oxigenation Index (OI) are linked to high risk of AKI.

**Results:** 9 patients (43%) developed AKI, defined as RIFLE Risk category. SVV and OI (Table 1) were significantly higher at aortic clamping (p<0.0001) and declamping (p<0.0001) in patients that will develop AKI. Similarly, OI was significantly higher in AKI than non-AKI at aortic clamping (AKI, median 8.0, IQ 8.7-11.1; non-AKI, median 4.1, IQ 3.1-4.5; p<0.0001) and declamping (AKI, median 7.3, IQ 6.4-11.1; non-AKI, median 4.4, IQ 3.8-5.2; p<0.001).

**Conclusions:** SVV and OI during and after suprarenal AAA surgery are associated with high risk of AKI.

**MP128**

**TUBULAR FUNCTION OF SURVIVORS OF SEVERE ACUTE KIDNEY INJURY SUBMITTED TO DIALYSIS**

Bianca M. Chella1, Carmen Pilla2, Antonio Balbinotto1, Veronica H. Antunes1, Alessandra Hegler1, Fernanda M. Colares1 and Fernando S. Thomé1,2

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**Introduction and Aims:** Acute kidney injury (AKI) occurs in up to 50% of critically ill patients and is associated with high mortality. Survivors have a greater chance of developing chronic kidney disease (CKD). Early tubular dysfunction is found in CKD patients compared to healthy persons with similar estimated glomerular filtration rates (EGFR). The study aim was to study tubular function in survivors of an episode of severe AKI and critical illness.

**Methods:** A cohort of critically ill patients on intermittent or continuous dialysis for AKI stage 3 was followed prospectively from 2006 to 2011. Survivors with EGFR > 60 mL/min/1.73m² (CKD-EPI), were included, except those with previous CKD, chronic hepatitis, HIV/AIDS, transplants, plants and chronic complications, severe vascular disease or single kidney (pAKI group). Healthy volunteers paired by sex and age were controls (C). We measured urinary alkaline phosphatase (ALP), N-acetyl-β-D-glucosaminidase (NAG), lactate dehydrogenase (LDH), β-2-microglobulin (ß2M), proteinuria (PCr), microalbuminuria (MICA), transtubular potassium gradient (TTKG) and the fractional excursions of potassium (FEK₆), phosphorous (FEP), uric acid (FEUA), and magnesium(MFEG₆). Students t or Mann Whitney test for continuous and chi-square test for categorical variables were used, with SPSS, version 18, and p<0.05.

**Results:** The cohort had 1038 patients, 302 (23%) discharged alive. Eighty nine subjects met inclusion criteria, but 72 were excluded: 31 were not alive, 83 were not reached, not willing to participate or had cognitive/physical impairment, 3 had current ARF. Baseline characteristics were similar: age=54.1±12.4 (pAKI) vs. 54.4±12.4 (C) years; body mass index=27.0±6.5 (pAKI) vs. 27.8±1.1 Kg/m² (C), EGRF 87.9±13.8 (pAKI) vs. 81.0±13.8 mL/min (C). Mean time between discharge and the study was 3.2±1.1 years. There were no statistically significant differences between groups in B2M, ALP, NAG, LDH, FEK₆, FEP, FEUA, TTKG. MICA was higher in pAKI 5.5 (3.5-6.6) vs 3.0 (3.0-8.5) mg/g (p=0.04), MICA>30mg/g was present in 29.4% of pAKI and none in C. PCI was higher in pAKI (0.08 (0.06-0.21) vs 0.04 (0.04-0.08) mg/mg (p<0.01). Serum Mg was lower in pAKI (2.1±1.8 vs. 2.2±1.9 mg/dl, p=0.01). Excluding patients taking drugs that might interfere with tubular function, this difference persisted, associated with higher FEP and lower PCI in pAKI 4.4±2.9-8.8 vs 2.1-9.3 (p<0.03).

**Conclusions:** Survivors of critical illness and dialysis requiring AKI present sub-clinical tubular abnormalities when compared to controls, despite similar EGFR: high FEK₆, MICA and PCI. Whether this was present before AKI or is a consequence, this nested case-control study design could not answer.

**MP130**

**ACUTE KIDNEY INJURY AFTER CARDIAC SURGERY ACCORDING TO RIFLE: ADULTS VS PEDIATRICS**

Albania Gjyzari1, Nestor Theressa2 and Ornela Xhango3

1UHC Tirana Albania, 2UHC Tirana Albania, 3UHC Tirana Albania

**Introduction and Aims:** Aim was to evaluate incidence, risk factors, outcome of acute kidney injury (AKI) in adult and pediatric patients after cardiac surgery in intensive care unit (ICU), based on RIFLE and RIFLE modified criteria, and predictive factors for ICU mortality.

**Methods:** All patients admitted in the cardiac surgical ICU, tertiary care center, during 2007 were reviewed retrospectively. Transplanted and chronic dialysis patients before admission to the ICU were excluded. AKI was classified according to the maximum RIFLE criteria using both estimated creatinine clearance (eGFR) and urine output (UO) criterion during the first week of stay. For pediatric patients (≤18 years) RIFLE modified was used. For baseline creatinine, was used that of hospital admission. Results: 315 ICU patients were included for the study. Among 284 adult patients, 181 (57.2%) patients met criteria for AKI during the study period: non AKI 133 (42.2%), Risk 84 (26.7%), Injury 43 (13.7%), Failure 24 (7.8%), among 31 pediatric patients, 18 (58%) patients met criteria for AKI during the study period: non AKI 13 (41.9%), Risk 10 (32.3%), Injury 8 (25.8%). Type of intervention for adults: 34.5% valve operation, 51% aortocoronary bypass (20.8% CABG), other 14.4%. For pediatrics was: 58% septal defects, 22.5% tetralogy of Fallot, 19.5% other (aortic stenosis and coarctation). Adult AKI patients were aged, median UOF (IQR) 58 (52-65) vs. non-AKI patients 54 (44-61), p=0.01 and had higher SOFA score: AKI 5 (3-6) vs. non-AKI patients 3 (1-4), p<0.001. Pediatric AKI patients, median age (IQR) 9 (4-13) vs. non-AKI patients 9 (4-18).
Abstracts

(5.5-14.5); p = 0.644. For the total cohort study hospital mortality was 13 (41%) patients. Mortality according to the groups: all pediatric patients 0 (0%); adult non AKI patients 1 (0.8%); Risk class 1 (12.6%); Injury class 9 (3.3%); Failure class 7 (29.2%); p = 0.001. Multivariate logistic regression analysis showed age (OR: 1.02, 95% CI: 1.01-1.025), SOFA score (OR: 1.43, 95% CI: 1.25-1.65, p = 0.001) as independent factors associated to AKI development for adults. Multivariate logistic regression analysis showed independent risk factors associated to mortality, Failure (OR: 2.77, 95% CI: 0.16-47.2, p < 0.001); SOFA score (OR: 4.94, 95% CI: 1.69-96.5, p < 0.001). Kaplan-Meier curve for hospital survival by RIFLE class with Cox regression analysis was statistically significant, p = 0.0001.

Conclusions: According to RIFLE and RIFLE modified criteria high incidence of AKI after cardiac surgery in ICU patients was observed. AKI was more severe and had worse outcome in adult then pediatric patients. Advanced age and higher SOFA score are independently associated to AKI development in adults. Higher SOFA score and failure of renal function according to RIFLE were found independent factors associated to hospital mortality.

MP131

**ACUTE KIDNEY INJURY INFLUENCES MORTALITY IN LUNG TRANSPLANTATION**

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1The Department of Nephrology WuXi People’s Hospital, the Affiliated Hospital of NanJing Medical University WuXi Jiangsu China; 2The Department of Thoracic Surgery WuXi People’s Hospital, the Affiliated Hospital of NanJing Medical University WuXi Jiangsu China

**Introduction and Aims:** Acute kidney injury (AKI) is a common complication after lung transplantation (LTx). But there is no consistent result about the influence of AKI after LTx. We studied the prevalence of AKI and its association with long-term mortality in lung transplant patients in our hospital.

**Methods:** We retrospectively analyzed clinical data of 88 patients who underwent LTx at our institution between September 2002 to December 2011. Primary outcomes were the incidence of AKI, as defined and divided into three groups based on creatinine criteria from the Acute Kidney Injury Net (AKIN) classification. A multivariable logistic regression model evaluated risk factors for AKI. Secondary outcomes were 5-year survival. Risk adjusted multivariable Cox proportional hazards regression examined the association between AKI and mortality.

**Results:** AKI developed in 47 (53.40%) of patients (27 [30.7%] AKIN 1 and 20 [22.7%] AKIN 2-3) in the first week after LTx. Multivariate analysis identified pre-LTx hypertension (OR: 1.37 [0.06 to 2.68], p = 0.041) and mechanical ventilation (OR: 0.05 [0.01 to 0.09], p = 0.022) were risk factors for post-operative AKI.

**Five-year survival was 48.8%, 37.0%, 30.0% in the no-AKI, AKIN1, and AKIN 2-3 respectively. Adjusting for age, sex, type and cause of LTx, hypertension and diabetes, the hazards ratio for death was 1.481 ([1.040 to 2.107], p = 0.029) for AKI.**

**Conclusions:** AKI is a common occurrence after LTx and increases long-term mortality. Several variables, including pre-LTx hypertension and mechanical ventilation, are associated with AKI after LTx.

MP132

**IMPACT OF BODY MASS INDEX ON OUTCOMES AFTER ACUTE KIDNEY INJURY IN POST-OPERATIVE GERIATRIC PATIENTS**

Hung-Bin Tsai2, Wen-Je Ko1 and Chia-Ter Chao2

1Department of Traumatology National Taiwan University Hospital Taipei Taiwan Republic of China; 2Department of Traumatology; Department of Internal Medicine National Taiwan University Hospital Taipei Taiwan Republic of China

**Introduction and Aims:** Acute kidney injury (AKI) frequently occurs in critically ill patients, but studies on outcome-modifying factors in geriatric patients with AKI are few. The influence of body mass has not been determined previously.

**Methods:** We performed a multicenter prospective observational study and enrolled elderly patients (>65 years) that developed AKI after major surgery in the intensive care units. We analyzed in-hospital mortality within each body mass index (BMI) category utilizing Cox proportional hazard regression analysis and generalized additive modeling (GAM).

**Results:** A total of 2015 postoperative elderly patients (age 75.2±4.6, mean 57.8%) were studied. The survivors were significantly younger and had higher BMI (23.2±3.9 kg/m² vs. 22.4±4.2 kg/m², p = 0.001). GAM modeling showed that elderly AKI patients with a BMI between 21 and 31 kg/m² (normal) had a lower mortality risk than those with a BMI ≥21 (underweight) or ≥31 (obese). Regression model showed that both underweight and obese individuals had a greater risk of mortality compared with patients with normal BMI (underweight vs. normal, hazard ratio [HR] 1.60, 95% confidence interval [CI] 1.05-2.61; p = 0.046; obese vs. normal, HR 1.22, 95%CI 1.01-1.49; p = 0.042).

**Conclusions:** Both underweight and obese patients had a greater risk of mortality compared with patients with normal BMI. Underweight and obese individuals had a greater risk of mortality compared with patients with normal BMI.
Conclusions: This study is the first to demonstrate the effects of BMI on in-hospital mortality in geriatric AKI patients. The U-shaped association of BMI with hospital mortality in geriatrics is unique, and should alert physicians of factors potentially affecting the outcomes of these elderly.

**MP134**

**THE IMPACT OF ACUTE KIDNEY INJURY ON MORTALITY AND RENAL FUNCTION IN PATIENTS WITHOUT PRE-EXISTING DISEASE**

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1Nephrology Erasmus Medical Center Rotterdam The Netherlands, 2Intensive Care Erasmus Medical Center Rotterdam The Netherlands

Introduction and Aims: Acute kidney injury (AKI) necessitating renal replacement therapy (RRT) is associated with excessively high mortality and increased risk for progression towards end stage renal disease (ESRD). However, it is unknown if this risk applies to all patients with severe AKI especially to those with an unremarkable medical history prior to hospital admission. This study describes the effects of AKI necessitating RRT in critically ill patients without pre-existing disease on mortality and renal function.

Methods: A retrospective cohort study was performed in a tertiary care center, between January 1994 and April 2010, selecting for critically ill patients ≥ 18 years with AKI necessitating RRT. Patients were categorized as patients with pre-existing disease versus patients without pre-existing disease (study population). Additionally, the patients in the study population were randomly one-to-one matched for age and sex to patients with pre-existing disease admitted in the same period (matched population). Data were analyzed using logistic regression and survival curve analyses.

Results: Of the 1220 critically ill patients recruited, only 94 (7.7%) had no pre-existent disease. The mean age in the study population was 46.9 (SD = 15.2). AKI due to sepsis was most frequent (59.6%), followed by ischemia (24.5%), drug-associated (8.5%) and any other cause of AKI (7.4%). The mean rate for admitting patients to the ICU was sepsis (38.3%) followed by trauma (30.9%), post-operative (12.8%), intoxication (9.6%), and other (9.6%). In hospital mortality was 43.6%, which was equally high as the group of patients matched for age and sex with pre-existing disease. Those who survived hospital admission had a mean follow-up of 8.6 years (range = 0 - 17) and 49.1% left the hospital with an estimated glomerular filtration rate (eGFR) <90 ml/min/1.73m2 of which two were dialysis dependent. The 1-year, 5-year and 10-year cumulative survival rates for patients that survived hospital admission were 96.2%, 91.4% and 85.6%, respectively. Cumulative survival rates for the matched patients with pre-existing disease were 89.8%, 65.7% and 57.0%, respectively. Compared to the predictive survival rate in the average Dutch population, the 10-year survival rate in this study was 7% lower. Besides the two survivors that progressed towards ESRD during hospital admission, one additional patient reached ESRD during follow-up after 7.5 years, which constituted a 10-year renal survival of 93%.

Conclusions: Critically ill patients with RRT-requiring AKI have an excessively high in-hospital mortality risk, even in the absence of pre-existing disease. However, those without pre-existing disease have a relative good long-term prognosis. These results are indicative that comorbidity and not the episode of AKI itself may be a major determinant of renal function, ESRD and mortality after hospital discharge.

**MP135**

**POVIDONE-IODINE A POSSIBLE CAUSE OF CONTRAST INDUCED AKI? – OUR CENTER ANNUAL REPORT**

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Introduction and Aims: Nowadays, it is worldwide recognized that acute kidney injury (AKI) represents one of the most important and increasingly common death- and ESRD progression-related cause. Therefore, each year our Center assesses data regarding AKI possible etiology of hospitalized cases for a future better management and control.

Methods: In 2012, 75 patients were diagnosed with AKI and 68% (n = 51) – Group A – of them presented acute-on-chronic kidney disease and 32% – Group B – associated no known renal impairment. All patients were age and sex matched and routine lab tests (e.g.: hemoglobin, BUN, creatinine, ESR, C-protein, uric acid, albumin levels, coagulation profile etc) were performed including eGFR measurement using Cockcroft-Gault formula. In the present report we focused on Group B patients and all data were statistically analyzed using SPSS 17.0 software.

Results: Group B included 24 individuals with the following possible etiologies: 57% post-surgical related AKI causes, 21% contrast induced AKI (CI-AKI), 17% drug induced AKI and 5% other causes. The most interesting aspect we observed was regarding the CI-AKI cases. 4 of these patients, all women, presented CI-AKI following non-intravascular use of iodinated substances (povidone-iodine); the patients underwent hysterectomy for diagnosis of primary sterility. 2.5 ± 1 days after the procedure, the subjects were hospitalized due to an acute elevation in serum creatinine (Cr mean level = 9.32 ± 1.3 mg/dL; p < 0.001) and BUN (BUN mean level = 230.35 ± 5.7 mg/dL; p = 0.001) values, associating oligosanuria, dizziness, nausea and vomiting. In all cases, except standard AKI management, HD was required and after 10.3 ± 2.7 days of RRT, 3 of them returned to normal renal function and 1 patient remained on chronic HD program. There was a clear correlation between povidone-iodine exposure and increased nitrogen waste products values and consequently, acute renal failure (p < 0.001; α = 0.05; χ² = 33.523; df = 2).

Conclusions: Our findings highlighted the possibility of CI-AKI even in non-intravascular administration situation and should raise the attention of the practitioners to consider this diagnosis when iodine substances, injected or not, were recently used. Further larger clinical trials are needed to confirm our results for assure a better management and control of AKI patients with related or not preexistent renal impairment.
per 10000 person years in the AKI-dialysis-recovery group. The Cox proportional-hazards regression model showed that the AKI-dialysis-recovery group had an increased long-term risk of dementia (HR, 2.01; P< .01). The conditional effect plot showed that the risk of dementia was amplified in patients who were older than 58 years when the temporary dialysis was discontinued. The development of dementia following recovery from AKI requiring dialysis was associated with an increase in all-cause mortality (HR, 2.38; P< .001). Diagram of the patient selection process Independent predictive factors for long-term dementia were estimated by the time-varying Cox regression model. Conditional-effect plots of the estimated risk of dementia versus patient age.

Conclusions: Patients who recover from AKI requiring temporary dialysis have a greater risk for the subsequent development of dementia than patients without AKI, and patients who develop dementia subsequent to recovery from AKI requiring dialysis are at increased risk for mortality.

**Covariates**

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Odds Ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>1.10 (1.08-1.11)</td>
<td>&lt; .001</td>
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<tr>
<td>Acute dialysis</td>
<td>2.01 (1.19-3.39)</td>
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<tr>
<td>Stroke</td>
<td>1.80 (1.00-3.25)</td>
<td>.05</td>
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<tr>
<td>Neurologic comorbidities</td>
<td>4.82 (1.15-20.14)</td>
<td>.03</td>
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<tr>
<td>Ongoing ESRD after discharge</td>
<td>0.96 (0.37-2.49)</td>
<td>.93</td>
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**Introduction and Aims:** Patients undergoing liver transplantation often have acute kidney injury (AKI) as a complication in the early postoperative, presenting a greater number of complications and high mortality rates. The aim of this study is to determine the incidence of AKI and mortality in patients undergoing orthotopic liver transplantation (OLT) in our hospital.

**Methods:** We conducted a retrospective cohort study where we reviewed the medical records of all patients older than 18 years undergoing OLT between April 2008 and April 2011, and excluded patients with glomerular filtration rate (GFR) estimated lower than 60 ml/min using the MDRD formula or with acute kidney injury or need for renal replacement therapy at the time of transplantation. AKI was defined as a percentage increase of 150% from preoperative creatinine during hospitalization of transplantation.

**Results:** We performed 158 orthotopic liver transplants in 152 patients in our hospital during the period. 39 patients were excluded (23 GFR below 60 ml/min, 4 combined transplantation of kidney and liver, 10 with acute renal failure before renal transplantation, 1 bellow eighteen years, 1 immediate postoperative death). 113 patients were selected, 78 (69%) patients were male, 94(83.2%) caucasians, median age 55 years, mean body mass index 26.21, 40 (35.4%) had systemic arterial hypertension and 30 (26.6%) diabetes, mean preoperative creatinine 0.9 mg/dl, GFR MDRD 82.76 ml/min, calculated MELD 13, serology for hepatitis C in 78.8% (88), hepatitis B 11.5% (13), diagnosis of hepatocellular carcinoma in 75.2% (85) and intrahepatic ductal alcohol in 81.9%. The mean age of patients. The incidence of acute kidney injury in the postoperative period was 56.6% (64 patients) of these 22 patients (19.4%) required renal replacement therapy and 42 patients (37.2%) were maintained in clinical treatment. The hospital mortality in the group with acute renal failure was 25% (16 patients) in those who required renal replacement therapy (RRT) was 54.5% (12 patients) and 9.5% (4 patients) among those who had acute kidney injury and did not require RRT, and in group without acute renal failure 6.1% (3 patients), OR 5.11 (1.39-18.71), p <.01. Among patients who required renal replacement therapy in hospital mortality was 54.5% (12 patients) compared to 7.7% (7 patients) who don’t need for renal replacement therapy, OR 14.40 (4.60-45.00), p<.01.

Conclusions: The study demonstrates the high incidence of acute kidney injury in this group of patients and increased risk of mortality in patients who need renal replacement therapy.

**Introduction and Aims:** 1. To know the prevalence of acute kidney injury in cirrhosis patients 2. To study clinical profile and laboratory characteristics in these patients 3. To analyze precipitating factors of acute kidney injury in these patients 4. To measure all cause in hospital mortality in these patients.

**Methods:** Prospective study conducted on 120 cirrhosis of liver patients admitted serially with acute kidney injury to the hospital. These patients were classified as per AKIN criteria. These patients were evaluated after clinical examination for precipitating factors of Acute kidney injury. Factors affecting in hospital mortality were studied.

**Results:** This study observed male predominance. The prevalence of acute kidney injury in cirrhosis of liver patients was 33.5% in this cohort. In hospital mortality was 36.6%. Mean MELD Score of study cohort was 27.8 ± 7.40 (SD) and mean CTP score was 10.84 ± 1.84 (SD). Most common source of sepsis was spontaneous bacterial peritonitis (27.4%), followed by urosepsis 22.58% on univariate analysis between survivor and non-survivor presence of sepsis, GI losses, encephalopathy, higher MELD score and child Pugh score. Presence of tachycardia and low mean blood pressure were commonly present in non survivors. Patients in AKIN stage I had maximum survival rates (80.3%), and maximum mortality was seen in AKIN Stage III renal injury (65.9%). Multiple logistic regression analysis showed presence of AKIN stage II and III presence of sepsis, serum creatinine of more than 1.5mg/dl as important predictors of in hospital mortality.

**Conclusions:** Prevalence of Acute kidney injury is high in cirrhosis of liver patients. Sepsis was the most common cause of precipitating Acute kidney injury followed by duodenal ulcer, gastrointestinal fluid loss, encephalopathy. GI Losses. Spontaneous bacterial peritonitis followed by urosepsis is the frequent cause of sepsis. Patients with AKIN stage II and III have significantly high mortality. AKIN criteria is useful in cirrhosis of liver patients in predicting patients prognosis.

**Introduction and Aims:** To develop a clinical predictive score to predict the acute kidney injury (AKI) after cardiac surgery by incorporating the effects of all of its major risk factors.

**Methods:** We analyzed data on consecutive patients receiving cardiac surgery from June, 2010 to April, 2011 at Beijing Anzhen Hospital. All the patients were divided into two groups, AKI group and non-AKI group, with the definition of AKI by Acute Kidney Injury Network. The univariable analysis and logistic regression model were used to establish the predictive score.

**Results:** The total cohort consisted of 3500 patients. The derivation cohort consisted of 2380 patients and the validation cohort consisted of 1115 patients. In the derivation cohort, the rate of AKI was 40.5%, while rate of acute renal failure (ARF) requiring dialysis was 2.5%. In the validation cohort, the rate of AKI was 39.6%, while rate of ARF requiring dialysis was 1.4%. In both the derivation cohort, the mortality rate was 5.6% for AKI patients, while 45.8% for ARF requiring dialysis. In the validation cohort, the mortality rate was 4.3% for AKI patients, while 68.8% for ARF requiring dialysis.

**Variables selected for the logistic regression model and then predictive score were the**
following: male (2 points), older age (score is increased 1 point with every 5 years increment from 60 years old), diabetes mellitus (2 points), preoperative use of ACEI/ARB (1 point), eGFR (score is increased 1 point with every 10 ml/min/1.73m²) deteriorations from baseline (≥1 ml/min/1.73m²), NYHA class >3 (1 point), NYHA class >2 (0 point), intraoperative hypotension time >60min (2 points), postoperative hypotension time >60min (3 points), postoperative use of loop diuretics 60-100mg per day (2 points), postoperative use of loop diuretics >100mg per day (3 points), postoperative ventilator use >24h (1 point), inotropic support >2 points, postoperative mechanical ventilation time >24h (2 points). The stratification of risk factors is as follows: low-risk (within 0-5 point), intermediate-risk (6-11 point), and high-risk (≥12 point). The frequencies of AKI were 20.7%, 44.3%, and 83.6% respectively. In the validation cohort, the predictive score presented a good discrimination with a c-index of 0.71 under the curve of receiver operating characteristic of 0.738 (95%CI, 0.707–0.768), while it also presented a good calibration with Hosmer-Lemeshow statistic (P=0.305).

Conclusions: we developed a clinical predictive score for AKI after cardiac surgery. This predictive score presented good discrimination and calibration. It would help the clinicians to make decision for preventive intervention.

MP142 IMPROVING KNOWLEDGE AND CONFIDENCE OF GENERAL PHYSICIANS AND TRAINEES ON THE SUBJECT OF ACUTE KIDNEY INJURY THOUGH NOVEL EDUCATION TOOLS; RESULTS FROM 2 UK TEACHING HOSPITALS

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Introduction and Aims: Acute Kidney Injury (AKI) causes significant morbidity and mortality. In the United Kingdom (UK) it has been recognized that the management of patients with AKI can be improved significantly. Most of patients with AKI in the UK are currently managed by non-nephrologists, who may lack the knowledge and confidence on the topic of AKI. Aims: We aimed to improve the confidence and knowledge of general physicians and trainees in two large UK teaching hospitals (University Hospitals of Leicester and Royal Derby Hospital) on the topic of AKI.

Methods: An integrated education package was produced on the topic of AKI. This included an e-learning tool, face-to-face teaching on admissions wards, and sessions integrated into already established teaching programs. A MCQ (Multiple choice question) survey consisting of questions designed to test knowledge and confidence was carried out before (pre-survey) and after post-survey) the dissemination of the education package. The survey was carried out in a face-to-face setting.

Results: Less than 5% of doctors had received no teaching at all on AKI before the education package was delivered. In total 457 doctors completed the survey; 319 in the initial survey and 138 in the post survey. 50% of doctors in the initial survey thought AKI was always diagnosed when it occurred, and 37% would always initiate a management plan in patients with AKI. In the initial survey being aware of local guidelines on AKI wasn’t associated with a higher MCQ score (45% vs 44%, p = 0.62). There was also no association between being aware of guidelines and increased confidence to initiate investigations or basic management plans for patients with AKI (p = 0.6 and p = 0.8). After the education package was disseminated all grades were more confident about diagnosing, investigating, and managing patients with AKI (p < 0.05) overall doctors scored an MCQ of 47% in post-survey (p = 0.06). 292 individuals accessed the e-Learning tool over a period of 4 months; the completion rate of the module was 65%. 20% of junior doctors who had access to the e-Learning tool completed the e-Learning module. This reflects the finding in the initial survey that showed doctors have more formal education sessions related to AKI.

Conclusions: Confidence and knowledge of AKI in general physicians can be improved using an integrated education package, even if the majority of the target audience has already received education on AKI. Being aware of local guidelines on AKI did not guarantee better knowledge or more confidence. Overall the scores of 15 MCQs designed to test knowledge was higher post exposure to the educational package, suggesting better education may be a powerful tool in helping to improve the outcomes of patients with AKI.

MP141 EFFECTS OF CONTRAST MEDIA ON DIFFERENT URINARY BIOMARKERS OF KIDNEY INJURY

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Introduction and Aims: Contrast media (CM) induced nephropathy accounts for up to 15% of hospital-acquired acute renal failure. Given the huge number of percutaneous coronary interventions, early detection of is of utmost clinical relevance, however, the standard clinical tests for detection of kidney injury especially serum creatinine measurements are insensitive and detect only after the injury is advanced. Therefore, a variety of urinary biomarkers is currently under evaluation.

Methods: 282 urine samples from 72 patients (age 67±11 years, BMI 28±3) were collected before and after CM application for invasive cardiology and compared with 154 spontaneous urine samples from 44 healthy volunteers (HV, age 41±10 years, BMI 24±4). Urine samples were analyzed for different renal biomarkers using clinical chemistry, Luminex-based technology and NMR. An interim analysis is reported.

Results: Within the patients, 29% suffered from diabetes and 89% from hypertension. 72% of patients were treated with ACE-inhibitors or ARBs and 44% with diuretics. Compared to HV, several patients showed higher values of the urinary biomarkers already before contrast media. Elevated urine protein biomarker levels were especially found in patients with elevated serum creatinine and in diabetic patients with poor glucose control. Increases in the NMR score before CM application are seen in nearly all patients with increased serum creatinine values and are high in those samples with increased urinary protein excretion. After application of contrast media, there was a fast increase in most biomarkers reaching a maximal effect within 6 hours after CM application. The increase was most pronounced for ßNAG (ß-acetyl-beta-D-glucosaminidase), LDH, GGT, TIMP-1 (lissu inhibitor of metalloproteinase 1), a1MG (alpha1-microglobulin) and a NMR score. Within these, TIMP-1, LDH and GGT recovered within 12 hours. Other protein biomarkers like NGAL (neutrophil gelatinase-associated lipocalin), KIM-1 and Clueterin showed only slight to moderate increases after contrast media. Albumin, ALP and LDL levels after CM were only elevated in patients with hypertension. Increases of ßNAG, LDH, a2M (ß-2 microglobulin) and NMR score were higher with higher iodine dose of the contrast media. NMR scores were the most sensitive parameter and independent from age, BMI, hypertension or diabetes. Patients treated with diuretics showed lower levels of ALP, GGT and TIMP.

Conclusions: Within the tested biomarkers ßNAG, LDH, GGT, TIMP-1, a1MG and the NMR score showed the strongest reaction to contrast media. These biomarkers react within a short timeframe. Analysis of multiple parameters is needed for interpretation of confounding effects.

MP142 RENAL SAFETY EVALUATION AFTER DOTAREMO-ENHANCED-MRI COMPARED WITH NON-ENHANCED-MRI IN PATIENTS AT HIGH RISK OF DEVELOPING CONTRAST MEDIUM INDUCED NEPHROPATHY

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Introduction and Aims: To assess the safety profile of Dotarem® in patients with chronic renal failure.

Methods: Phase IV, open-label, non-randomized, comparative and multinational study, including 155 patients (male or female, aged ≥18 years), presenting with a known stable stage III to stage IV renal insufficiency (i.e. ≤ 15 % estimated glomerular filtration rate (eGFR) ≤ 60 ml/min/1.73m²) scheduled to undergo a contrast-enhanced-MRI (gadoteric acid, Dotarem®) or unenhanced-MRI examination. The primary endpoint was the percentage of patients presenting with a nephrotoxicity, defined as a serum creatinine level increase at 72±24h of at least 5% or 0.5mg/dl compared to baseline, using a non-inferiority analysis. Main secondary criteria were eGFR and serum creatinine variations, influence of hydration protocol and/or prophylactic treatment on the renal function, laboratory parameters, and adverse events through a follow-up of 72±24h.

Results: The difference (unenhanced-MRI – Dotarem® MRI) in terms of nephrotoxicity incidence was -1.4% and significantly (p<0.001) superior to the clinical non-inferiority limit, demonstrating the non-inferiority. The serum creatinine variation from baseline was -1.4 ±10.4% for Dotarem® MII and -3.5 ±9.9% for unenhanced-MRI (p=0.291). Globally for the secondary endpoints, no relevant differences between the two groups were observed. The good general safety profile of Dotarem® was also confirmed (5 adverse events post-injection mostly mild and unrelated).

Conclusions: The non-inferiority of Dotarem® over unenhanced-MRI in terms of nephrotoxicity was demonstrated. Among the few contrast medium induced nephropathy studies with gadolinium products, this prospective study involved a comparison to a control group emphasizing the very good renal tolerance of Dotarem® in at risk patients.

MP143 DEVELOPMENT OF A RISK SCORE FOR PREDICTION OF CONTRAST INDUCED NEPHROPATHY AFTER CORONARY ANGIOGRAPHY AND INTERVENTION IN CHINA

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Abstracts

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**Introduction and Aims:** Contrast induced nephropathy (CIN) is the third most common cause of hospital-acquired renal failure. Although many individual risk factors for the development of CIN have been reported, the cumulative effect of these risk factors on renal function has been assessed with risk score models in the small number of studies. Furthermore, none of the databases based on the general settings (previous risk scores were derived from patients undergoing primary PCI or elective PCI). The aim was to develop a risk score that could be readily applied by clinicians to evaluate individual patient risk for developing CIN after coronary angiography and percutaneous coronary intervention based on unselected population.

**Methods:** A total of 3,957 patients undergoing coronary angiography and percutaneous coronary intervention were randomly assigned to a development and a validation dataset. Several baseline clinical and procedural characteristics of 2,773 patients in the development dataset were considered as candidate univariate predictors of CIN (increase ≥ 0.5 mg/dL in serum creatinine level within 72 hours following the procedure vs. baseline). Multivariate logistic regression was then used to identify independent predictors of contrast induced nephropathy. Based on the odds ratio and clinical characteristic, the independent predictors were assigned a weighted integer and a risk score system was derived. The risk score was validated in a second cohort of 1,184 patients.

**Results:** CIN occurred in 4.4% of patients (176/3957). In the development dataset, the following factors were independent predictors of CIN: age ≥ 65 years (OR = 1.98), acute myocardial infarction (OR = 2.30), 10/μmol/L < baseline serum creatinine ≤ 177/μmol/L (OR = 1.52), baseline serum creatinine > 177/μmol/L (OR = 3.39), periprocedural heart failure (OR = 2.11), periprocedural intra-aortic balloon pump (OR = 3.86), pre-procedural ACEI or ARB therapy (OR = 1.69), 200 mL < contrast media < 300 mL (OR = 1.49), contrast media > 300 mL (OR = 3.02). The risk score system based on these variables, the patients in development cohort were further categorized into three groups: low risk (0-3 points), moderate risk (4-6 points), 21.6% (95% CI 0.66-0.8). The risk score system demonstrated good discriminative power (ROC 0.73, 95% CI 0.66-0.8).

**Conclusions:** We developed and validated a clinical prediction tool based on to determine which patients are at high risk for CIN. Use of this risk score system may help physicians perform targeted intervention to reduce this risk.

**Introduction and Aims:** Acute kidney injury (AKI) is defined and staged according to the rise in serum creatinine. Some studied reported the rapid reversal of post surgical AKI had good prognosis comparing to long duration AKI. This suggested the duration of AKI has additional prognostic information in surgical patients. Here we sought to determine if the duration of AKI has clinical information in hospital acquired AKI patients.

**Methods:** We prospectively enrolled hospital-acquired AKI in single referral center Sep. 2007 to August 2008 and followed up the long-term outcome until 2011. Duration of AKI was categorized as AKI for 1 to 2 (short duration), 3 to 6 (medium duration), at least 7 days (long duration). We defined persistent AKI if the patient still had AKI at baseline at the time of discharge. And the severity of AKI was classified by AKIN criteria. Interrupted time series with segmented regression analysis of intervention effect was carried out in the two years before and after the policy change (Chi squared = 6.12, p=0.049).

**Results:** Of 1,091 AKI patients, 41% (445) were active treatment patients, one hundred twenty three had hospital acquired AKI patients. Short duration of AKI, 32° (26%), medium 23 (18.7%), long duration 27 (22%), persistent AKI (41; 33.3%) were categorized. AKI stage was classified as stage 1, 28.5%, stage 2, 30.9%, and stage 3, 40.7%. The median follow-up duration was 248 days (53 - 1,428 days). There was no difference in long-term outcome between each duration group (p = 0.365). Our data showed that persistent AKI and AKIN stage 3 were associated with high mortality (p < 0.001, p = 0.023).

**Conclusions:** Rapid reversal AKI has same effects in long-term outcome compared to slow reversal group. Severity and reversibility of AKI impact mortality in hospitalized patients.

**Introduction and Aims:** Acute tubulo-interstitial nephritis (ATIN) is a common and reversible cause of acute kidney injury (AKI). Recent evidence suggests that the incidence of ATIN is increasing. The aim of this multicentre retrospective study was to compare renal outcomes in patients with biopsy proven ATIN treated with corticosteroids and those managed conservatively.

**Methods:** Cases presenting between January 2000 and December 2011 (12 years) were identified by searching the Renal and Pathology databases of three Scottish health boards (together serving around 1.9 of Scotland’s 5 million population). A review of casenotes and the electronic laboratory data archive was undertaken to determine patient demographics, presenting features, aetiological factors, pathological features, management and outcome.

**Results:** There were 177 native renal biopsies where a histopathological diagnosis of ATIN was made. This represented 5.4% of the total number of renal biopsies performed in the time period. There was a trend towards increasing relative incidence (Chi squared test for trend 10.45; p=0.0012). The aetiology was drug-related in the majority of cases. Proton pump inhibitors were thought to be causative in as many baseline clinical and procedural characteristics of 2,773 patients in the development dataset were considered as candidate univariate predictors of CIN (increase ≥ 0.5 mg/dL in serum creatinine levelwithin 72 hours following the procedure vs. baseline). Multivariate logistic regression was then used to identify independent predictors of contrast induced nephropathy. Based on the odds ratio and clinical characteristic, the independent predictors were assigned a weighted integer and a risk score system was derived. The risk score was validated in a second cohort of 1,184 patients.

**Conclusions:** Our data shows that incidence of ATIN in Scotland appears to be increasing. It does not provide evidence for the routine use of corticosteroids.
are few reports which focused on the detailed evaluation of course of cisplatin-induced AKI, and no validation study of new AKI definition proposed by Kidney Disease: Improving Global Outcomes (KDIGO 2012). We investigated clinical features of cisplatin-induced AKI.

Methods: In 54 cancer patients (165 times) treated with cisplatin between January 2007 and December 2011 at otorhinolaryngology/head and neck surgery and gastroenterology units in Hamamatsu University School of Medicine Hospital. The incidence, risk factors, outcomes, and electrolyte imbalances and infection as the complications were retrospectively assessed.

Results: 26 of 54 patients (48.1%) and 29 of 165 times (17.5%) were diagnosed with AKI at 6-7 days after cisplatin administration. AKI was developed in 20 patients (76.9%) after the first administration of cisplatin. Their serum creatinine levels peaked (1.78±0.23 mg/dl) at 7-8 days after cisplatin administration. Serum creatinine was higher at 4 weeks after before AKI (1.22±0.17 mg/dl vs 0.79±0.03 mg/dl, p<0.05). The patients with hypertension and ARB/ACE-1 use were more susceptible to AKI than those without them (hypertension; 38.46% vs 10.71%, p<0.05, ARB/ACE-1; 26.92% vs 3.57%, p<0.05). The patients developing AKI were susceptible to infection and hyponatremia (infection; 34.93% vs 14.71%, p<0.05, hyponatremia; 72.41% vs 43.38%, p<0.05). Among patients affected by AKI, cisplatin was not given to 15 patients but given to 11 patients affected by AKI developed AKI by the repeated treatment of cisplatin. The in-hospital mortality tended to be worsened in patients with AKI compared to patients without AKI but not significantly (23.1 % vs 14.3 %).

Conclusions: Based on the new definition of AKI by KDIGO, we found that cisplatin-induced AKI frequently occurred at the first chemotherapy treatment. Serum creatinine did not decline to the baseline level at 4 weeks after AKI in most patients. The repeated administration of cisplatin to patients undergoing AKI seemed not to induce AKI again, suggesting an example of clinically acquired cytoresistance.

Introduction and Aims: Information of renal prognosis of post-renal acute kidney injury (PR-AKI) is exceedingly scarce. The purpose of this study is to identify 6 months renal prognosis and its predictors of post-renal AKI after the release of obstruction.

Methods: A single center retrospective observational study of 76 consecutive patients who were diagnosed as PR-AKI from December 2006 to February 2010 was conducted at the St. Marianna University Hospital, a university affiliated tertiary care center. Clinical information and laboratory data were obtained from medical charts and electrical records and kidney function was followed for at least 6 months after the release of obstruction. Baseline kidney function were obtained within 6 months before the intervention or estimated as 75 ml/min/1.72m² if the data was not available. The major outcome measure is estimated GFR (eGFR) calculated by MDRD study equation or estimated as 75 ml/min/1.72m² if the actual data was not available. The complications were retrospectively assessed.

Results: Participants had a mean age of 68.5 years, 52.6% were male and mean baseline eGFR was 67.1±12.6 ml/min/1.73m². The most frequent cause of urinary tract obstruction was malignancy, which associated with 40.8% of the AKI. The most common type of cancer was cervical cancer (18.4%) and prostate cancer (7.8%). Six months after the procedure, eGFR decreased significantly from eGFR at the time of admission (P<0.001). Factors associated with 6 months eGFR were older age (P=0.04), malignancy as the cause of obstruction (P=0.04), lower blood hemoglobin on day of admission (P=0.01) and lower eGFR on admission (P<0.01). Stepwise multivariate analyze showed that predictors of eGFR decreased significantly from eGFR at the time of admission (P<0.001). Factors associated with risk for death were: percentage of PC (HR=1.06, 95%CI 1.01-1.12, p=0.01), higher levels of serum paraprotein (HR=1.05, 95%CI 1.1-1.11, p=0.037) and lower levels of proteinuria (HR= 0.28, 95%CI 0.09-0.93, p=0.037). 12-month mortality was higher in the AKI than NRI group (28 vs. 11% p=0.003). We also found a higher 12-month mortality tended to be worsened in patients with AKI compared to patients without AKI but not significantly (23.1% vs 14.3%).

Conclusions: This study demonstrated that PR-AKI only partially recovered and could lead to CKD. Older age and lower baseline eGFR but not etiology of obstruction or method of intervention was independent predictors of lower eGFR 6 month after the release of obstruction.

Introduction and Aims: Pregnancy related Acute Kidney Injury is common cause of Acute Kidney Injury in tertiary referral hospital and is associated with substantial maternal and fetal morbidity and mortality. We conducted the study to ascertain the etiology, contributing factors and outcome in patients with Pregnancy related Acute Kidney Injury from July 2012 to December 2012.

Methods: In this prospective study, 120 consecutive cases of Acute Kidney Injury were enrolled during the study period, out of which 24 were Pregnancy related.Accute Kidney Injury was diagnosed by oliguria, azotemia ( Serum Creatinine >1.5 mg/dl or 0.3 mg/dl increase above baseline) with or without requirement for Hemodialysis. Renal Biopsy was performed when patient was oliguric or dialysis dependent at the end of 3 weeks.

Results: The incidence of Pregnancy related Acute Kidney Injury was 20%. Approximately 14% cases occurred in early pregnancy and 86% cases in late pregnancy. Puerperal sepsis was commonest cause (62.5%) followed by Preeclampsia (20.8%). Two third patients required dialysis and supportive care. Renal biopsy was done in three patients and outcomes of acute cortical necrosis was present in two of them. Mortality rate was 20.8 %.

Conclusions: Pregnancy related Acute Kidney Injury was the commonest cause Acute Kidney Injury in our hospital. Puerperal sepsis was the leading cause. Sepsis, thrombocytopenia, Disseminated intravascular coagulation and prolonged involvement was associated with maternal mortality. Pregnancy related Acute Kidney Injury continues to be a important cause of Acute Kidney Injury in developing countries and contributes significantly to maternal mortality and morbidity.
Introduction and Aims: An accurate measure of kidney function is essential, not only to protect acute kidney injury, but also for identification of patients with autonomic renal clearance (ARC)—defined as the increased renal elimination of circulating solutes and drugs as compared with normal baseline. The accuracy of glomerular filtration rate (GFR) estimates has been questioned and several authors recommend routine use of measured CLCR in the intensive care unit (ICU). The present study aims to compare estimates of GFR using the Cockcroft-Gault (CG) formula with measured CL\textsubscript{CR} in a population of critically ill patients with normal serum creatinine.

Methods: We undertook a prospective, observational study of 54 patients admitted to the ICU over a four month period (50% medical admissions, 28.2% trauma patients, 20.4% surgical admissions). Daily eight-hour CL\textsubscript{CR} and GFR estimates (CG formula) were calculated. Reported reference ranges for serum creatinine concentrations are 0.6-1.2 mg/dL. ARC was defined as CL\textsubscript{CR} > 130 ml/min/1.73m\textsuperscript{2}. Correlations were assessed using a scatter graph and Pearson correlation coefficient and accuracy was assessed using a Bland-Altman plot.

Results: A total of 645 determinations were obtained in the 54 patients (72.2% male, mean age 54.7±12.5 years), with the eight-hour CL\textsubscript{CR} ranging from 20 to 800 ml/min/1.73m\textsuperscript{2} and mean serum creatinine of 0.6±0.17 mg/dL. The 645 samples were matched with respective GFR estimates, showing no significant difference between mean values (137.7 vs. 135.9 ml/min/1.73 m\textsuperscript{2}; p=0.54). Although a statistically significant correlation was noted between eight-hour CL\textsubscript{CR} and CG (p<0.05), the strength of this correlation was very poor (r\textsuperscript{2}=0.02). Additionally, the Bland-Altman plot shows poor agreement between both methods in terms of their precision (42.6%) and their limits of agreement (-81% and +82.5%). ARC was present in almost half (49.7%) of the studied samples. When sub-groups of measurements were analysed according to different cut-offs of CL\textsubscript{CR}, there was an evident and progressive underestimation of CL\textsubscript{CR} for values above 120 ml/min/1.73 m\textsuperscript{2} when using CG, and a progressive overestimation for values under 120 ml/min/1.73 m\textsuperscript{2} when using CG (p<0.05).

Conclusions: The evaluation of GFR in critically ill patients is fundamental for early identification of patients with undetected renal dysfunction or ARC. ARC was present in almost half (49.7%) of the studied samples. Estimates of GFR using CG formula are flawed in the critically ill, with a trend to significantly underestimate renal function in those with ARC and to overestimate renal function in those with normal or decreased renal function. The routine use of measured CL\textsubscript{CR} is highly recommended, as a surrogate of GFR in the ICU.
**Results:** We identified 448 AKI patients who had dialysis and survived 90 days after index hospital discharge and did not require subsequent dialysis. Among these, 273 were male (60.9%), with a mean age of 61.4±16.6 years. The control group included 1,792 hospitalized HIV-infected patients without AKI, dialysis, or history of bone fracture. The incidence of bone fracture was 320 per 10,000 person-years in the AKI recovery group. The hazard ratio (HR) of long-term bone fracture in the AKI recovery group was 2.15 (p=0.049) compared to the control group, independent of progression to ESRD (HR=1.55, p=0.01). Both AKI recovery status (SCr > 1.5 mg/dL) and time-varying bone fracture (HR=1.43, p<0.001) were independent predictors of mortality compared to controls.

**Conclusions:** Our study has shown that AKI requiring temporary dialysis seems to independently increase the long-term risk of bone fracture, regardless of subsequent progression to ESRD. In addition, our study has provided greater understanding of the long-term effects of AKI, specifically that bone fractures then lead to further negative impact on patient mortality.

**INTRODUCTION AND AIMS:** Acute kidney injury (AKI) is common in hospitalized human immunodeficiency virus (HIV)-infected patients and is associated with hospital mortality. We aimed to evaluate the impact of AKI on long-term mortality of hospitalized HIV-infected patients.

**METHODS:** Retrospective analysis of a cohort of 433 HIV-infected patients who were discharged alive from the hospital. AKI was defined according to the Risk Injury Failure Loss of kidney function End-stage kidney disease (RIFLE) criteria. An evaluation of all clinical manifestations and laboratory tests at admission in the period from January 2009 to July 2012. AKI was defined according to the RIFLE criteria.

**RESULTS:** Sixty-four patients (14.8%) had AKI. Median follow-up was 37 months. At follow-up, 81 patients (18.7%) died. The cumulative probability of death of patients with AKI was 21.2, 25, and 31.3%, respectively, as compared with 10, 13.3, and 16.5% in patients without AKI (log-rank, P = 0.011). In multivariate analysis AKI was associated with increased mortality (adjusted HR 1.7, 95% CI 1.1; 3; P = 0.049).

**Conclusions:** AKI was independently associated with long-term mortality of hospitalized HIV-infected patients.

**MP157 LONG-TERM RISK OF MORTALITY FOR ACUTE KIDNEY INJURY IN HIV-INFECTED PATIENTS: A COHORT ANALYSIS**

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**Prevention of Contrast-Induced Acute Kidney Injury by Oral or IntraVenous Hydration: Markers of Renal Damage: Neutrophil gelatinase-associated lipocalin (NGAL) and Interleukin-8 (IL-8)**

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**Introduction and Aims:** Contrast-induced acute kidney injury (CIAKI) is the third most frequent aetiology of hospital-acquired AKI. There is evidence of a protective effect of hydration with intravenous solutions but information about oral hydration is scarce. Because accumulation of creatinine is relatively slow, it requires 48 to 72 hours to identify many cases of CIAKI. Neutrophil gelatinase-associated lipocalin (NGAL) and IL-8 could be early markers. Objectives: To study the change of urine and serum NGAL and IL-8 in patients who have received intravenous contrast with different hydration protocols.

**Methods:** A prospective, randomized, single-centre trial was performed in hospitalized non-diabetic patients with estimated glomerular filtration rate (eGFR) calculated by MDRD-4 higher than 30 ml/min, undergoing procedures with contrast media. Patients were randomized in three groups: G1: intravenous (IV) bicarbonate, G2: Oral hydration and G3: control. NGAL and IL-8 in serum and urine were studied before and after contrast administration.

**Results:** 132 patients were included in the study. 57.7 years old (S.D:15.8), 82 males. There were no significant differences (p<0.05) between groups regarding NGAL and IL-8 baseline levels. However, absolute change in serum and urine NGAL and IL-8 after contrast administration was non-significant (p<0.05) across the 3 groups.

**Conclusions:** In patients with low risk of CIAKI, different hydration protocols do not determine differences both in plasma and urine change of NGAL or IL-8 level.

**Abstracts**

**MP158 ACUTE KIDNEY INJURY DUE TO ANABOLIC STEROIDS AND VITAMIN SUPPLEMENT ABUSE - SERIES OF 10 CASES IN FORTALEZA, CEARA, BRAZIL**

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**Introduction and Aims:** The use of anabolic steroids and vitamin supplements has reached alarming proportions in the last decades and is now a public health problem. The aim of this study is to describe the occurrence of acute kidney injury (AKI) as a complication of the use of anabolic steroids and vitamin supplements.

**Methods:** This is a case series of 10 patients with AKI due to anabolic steroids and vitamin supplement abuse admitted to the General Hospital of Fortaleza, Ceara, Brazil, in the period from January 2009 to July 2012. AKI was defined according to the RIFLE criteria. An evaluation of all clinical manifestations and laboratory tests at admission and during hospital stay was done.

**Results:** The patients reported the use of anabolic steroids and vitamin supplements with vitamin A (20,000,000IU/dose), vitamin D (35,000,000IU/dose) and vitamin E (6,000IU/dose). The mean age was 23.7± years (range 16-34 years), and they were all male. The main clinical manifestations were fever (66.6%), nausea (88.8%), vomiting (77.7%), anorexia (44.4%), weight loss (44.4%), hypertension (33.3%), headache (33.3%), tachycardia (33.3%) and dyspnoea (44.4%). All patients had AKI classified as “Injury” according to the RIFLE criteria. The mean time of hospital stay was 36±28 days. The laboratory tests at admission showed: U 70±17mg/dL, Cr 3.3±0.7mg/dL, Na 137±1.9, K 3.7±0.6, Hb 11.2±2.2g/dL, Ht 33.4±6.6%, white blood count 11340±5982/mm3, Platelets 37 6000±1 7589/mm3. The maximum levels of urea and creatinine were 120±85mg/dL and 5.3±3.0mg/dL, respectively, and calcium was 14.1±1.2mg/dL. Urinalysis showed proteinuria in 3 cases (33.3%) and hematuria in 1 case (11.1%). Hemodialysis was required for 2 patients (22.2%). Renal biopsy was done in 4 cases and showed inflammatory interstitial infiltrate, with eosinophils, calcium deposit in the interstitial space and acute tubular necrosis, without significant glomerular abnormalities.

**Awareness**

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Conclusions: AKI is an important complication of anabolic steroids and vitamin supplements abuse. The main cause of renal dysfunction in these cases seems to be the vitamin D intoxication and drug induced interstitial nephritis. Further studies are required to better understand the pathophysiology of this type of AKI.

MP159

EARLY INITIATION OF CONTINUOUS RENAL REPLACEMENT THERAPY MAY IMPROVE PATIENT SURVIVAL IN ACUTE KIDNEY INJURY

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Introduction and Aims: The effects of the timing of continuous renal replacement therapy initiation and the characteristics of the infectious process on the clinical outcomes in sepsis patients seem to be controversial. In this study, we tried to elucidate whether the timing of CRRT application, based on the interval between the start time of vasopressors infusion and CRRT initiation, was an independent predictor for mortality in critically ill patients with AKI.

Methods: We evaluated patients with AKI who were treated in ICU of Kosin University Gospel Hospital from January 1, 2010 to December 31, 2011. A total of 200 consecutive patients were included over a 48 month period. Predictors of all-cause death were examined using the Kaplan-Meier and Cox proportional hazards analyses in both treatment groups.

Results: The main contributing factors of AKI were sepsis (38%) and cardiac dysfunction (40%). 28-day overall mortality rates in the early CRRT group were significantly lower than those in the late CRRT group (P = 0.001). Furthermore, early CRRT treatment was independently associated with a lower mortality rate even after adjustment for age, sex, DM, and number of failed organ (P = 0.023).

Conclusions: Early initiation of CRRT may be of benefit.

MP160

INSULTED AT THE FRONT DOOR? DOES IDENTIFICATION OF AKI IMPACT CLINICAL CARE?

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Introduction and Aims: Acute Kidney Injury (AKI) is a common biochemical finding, however it is not always considered as a primary diagnosis on admission to hospital when other conditions co-exist. It can have a poor prognosis with mortality rates ranging from 10–80%. The AKIN criteria give clear guidelines on the classification of AKI. This study audited the identification and management of AKI in MAU and associated outcomes of length of hospital stay and death were analysed.

Methods: We retrospectively reviewed 529 patient admissions who had a creatinine reading within 1 year prior to admission to Medical Admissions Unit (MAU) during July 2011. 98 patients were identified as having a biochemical diagnosis of AKI according to AKIN criteria. 67 AKI notes were reviewed and 4 patients excluded as already established on dialysis. Clinical data was collected on admission diagnoses and management according to the standard set by the UK Renal Association.

Results: The mean age (years) was 70.8 ± 17.5 and 61.8% were female. 36.5% of patients had diabetes and 49.2% vascular disease. Only 15(23.4%) patients were identified as having AKI. Analysing these according to AKIN criteria , 9 (60%) had stage 1 AKI, 5 (33.3%) had Stage 2 and 1 (6.7%) had stage 3. Overall (n=63) 57 patients were AKIN 1, 5 were AKIN 2 and 1 was AKIN 3. Only 17.5% of all stage 1 AKI patients were identified clinically. Only 7(46.7%) of all AKI identified had a cause suggested with majority being dehydration (57.1%). 12 (80%) of clinically identified patients had a urinalysis performed within 24 hours of admission. 3 (20%) were referred to the renal team within 48 hours. 10 (66.7%) were taking nephrotoxic drugs on admission and 8 (80%) had them stopped. No patients had urine output measured on an hourly basis and so no data could be collected on this. AKI stage 1 has significantly increased LOS compared to those without AKI (median 4.5 days range 0-78 vs median 1 day range 0-149, p<0.001) as does AKI stage 2 compared to no AKI (median 13 days range 2-30 vs median 1 day range 0-149, p<0.005).

Conclusions: This study highlights underdetection of AKI stage 1, which is associated with a significantly higher LOS. Clinical identification of AKI is associated with higher rates of urinalysis – however further investigations and referrals are not instigated. AKI is a common co-existing condition on admission and acute physicians should determine delta creatinine on admission. Informatics support may aid clinician in early trends in creatinine, which may aid AKI detection in MAU as well as further training. By not identifying AKI as an important diagnosis, key investigations and expertise are absent, in particular urine output monitoring.

MP161

KIDNEY FUNCTION IN VISCERAL OBESITY IS NOT RELATED TO THE ADIPONECTIN

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MP158

ACUTE KIDNEY INJURY AFTER OFF-PUMP CORONARY ARTERY BYPASS SURGERY

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Introduction and Aims: To investigate the risk factors of acute kidney injury (AKI) after off-pump coronary artery bypass graft (OPCAB), develop a clinical predictive score and validate its discrimination and calibration.

Methods: Clinical data of 1513 patients undergoing coronary angiography (CAG) and OPCAB from June, 2010 to December, 2011 at Beijing Anzhen Hospital were retrospectively analyzed. All the patients were divided into AKI group and non-AKI group. Univariable analysis and multivariate logistic regression analysis were used to establish the predictive score.

Results: 436 patients (28.8%) developed AKI. In a multivariable model about AKI included: increased age, male, hypertension, diabetes, New York Heart Association class III or IV, lower estimated glomerular filtration rate (eGFR), shorter time interval between CAG and elective OPCAB, much numbers of grafts, intraoperative or postoperative intra aortic balloon pump, longer postoperative hypotension time, larger dosage of loop diuretics. The predictive model was discriminated well (ROC=0.71) and had well calibrated according to the Hosmer-Lemeshow test (P=0.30).

Conclusions: We developed a clinical predictive score for AKI after CAG and OPCAB. This predictive score presented good discrimination and calibration.

MP164

ASSOCIATION BETWEEN QUALITY OF LIFE AND DEPRESSION IN PATIENTS ON CHRONIC HEMODIALYSIS

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Introduction and Aims: To investigate the relationship between quality of life (QoL) and depression in patients on chronic hemodialysis.

Methods: We conducted a cross-sectional study with 100 patients on chronic hemodialysis. Depression was assessed with the Beck Depression Inventory (BDI). QoL was evaluated with the Short Form 36 (SF-36). The study was approved by the Ethics Committee of the local hospital.

Results: 16% of patients presented depression. A lower QoL in physical and mental health domains was observed in depressed patients compared to non-depressed patients. No significant differences were found in demographic and clinical characteristics between the two groups.

Conclusions: Depression is common in patients on chronic hemodialysis and is associated with a lower QoL. Further studies are needed to investigate the potential mechanisms underlying this relationship and to develop interventions to improve QoL in these patients.
Introduction and Aims: The World Health Organization (WHO) states that the prevalence of chronic non-communicable diseases (NCDs) is increasing in most developing countries. It is estimated that in Brazil there are about twenty-five million people living with NCDs. The DRC is included in this group and is currently a significant public health problem, affecting the quality of life of patients and the incidence of mood disorders. The objective of this study was to assess the level of quality of life (QOL) and the presence of depression in patients with chronic kidney disease (CKD) on hemodialysis chronic (4 h/session/3 times/week).

Methods: Patients of two dialysis clinics in São Paulo, Brazil, (n=100) took part in the research. They all answered an informed consent (IC), the Kidney Disease Quality of Life Short Form (KDQOL-SF26) and Beck Depression Inventory (BDI).

Results: 48% were male (n = 48) and 52% female (n = 52). Mean age was 55.14 years, standard deviation (SD) = 14.43; Age = 24-85. 14% of hemodialysis patients had reduced quality of life associated with depressive symptoms. Among them, 73% had levels of poor quality of life. It is noteworthy that patients who did not have depressive symptoms, have a better quality of life (19% very good and 79%, good).

Conclusions: The quality of life is preserved in patients with CKD undergoing chronic hemodialysis treatment. However, the presence of depression in these patients is associated with poor quality of life. We can consider depression as a predictor of poor quality of life in patients with CKD on chronic HD.

### MP165 IMPACT OF LIVER RESECTION ON PORTAL VENOUS PRESSURE AND RENAL FUNCTION

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Introduction and Aims: Liver dysfunction – in correlation to the severity of functional impairment – but also any increase in portal pressure per se (“hepaticorenal reflex”) can induce alterations in renal function and ultimately result in hepatorenal syndrome (HRS). In this prospective investigation we determined the impact of liver resection on portal venous pressure by measuring the hepatic venous pressure gradient (HVPG), on concentrations of vasoactive peptides and on renal function.

Methods: Twenty patients (mean age 66.3 years) undergoing elective liver resection surgery because of malignant tumor were assessed and grouped according to resection size: (1) hemihepatectomy, n=13 vs. (2) segmentectomy, n=7. HVPG was measured before and after resectionary canulation of a hepatic vein under fluoroscopic guidance, liver function was assessed by indocyanine green plasma disappearance rate (ICG-PDR).

Results: HVPG increased in group 1 from 3.7 to 5.4 mmHg (p<0.05) and decreased in group 2 (4.8 to 4.3 mmHg, p=ns) (table). Liver function as assessed by ICG-PDR decreased in group 1 during operation. Group 2 showed a significant rise only in ADH and dopamine. Acute kidney injury occurred in 5 of 13 patients in group 1, including (p<0.05) in group 1 during operation. Group 2 showed a significant rise only in ADH and dopamine. Acute kidney injury occurred in 5 of 13 patients in group 1, including two patients developing renal and liver failure. These two patients required dialysis and extracorporeal liver support and eventually died on day 5 and 15, respectively.

Conclusions: Depending on resection size liver resection acutely increases portal venous pressure and induces neurohumoral activation resulting in compromised renal function and increased risk of developing AKI.

### MP166 ISCHEMIA MODIFIED ALBUMIN AND ACUTE KIDNEY INJURY IN PUMP-ON CARDIAC SURGERY

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Introduction and Aims: Neutrophil gelatinase-associated lipocalin (NGAL) is one of the biomarkers of acute kidney injury (AKI). Ischemia Modified Albumin (IMA) is a new marker used to detect acute ischemic events. The aim of our study was to determine the role of IMA in the development of AKI and/or IMA is a marker of AKI in patients undergoing pump-on cardiac surgery.

Methods: This is a prospective study of patients who were underwent pump-on cardiac surgery due to coronary artery bypass grafting and/or cardiac valve surgery. AKI defined according to KDIGO AKI guideline. Blood samples for measurement of IMA, NGAL and creatinin levels were collected prior to cardiac surgery (0h) and in the time course on 2nd, 12th and 24th hours after conducted surgery (2h 12h and 24h respectively), and neutrophil-to-lymphocyte ratio (NLR) was calculated from hemogram as well. Patients with developed AKI were divided in to two subgroups that had non progressed and progressed AKI. Criteria for progression of AKI included: the transition from the I stage to the II or III, from the II stage to the III stage and the beginning of CRRT.

Results: Forty eight patients (31 male, 17 female) were included to the study. After cardiac surgery 33 patients developed any stage of AKI, 22 of them non-progressed AKI, 11 – progressed AKI. The basal characteristics of patients showed in table. All of the markers significantly increased after cardiac surgery, but IMA and NLR levels not differed between groups. ROC analysis of 2nd hours markers showed that NGAL and creatinin had significantly large area under the curve (AUC) than IMA and NLR to predict AKI developed at 24 hours.

Conclusions: IMA as well as NLR increased after cardiac surgery, but not predicted development of AKI.
**Introduction and Aims:** Aim of the present study is to estimate the actual dietary intakes (DI) of trace elements, minerals and vitamins in HD patients of three centers of one metropolitan and two urban areas of a Mediterranean country such as Italy.

**Methods:** The study was performed at the Hemodialysis Units of the following centers: Catholic University of Rome, Hospital “A. Murri” of Jesi and Hospital “Principe di Piemonte” of Senigallia. The study was performed in autumn. Dietary intake was recorded for three days by means of 3-day diet diaries starting on Monday for those undergoing HD on Monday/Wednesday/Friday and on Tuesday for those undergoing HD on Tuesday/Thursday/Saturday.

**Results:** One hundred and twenty eight patients were included in the study. The mean zinc DI was 7.6±5.4 mg. Most patients were under these recommended values (7-10 mg/d). The mean copper DI was 14.3±11.8 mg. Most patients had a DI higher than the recommended value (8.8-1.2 mg/d). The mean selenium DI was 28.8±18.15 mg. A DI of is recommended in the Italian general population and of 55 μg in HD. Most HD had a selenium DI under the recommended value (35-55 μg/d). The mean iron DI was 7.2±4.1 mg, 7.8±2.6 mg in women and 6.9±2.4 mg in men, much below the intake recommended. The mean phosphorus DI was 842.6±576.8 mg. Most HD had a phosphorus DI under the recommended value (800-1000 mg/d). The mean calcium DI was 371.8±363.7 mg. Most HD had a calcium DI under the recommended value (500-800 mg/d). The mean magnesium DI was 174.4±94.3 mg. The required intake of magnesium for HDP is unknown. Most HD had a magnesium DI under the recommended value. The mean potassium DI was 1616.2±897.3 mg. Most HD had a potassium DI under the recommended value (1950-2730 mg/d). The mean sodium DI was 1350±1281 mg. Most HD had a sodium DI under the recommended value (2000-2300 mg/d). The mean daily vitamin A intake was 486±1544.6 μg. Most HD had a vitamin A DI under the recommended values (800 to 1000 μg/d in HDP). The mean daily vitamin B1 intake was 0.86±0.97 mg. Most HD had a vitamin B1 DI under the recommended value for HDP (1.1-1.2 mg/d). The mean daily vitamin B2 intake was 1.11±0.7 mg. Most HD had a vitamin B2 DI under the recommended value for HDP (1.1-1.3 mg/d). The mean daily vitamin B3 intake was 13.3±8.1 mg. Most HD had a vitamin B3 DI under the recommended value for HDP (14-18 mg/d). The mean daily vitamin C intake was 47.8±50.3 mg. Most HD had a vitamin C DI under the recommended value for HDP (75-90 mg/d). The mean daily vitamin E intake was 9.5±3.6 mg. Most HD had a vitamin E DI under the recommended value for HDP (8-10 mg/d).

**Conclusions:** In conclusion, the present study shows that many HD patients have daily dietary intake of trace elements and vitamins lower than the recommended values. Conversely, the daily dietary intake of copper is much higher.

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**References:**

1. Hemodialysis Service Catholic University Rome Italy, 2Hospital “A. Murri” Jesi Italy, 3Hospital “Principe di Piemonte” Senigallia Italy

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**MDP167 COMPARISON OF CIRCUIT COAGULATION AFTER AND BEFORE APPLICATION OF AN ANTI-CLOTTING FLOW-CHART. A RETROSPECTIVE MONOCENTRIC ANALYSIS**

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**Introduction and Aims:** Premature circuit clotting is a key problem in AKI patients undergoing CRRT. Prolonged Intermittent Renal Replacement therapy (PIRRT) represents a dialysis modality combining the detoxification and hemodynamic stability of CRRT with the advantage of conventional intermittent dialysis. However, an unpublished study in our Unit, pointed out a coagulation rate of almost 50% of dialysis sessions, and tried to elaborate a flow-chart to avoid circuit clotting and down-time. This study aims to compare clotting episodes in two groups of PIRRT, after the introduction of the anti-coagulant flow chart.

**Methods:** A comparison between: (a) clotting episodes in all PIRRT performed in the period 2009-10 and (b) a sample of PIRRT in 2011-12 in 100 consecutive patients hospitalized in 4 Intensive Care Units (duration 8-12 hr, blood flow 200-250 ml/min, predilution 50-80%, no selection by filter membrane). The clotting rate in single patients was extrapolated, to highlight the improvement of treatment technique after the use of the flow chart.

**Results:** The 2 groups were comparable in terms of severity of illness, while sample sizes were different (1318 dialysis in 256 patients vs 898 in 100 patients), but compatible with the study’s aim. Patients characteristics were similar in both groups (68% vs 66% male; age 66.5 vs 59; septic patients 28 vs 20%). An important difference between the two groups is the average number of dialysis sessions/patient (5 vs 9).

**Conclusions:** Introduction of the anti-coagulant flow chart allowed to significantly reduce clotting rate, also in case of sepsis, catheter malfunction and impossibility to heparinize circuit. This is a preliminary analysis, of about half treatment performed in our Unit. The final aim will be to correlate the reduction of clotting rate to each point of the flow-chart.
Introduction and Aims: Urinary Tract Obstruction (UTO) is an important cause of renal impairment, which may progress to chronicity. The factors involved in recovery of renal function are not yet fully studied. The aim of this study was to evaluate the factors associated with recovery of renal function after obstruction relief.

Methods: Patients bilateral UTO, diagnosed by image methods, submitted to relief procedure at a referral center. The glomerular filtration rate (GFR) was estimated by MDRD.

Results: Overall, 130 patients (73% men) were prospectively included over a period of 9 months, with a mean age of 65.8 ± 16.5 years. The main comorbidities were hypertension in 46.2% and Diabetes Mellitus in 18.5% of cases. Direct malignant infiltration was the cause of UTO in 30.8% of patients. The average period of hospitalization was 13 ± 6 days. Dialysis was required in 54.6% of cases and mortality rate 13.1% of the patients. At hospital discharge, maintenance dialysis was required in 27/113 patients (23.9%). The independent risk factors for mortality were neoplastic obstruction (OR: 95% CI: 7.2-22.4, p <0.001) and need of dialysis during hospital stay (OR: 18.08 95% CI: 4.65-32.89, p <0.001). Partial renal function recovery (eGFR>30mL/min/1.73m²) occurred in 46/113 patients (40.7%) and eGFR> 60mL/min in only 18/113 patients. Patients with partial recovery of renal function (eGFR>30mL/min) were younger (62.2±16.1 vs. 69.6±14.7 years, p = 0.019) and had non-tumoral causes of obstruction more frequently (79 vs. 60%, p=0.03). Need for dialysis was similar between in patients with or not partial renal function recovery (40.7 vs. 45%, p=ns), however patients with partial renal function recovery needed less dialysis sessions (1.14±0.81 vs. 3.78±1.42 sessions, p <0.001). No differences were observed in admissional serum Cr (8.2 ± 5.5 vs. 7.2 ± 4.6mg/dL, p=0.315) nor serum urea (184 ± 89 vs. 173 ± 79mg/dL, p=0.04) between groups. The degree of pelvis dilatation and cortical thickness were not associated with renal function recovery.

Conclusions: UTO has a high mortality rate, mainly in patients with neoplasia obstruction causes. Partial renal function recovery occurs in less than half of the cases, being associated with age and obstruction cause. Severity of renal impairment at admission is not associated with recovery of renal function, as evidenced by similar need of dialysis and similar levels of serum Cr on admission.
**EPIDEMIOLOGY - CARDIOVASCULAR OUTCOMES**

**MP170**

THE EFFECT OF VITAMIN K2 SUBSTITUTION ON Atherosclerosis and Vascular Calcification MARKERS in NON-DIALYZED PATIENTS in CHRONIC Kidney Disease STAGE 3-5

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Introduction and Aims: The prospective, randomized study was designed to compare the effect of oral administration of vitamin K2 plus low-dose vitamin D or vitamin D alone on the progression of coronary artery calcification score (CACS) and common carotid intima media thickness (CCA-IMT). Methods: 42 non-dialysis patients with CKD stage 3-5 and CACS≥10 Agatston units were randomized into two treatment arms: group K received daily vitamin K2 plus 10 μg cholecalciferol or 10 μg cholecalciferol (group D); for 270 days. CCA-IMT and CACS were measured at baseline and at the end of treatment, along with serum mineral parameters, lipids, 25-hydroxyvitamin D (25OHD) and calcification modulators: matrix Gla protein (MGP), osteoprotegrin (OPG), fetuin A, osteocalcin (OC) and fibroblast growth factor (FGF-23).

Results: A significant increase of CCA-IMT during the intervention period was noticed in both groups (in K+D from 0.95±0.2 at the beginning to 1.01±0.3 mm, p=0.005 at the end of the study and in D group from 1.02±0.2 to 1.16±0.2 mm, p=0.008). The change of CCA-IMT during the treatment was smaller in K+D than in D group (0.063±0.07 vs 0.14±0.05 mm, p=0.006; 6% vs 13.8, p=0.02). A significant increase of CACs was noted in both treatment arms but the change of CACS (ΔCACS) was numerically but not significantly lower in K+D than in D group (58.1±106.5 vs 74.4±127.1 A.u.). When the patients with CACS≥100 at baseline were excluded from the analysis, the difference of ΔCACS between both treatment groups was at the border of statistical significance (18.2±29.1 vs 39.2±49.8, p=0.06, respectively). Total serum MGP tended to increase during the supplementation with vitamin K+D (from 63.3±41.4 to 56.5±42.0 ng/mL, p=0.03). In contrast, in K+D group the serum concentration of OC decreased (from 63.3±41.4 to 56.5±42.0 ng/mL, p=0.03). In multiple regression analysis the variability of serum MK-4 levels in HD patients (N=42) were explained by consumption of vitamin K2 (r=0.38, p=0.04) and vitamin D (r=0.40, p=0.03, respectively). Other consumption like calcium, phosphate, sodium and potassium content were assessed on addition to monthly, routinely measured parameters. Daily energy intake and dietary vitamin K1, K2, calcium, phosphate, sodium and potassium content were assessed on the basis of 3-day food record.

Conclusions: Decreased vitamin K2 consumption, mainly as a result of milk products intake, may explain markedly lower serum MK-4 concentrations in haemodialysis patients.

**MP171**

VITAMIN K2 (MENAQUINONE) INTAKE AND ITS SERUM CONCENTRATION IN HAEMODIALYSIS PATIENTS

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Introduction and Aims: Vitamin K2 (menaquinone-4, MK-4) deficiency seems an important risk factor for vascular calcification in dialysis patients. The optimal daily intake as well as the serum concentrations reference value for vitamin K2 in haemodialysis patients (HD) have not been yet determined. The aim of the present study was to assess the daily intake and serum concentrations of vitamin K2 in HD patients.

Methods: 85 stable, prevalent HD patients (51 males and 34 females) and 22 apparently healthy subjects (9 males and 13 females) with normal kidney function (control group) were included into the study. The study protocol assumed measurement of serum MK-4 concentration by HPLC (sensitivity 0.055 mg/mL) in addition to monthly, routinely measured parameters. Daily energy intake and dietary vitamin K1, K2, calcium, phosphate, sodium and potassium content were assessed on the basis of 3-day food record.

Results: Daily vitamin K2 consumption in HD patients and the control group was similar, while the level of vitamin K2 was significantly lower (by 29%) among HD patients due to lower milk product intake. Serum MK-4 concentration was detectable in 59 of 85 HD patients (59%) and in 21 out of 22 control group subjects (95%). The difference was statistically significant (p<0.001). The detectable serum MK-4 levels were significantly lower in HD patients than in the control group (by 42%; p<0.001). The correlation between serum MK-4 levels and both vitamin K2 and K1 daily consumption in HD patients (r=0.38, p=0.01 and r=0.30 p=0.05, respectively) was weaker than in the control group (r=0.47, p=0.03 and r=0.45 p=0.04, respectively). In multiple regression analysis the variability of serum MK-4 levels in HD patients (N=42) were explained by daily vitamin K2 (β=0.389 (0.001-0.617), p=0.05) but not K1 consumption (β=0.187 (-0.120-0.494), p=0.24).

Conclusions: Decreased vitamin K2 consumption, mainly as a result of milk products intake restriction, may explain markedly lower serum MK-4 concentrations in haemodialysis patients.

**MP172**

DOES VKORC1 POLYMORPHISM INFLUENCE CORONARY ARTERY CALCIFICATIONS in CHRONIC KIDNEY DISEASE PATIENTS?

Marion Morena1,2, Jean-Paul Cristol1,2,3, Isabelle Jaussent1, Leila Cherinin2, Célia Bruguesrole2, Hélène Leray-Moragues5, Jean-François Schwetz2, Bernard Canaud6,5,4, Anne-Marie Dupuy1 and Muriel Gianisli-Biaizot2

1Laboratoire de Biochimie CHRU Lapeyronie Montpellier France, 2Laboratoire d’Hématologie CHRU St Eloi Montpellier France, 3U 1061 INSERM Montpellier France, 4RDF Montpellier France, 5Service de Néphrologie, Hémodialyse et Soins Intensifs CHRU Lapeyronie Montpellier France, 6UMR 204 Nutripass Université Montpellier 1 Montpellier France

Introduction and Aims: Vitamin K epoxide reductase complex subunit 1 (VKORC1) haplotype combinations were found to be associated with the risk of developing vascular diseases. The C-allele of polymorphism rs339612 (VKORC1: c.283+387C>T) in the VKORC1 gene has been proposed to represent a major risk factor for coronary heart disease, stroke, and aortic dissection in Chinese non uremic patients. Chronic kidney disease (CKD) patients develop two to five times more widespread vascular calcifications than healthy age-matched subjects. However, to date no study reported any effect of VKORC1 genetic polymorphism on arterial calcifications in this population.

Purpose of this study was therefore to evaluate the risk of arterial calcifications associated with this polymorphism in CKD patients.

Methods: One hundred and ninety non dialyzed CKD patients (111M/79F, median age: 71 [27-95]) at various stages of kidney disease were tested for VKORC1 genotyping.

Results:VKORC1 c.283+387C>T allele

<table>
<thead>
<tr>
<th>Cases (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CC CT TT</td>
<td></td>
</tr>
<tr>
<td>A+837C&gt;T</td>
<td>0.098</td>
</tr>
<tr>
<td>CC CT TT</td>
<td>0.098</td>
</tr>
</tbody>
</table>

Conclusions: T allele of vitamin K2 haplotype (haplotype A) presented a tendency to higher atheromatous plaque after adjustment for confounder factors (p=0.098). By contrast, no association between VKORC1
polymorphism and both calcium scoring (p=0.28) and CV history (p=0.24) was observed.

Conclusions: Our results showed that in CKD patients, contrary to Chinese non uremic subjects, the VKORC1 polymorphism is not associated with a higher risk of coronary calcifications. These data have to be further confirmed by larger sample size studies.

Results: CKD group (n=54) suffered reduced patency rate compared with control group (n=67) (68.7 vs. 84.5% at 6 months, 55.8 vs. 76.6% at 12 months after revascularization respectively, p<0.01). One-year amputation-free survival rate showed the tendency to decrease in CKD group (88.4% vs. 92.1%, p=NS). Critical limb ischemia and eGFR < 60/m/min/1.73 m² were significant predictors of loss of patency after revascularization of PAOD in CKD patients (HR=2.65, 95% CI: 1.29-5.45; P<0.01, HR=2.15, 95% CI: 1.03-4.50; P<0.05, respectively).

Conclusions: Patients with CKD showed significantly lower patency rates after revascularization for PAOD. The presence of critical limb ischemia and chronic kidney disease (eGFR < 60/m/min/1.73 m²) could be used to identify the patients who are at risk for reduced patency rate after revascularization.

Introduction and Aims: Calcific uremic arteriolopathy (CUA, calciphiaxyis) is a rare disease (ORPHA380062) and devastating condition associated with high morbidity and mortality. CUA is characterized by painful, ischemic, partly necrotic skin ulcerations. Pathomorphologically, media calcification of cutaneous arterioles and extracellular matrix remodeling are the hallmarks of the disease. Little is known about the exact incidence and risk factors are only partially established. The aim of the German calciphiaxyis registry (www.calciphiaxyis.de) is to collect data concerning incidence and risk factors for CUA. We try to gain overview about current treatment strategies and link them to the clinical course. Serum analyses will particularly aim at the assessment of the role of inflammation as well as calcification inhibitors and inducers. This data collection is intended to be the basis for future prospective treatment trials.

Methods: We established an international internet-based registry in 11/2006 to allow online notification for all cases of established or suspected CUA. A comprehensive data base including various parameters concerning CUA and its clinical background and presentation as well as therapeutic strategies was established. Follow-up of the patients is planned by regular queries of long-term outcome. The diagnosis of CUA is made on clinical and/or histological grounds by the referring physician.

Results: Altogether 179 patients with CUA have been documented in 6 years: 60% females; 154 (85%) dialysis (HD and PD) patients, median age 67 (21-88) years; Stored serum samples were used for central laboratory analysis in core facility in n = 92 dialysis patients: PTH levels varied broadly between undetectably low and > 1100 pg/ml, mean 191 ±176 pg/ml; fetuin-A 0.21±0.01 g/L; Fetuin-A levels in control HD pts without CUA were significantly higher (n=65; 0.46±0.1 g/L, p<0.01). Oral anticoagulation with Vit K antagonists was common in ESRD CUA pts (47%). Cutaneous lesions were localized in 79% at the lower extremities or gluteal region. Among the most frequently observed infections, heart failure, autoimmune disease, hypercalcaemia, vitamin D treatment, however it is unclear whether it would be also significantly effective to CKD patients.

This study examined the effect of cholecalciferol supplementation on vascular function and circulating biomarkers in non-diabetic, CKD patients with low vitamin D. Methods: We assessed patients with CKD stage 3/4, aged 17-80 years and 25-hydroxy vitamin D levels < 30 nmol/L in the absence of diabetes, malignancy, infection, heart failure, autoimmune disease, hypercalcaemia, vitamin D treatment, recent MI or CVA. Flow mediated dilatation (FMD) of the brachial artery, pulse wave velocity and circulating blood biomarkers were evaluated at baseline and at 16 weeks. 300,000 units of cholecalciferol were administered at baseline and at 8-week follow up.

Results: Clinical characteristics of 26 recruited patients were: age 50±14 years, eGFR 41 ±11 ml/min/1.73 m², males 73%, dyslipidaemia 36%, smokers 39% and hypertensives 87%. At 16-week follow up vitamin D and calcium levels increased (43±16 to 84±29 nmol/L, p=0.000 and 2.37±0.09 to 2.42±0.09 mmol/L, p=0.004, respectively) and parathyroid hormone decreased (10.8±8.6 to 7.4±4.4; p=0.001). The eGFR, systolic and diastolic blood pressures did not change. FMD improved from 3.1±3.3% to 6.1±3.7%; p<0.001 (Figure 1). The pulse wave velocity (7.9±1.9 vs 7.7±2.2; p=0.59), augmentation index (22±16 vs 18±20; p=0.55) and central pulse pressure (33±14 vs. 35±14; 0.35) remained same (Figure 2). Endothelial biomarker concentrations decreased: E-Selectin from 566±2123 to 525±6208 pg/mL; p=0.032, ICAM, 3.45 ±0.01 to 3.10±1.04 ng/mL; p=0.038 and VCAM, 54±33 to 42±33 ng/mL; p=0.006, respectively. The levels of hsCRP, interleukin-6 and interleukin-10 levels remained unchanged.

Conclusions: This study demonstrates for the first time an improvement of endothelial function and blood biomarkers with vitamin D in non diabetic CKD patients; without any change in arterial stiffness. A randomised trial with larger number of patients and longer follow up is required to confirm the important findings of the present pilot study and established whether these are associated to improved patient outcome.

MP175 VITAMIN D THERAPY AND VASCULAR FUNCTION IN CKD

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St C. Georges Healthcare NHS Trust London United Kingdom, 1St Georges, University of London London United Kingdom, 2Guys’ and St Thomas’ Hospital NHS Foundation Trust London United Kingdom

Introduction and Aims: Cardiovascular events are frequent and vascular endothelial function is abnormal in patients with chronic kidney disease (CKD). We previously demonstrated endothelial dysfunction with vitamin D deficiency in CKD patients; however the impact of vitamin D supplementation on vascular function is unknown. This study examined the effect of cholecalciferol supplementation on vascular function and circulating biomarkers in non-diabetic, CKD patients with low vitamin D.

Methods: We assessed patients with CKD stage 3/4, aged 17-80 years and 25-hydroxy vitamin D levels < 30 nmol/L in the absence of diabetes, malignancy, infection, heart failure, autoimmune disease, hypercalcaemia, vitamin D treatment, recent MI or CVA. Flow mediated dilatation (FMD) of the brachial artery, pulse wave velocity and circulating blood biomarkers were evaluated at baseline and at 16 weeks. 300,000 units of cholecalciferol were administered at baseline and at 8-week follow up.

Results: Clinical characteristics of 26 recruited patients were: age 50±14 years, eGFR 41 ±11 ml/min/1.73 m², males 73%, dyslipidaemia 36%, smokers 39% and hypertensives 87%. At 16-week follow up vitamin D and calcium levels increased (43±16 to 84±29 nmol/L, p=0.000 and 2.37±0.09 to 2.42±0.09 mmol/L, p=0.004, respectively) and parathyroid hormone decreased (10.8±8.6 to 7.4±4.4; p=0.001). The eGFR, systolic and diastolic blood pressures did not change. FMD improved from 3.1±3.3% to 6.1±3.7%; p<0.001 (Figure 1). The pulse wave velocity (7.9±1.9 vs 7.7±2.2; p=0.59), augmentation index (22±16 vs 18±20; p=0.55) and central pulse pressure (33±14 vs. 35±14; 0.35) remained same (Figure 2). Endothelial biomarker concentrations decreased: E-Selectin from 566±2123 to 525±6208 pg/mL; p=0.032, ICAM, 3.45 ±0.01 to 3.10±1.04 ng/mL; p=0.038 and VCAM, 54±33 to 42±33 ng/mL; p=0.006, respectively. The levels of hsCRP, interleukin-6 and interleukin-10 levels remained unchanged.

Conclusions: This study demonstrates for the first time an improvement of endothelial function and blood biomarkers with vitamin D in non diabetic CKD patients; without any change in arterial stiffness. A randomised trial with larger number of patients and longer follow up is required to confirm the important findings of the present pilot study and established whether these are associated to improved patient outcome.
MP177

ATHEROSCLEROTIC PLAQUE CHARACTERIZATION AND HEME OXYGENASE-1 EXPRESSION IN CHRONIC KIDNEY DISEASE: THE 'VULNERABLE PLAQUE PHENOTYPE'

Kristen Daenen1, Inge Fourneau2, Eric Verbeek3, Marc F. Hoylaerts4 and Bert Bammens3

1Laboratory of Nephrology, Department of Microbiology and Immunology, KU Leuven, Leuven Belgium; 2Department of Cardiovascular Sciences, KU Leuven, Leuven Belgium; 3Laboratory of Nephrology, Department of Microbiology and Immunology, KU Leuven, Leuven Belgium; 4Molecular and Cellular Biology, Department of Cardiovascular Sciences, KU Leuven, Leuven Belgium

Introduction and Aims: CKD is characterized by accelerated atherosclerosis as compared to the general population. Heme Oxygenase-1 (HO-1), an inducible heme degrading enzyme with anti-oxidative, anti-apoptotic and anti-inflammatory properties is considered to be protective against atherosclerosis.

Methods: In patients planned for peripheral artery or aorta aneurysm surgery an arterial biopsy was retrieved during the procedure (n=82). We compared 23 biopsies of CKD patients with those of 36 non-CKD patients. Atherosclerotic plaques were scored blindly for lesion type (intimal thickening or xanthoma [IT] or IX, thin fibrous cap athroem [TJFCA] or fibrocalcific plaque [FCP]) according to a scoring system adapted from the AHA classification, presence of inflammatory cells and plaque complications (erosion, rupture, hemorrhage, not specified). HO-1 expression was judged semi-quantitatively on immunostained paraffin sections.

Results: CKD and non-CKD patients were well-matched for Framingham risk factors, cardiovascular event history and lipid lowering therapy. There was an equal distribution of lesion types in the 2 groups. Plaques of CKD patients showed higher inflammatory activity by higher number of foam cells. There were more complicated plaques in the CKD group. There was clear HO-1 expression, but the semi-quantitative scoring system didn't reveal any significant differences between CKD and non-CKD sections.

Conclusions: Atherosclerotic plaques of CKD patients show higher inflammatory activity and higher rates of complications, compared to non-CKD patients. These findings suggest a 'vulnerable plaque phenotype' of atherosclerosis in CKD. Expression of HO-1, assumed to play a role in plaque stabilisation, is comparable in the two groups. These findings suggest a relative lack of HO-1 effectivity in CKD.

Introduction and Aims: HO-1, an inducible heme degrading enzyme with anti-oxidative, anti-apoptotic and anti-inflammatory properties is protective against atherosclerosis. A functional (GT)n dinucleotide repeat polymorphism in the promoter region of the HO-1 gene has been reported to modify the susceptibility to atherosclerotic vascular disease: the short length allele has been linked to significantly increased HO-1 activity and protection against atherosclerosis an its complications.

Methods: Patients planned for PAD or abdominal aorta aneurysm surgery were asked for their consent to sample DNA for HO-1 genotyping (n=140). 42 patients with CKD stages 3 to 5 were compared with 88 patients without CKD for the present analysis. The HO-1 (GT)n dinucleotide repeat length was determined by fragment analysis on the ABI3730 sequence platform. Long (L) and short (S) alleles were defined as ≥25 and <25 repeats based on literature data. Patients were categorized as LL, LS or SS.

Results: The two patient groups were clinically well matched for Framingham risk factors, cardiovascular event history and lipid lowering therapy. Frequencies of HO-1 (GT)n dinucleotide repeat polymorphism categories are shown in the table. The overall distribution was comparable with the one seen in published data on patients with documented cardiovascular disease. Compared with non-CKD, however, the CKD group had a lower proportion of the LL and a higher proportion of the SS genotype (Chi2 P<0.05), which represents a shift towards the distribution seen in non-selected populations.

Conclusions: CKD and non-CKD patients with PAD show a different distribution of the HO-1 (GT)n dinucleotide repeat polymorphism. If confirmed in a larger cohort, the higher proportion of the "protective" SS genotype in CKD patients suggests that the effect of HO-1 is overruled by the burden of pro-atherogenic factors in these patients, or that the uremic environment may adversely affect the activity of HO-1, regardless of the genotype.

<table>
<thead>
<tr>
<th>Variable</th>
<th>No CKD (n=88)</th>
<th>CKD 3-5 (n=42)</th>
<th>CV disease</th>
<th>Non-selected (n=7647)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SS</td>
<td>8 (9%)</td>
<td>7 (17%)</td>
<td>12%</td>
<td>22%</td>
</tr>
<tr>
<td>SL</td>
<td>35 (40%)</td>
<td>23 (55%)</td>
<td>43%</td>
<td>57%</td>
</tr>
<tr>
<td>LL</td>
<td>45 (51%)</td>
<td>12 (29%)</td>
<td>43%</td>
<td>38%</td>
</tr>
</tbody>
</table>

** data retrieved from 15 papers.
Abstracts

Nephrology Dialysis Transplantation

**Methods:** The cohort included 33,125 subjects (22,297 males and 10,828 females), aged 33-60 years at baseline, in a representative, population-based study which enrolled subjects from 1974 to 1992, in the city of Malmo. Median follow-up time was 26 years. Every participant filled in a self-administered questionnaire on medical and personal history including family history of cardiovascular disease. Heredity for MI was defined as mother or father having had MI and/or died from MI, and/or brother or sister having had MI. Estimated GFR (eGFR) was calculated from serum creatinine using the CKD-EPI formula. Estimated GFR from serum creatinine was analyzed using kinetic albumin clearance away. There were no methodological changes during the study time. The impact of heredity was analyzed using both linear regression and binary logistic regression. A p-value less than 0.05 was considered as statistically significant.

**Results:** Data from CKD-EPI calculations show that 933/33125 (2.8%) of the whole cohort belong to CKD stages 2 and 3. Corresponding figures are 1.6% for males and 5.4% for females. Males with heredity for MI at the age of 43 years has a 2 times higher risk (p=0.02) of belonging to the group with GFR less than 45 ml/min/1.73m2 compared to those without heredity. For the whole cohort the increased risk was 1.6 times (p=0.07). Furthermore, in the whole cohort previous MI more than double-folded (HR 2.0, p<0.030) the risk of being in the group with GFR less than 60 ml/min/1.73m2. For males the HR was 2.1 (p=0.046), for women this was not significant. This was as an end-point at a cut-off of 45 ml/min/1.73m2 that seven-folded the risk (HR 9.2, p<0.001) for men but not significant for women.

**Conclusions:** Our findings point towards that genetic variants underlie predisposition to CKD in patients with MI. The association between MI and CKD was supported by our finding that males with previous MI demonstrated a nearly ten-fold of risk of belonging to CKD 3b or lower (<45 ml/min/1.73m2).

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**Abstracts**

**Title:** **SILENT CEREBRAL MICROBLEEDS PREDICT GLOBAL OUTCOME IN PATIENTS WITH CHRONIC KIDNEY DISEASE**

**Authors:** Hideaki Shimaa1, Tetsuo Shojib1, Yoshihide Nagamuraa1, Shinya Nakatanai1, Katsuhito Morii1, Eiji Ishimura1, Masanori Emott1, Mikio Okumura1, Tatsuuya Nakatani2 and Masaki Inahara2

**Institution:** 1Nephrology, Osaka Medical Center for Cancer and Excelence, Osaka, Japan, 2University of Osaka Japan

**Introduction and Aims:** Patients with chronic kidney disease (CKD) are at an increased risk of primary global outcome including cardiovascular and cerebrovascular outcome. Silent cerebral microbleeds (CMBs) by T2*-weighted magnetic resonance imaging (MRI) were reported to be a predictor of cardiovascular disease (CVD) in non-CKD populations. We previously reported that high prevalence of CMBs in CKD. However, the predictive value of CMBs for renal outcome is unknown. In the present study, we tested a hypothesis that CMBs predict poor global outcome in patients with CKD.

**Methods:** This is a prospective cohort study of consecutive 404 dialysis-independent CKD patients who underwent cerebral MRI including T2*-weighted images. We tested a hypothesis that CMBs predict poor global outcome in patients with CKD.

**Results:** Data from CKD-EPI calculations show that 933/33125 (2.8%) of the whole cohort belong to CKD stages 2 and 3. Corresponding figures are 1.6% for males and 5.4% for females. Males with heredity for MI at the age of 43 years has a 2 times higher risk (p=0.02) of belonging to the group with GFR less than 45 ml/min/1.73m2 compared to those without heredity. For the whole cohort the increased risk was 1.6 times (p=0.07). Furthermore, in the whole cohort previous MI more than double-folded (HR 2.0, p<0.030) the risk of being in the group with GFR less than 60 ml/min/1.73m2. For males the HR was 2.1 (p=0.046), for women this was not significant. This was as an end-point at a cut-off of 45 ml/min/1.73m2 that seven-folded the risk (HR 9.2, p<0.001) for men but not significant for women.

**Conclusions:** Our findings point towards that genetic variants underlie predisposition to CKD in patients with MI. The association between MI and CKD was supported by our finding that males with previous MI demonstrated a nearly ten-fold of risk of belonging to CKD 3b or lower (<45 ml/min/1.73m2).

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**Title:** **DIABETIC NEPHROPATHY IS AN INDEPENDENT RISK FACTOR FOR SEVERE SILENT ATHEROSCLEROTIC DISEASE**

**Authors:** Clara Barroso1, Sol Otero2, MaríaJosé Seco1, Eva Rodríguez1, Silvia Collado1, Anna Faura1, Sergi Moja1, Àngels Betriu1, Elvira Fernández1 and Julio Pascual2

**Institution:** 1Nephrology Hospital del Mar Barcelona Spain, 2Institute Mar for Medical Research Barcelona Spain, 3Nephrology Hospital Arnau de Vitanova Barcelona Spain

**Introduction and Aims:** Chronic kidney disease (CKD) and diabetes mellitus are well known risk factors for cardiovascular (CV) events. However, the contribution of different etiologies of primary renal disease such as diabetic nephropathy (DN) or vascular nephropathies (VN) with an increased risk of silent atherosclerotic disease (AD) has been scarcely evaluated.

**Methods:** In the prospective Spanish multicenter cohort NEFRONA study, we assessed 3040 subjects without any CV event: 2481 patients with CKD stages 2 to 5 and 559 controls with normal kidney function. Patients were divided according to primary renal disease in 4 groups: DN (n=357, 65% males, age 59.1±12.3y), VN (n=487, 66% males, age 56.3±11.9y), Glomerular/Systemic disease (n=463, 64% males, age 52.4±11.7) and other causes (n=1174, 59% males, age 56.7±12.6y). B mode and Doppler ultrasonography analysis of the carotid arterial walls were performed to measure intima media thickness (IMT, mm) and the presence of plaques. AD was scored according with the carotid ultrasonography findings. In a multivariate Cox models, a significant predictor of the composite endpoint independent of age, sex, hypertension, dyslipidemia, smoking behavior, diabetes mellitus, eGFR and urinary protein (HR 2.46, 95%CI 1.66-3.66). When CV and renal outcomes were separately analyzed, CMBs were not predictive of outcomes.

**Conclusions:** The presence of CMBs was a powerful and independent predictor of the composite CVD and renal endpoints in patients with CKD. Thus, CMBs predict poor global outcome in CKD.
Introduction and Aims: Renal tubular damage has an influence on renal deterioration, however the effect of renal tubular damage on mortality is unknown. To clarify this, we conducted a longitudinal study in community-based population.

Methods: Subjects of this study were 3443 Japanese over 40-year-old. Renal tubular damage was assessed using urinary beta 2-microglobulin-creatinine ratio (UBCR) in morning spot urine specimen. We investigated the association between the level of UBCR and mortality during 7-year observational period.

Results: At baseline, median value of UBCR was 112 μg/g, and high UBCR levels (≥200 μg/g) were detected in 394 (12.6%) subjects. During follow-up period, 138 deaths, including 41 cardiovascular deaths occurred. Kaplan-Meier analysis showed that all-cause, cardiovascular and noncardiovascular mortality was significantly increased along with an increase in UBCR values. The subjects with high UBCR showed significantly higher all-cause, cardiovascular and noncardiovascular mortality than those without it (P<0.05). Cox proportional analysis adjusted for age, gender, eGFR, albuminuria, and other confounding factors showed that high UBCR was an independent risk for all-cause mortality (hazard ratio 1.90, 95% confidence interval 1.10 to 3.29, P = 0.02).

Conclusions: This study revealed that renal tubular damage had a significant association with the mortality in general Japanese population.

**MP184 CELLULAR COMPONENTS OF THE IMMUNE SYSTEM CONTRIBUTE INDEPENDENTLY TO OVERALL MORTALITY IN CHRONIC KIDNEY DISEASE BEYOND THE CLASSIC MARKERS OF SYSTEMIC INFLAMMATION**

Ahad A. Abdalla1,2, Astrid Weiland1, Lian F. Casserly1, Cornelius J. Cronin1, Allish Hanning1, Hoang T. Nguyen1 and Austin G. Stack1,2

1Nephrology and Medicine University Hospital Limerick Limerick Ireland, 2Graduate Entry Medical School University of Limerick Limerick Ireland

Introduction and Aims: Systemic inflammation is common in chronic kidney disease (CKD) and predicts adverse clinical outcomes. The contribution of cellular components of the immune system to mortality remains unclear. The purpose of this study was to investigate the associations of the white cell count (WBC), lymphocyte (LYMPH) count and GRAN/LYMPH ratio with total and CV mortality in the setting of reduced kidney function.

Methods: A cohort of 15, 773 subjects age ≥20, representative of the U.S. population, were identified from the Third National Health and Nutrition Examination Survey (1988-1994). Vital status was obtained through linkage with the National Death Index conducted a longitudinal study in community-based population.

Conclusions: Cellular components of the immune system are significantly associated with mortality in CKD independent of classical measures of systemic inflammation. Incorporation of these simple measures into screening protocols for inflammation in CKD populations may yield important survival benefits.

**MP186 PULMONARY HYPERTENSION REFLECTS THE SEVERITY OF MYOCARDIAL DISEASE IN STAGE 2-5 CKD PATIENTS**

Davide Bolignano1, Rocco Tripodi1, Daniela Leonardis1, Francesca Mallamaci1 and Carmine Zoccali1

1CNR-Institute of Biomedicine and Molecular Immunology Reggio Calabria Italy

Introduction and Aims: Pulmonary Hypertension (PH) has a prevalence ranging from 19% to 60% in patients on dialysis (CKD-5D) and observational studies suggest that PH per se is a relevant risk factor for the exceedingly high cardiovascular (CV) mortality in this population. Left ventricular disorders and CKD-5D-related risk factors (e.g. volume overload, AV fistula, dialysis membranes and severe anemia) are implicated in PH in this population and kidney transplantation reverts pulmonary artery pressure (PAP) to normal in most patients. Although the risk for PH has been well-characterized in CKD-5D, only scattered data exist in the current literature in pre-dialysis CKD patients. In this study, we systematically screened an incident series of stage 2-5 CKD patients for PH and tested the relationship between PH and myocardial disease and background renal disease in the same population.

Methods: Eighty incident patients (50 M/ 30 F; age 60±11) with stage 2-5 CKD (median GFRMDRD :29 ml/min-1.73m2, IQ range 22-42 ml/min-1.73m2) were studied. Pulmonary Artery Pressure was estimated (ePAP) by Doppler echocardiography using a well-validated modified Bernoulli’s formula (1 Am Coll Cardiol 1985; 6:359–365) and PH was defined according to an established ePAP cutoff level ≥25 mmHg.

<table>
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<th>Variable</th>
<th>Total Population</th>
<th>CKD Population</th>
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<tbody>
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<tr>
<td>0-5.7 (referent)</td>
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</tr>
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<td>5.7-6.9</td>
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<td>1.48 (0.94-2.32)</td>
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<td>6.9-8.4</td>
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<td>1.66 (1.01-2.73)</td>
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<td>&gt;8.4</td>
<td>1.56 (1.11-2.20)</td>
<td>2.11 (1.39-3.18)</td>
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<tr>
<td>Lymphocyte count (10^3/L)</td>
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<tr>
<td>0-1.8 (referent)</td>
<td>0.62 (0.47-0.82)</td>
<td>0.77 (0.60-0.99)</td>
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<tr>
<td>2.2-2.7</td>
<td>0.50 (0.36-0.69)</td>
<td>0.74 (0.53-0.99)</td>
</tr>
<tr>
<td>&gt;2.7</td>
<td>0.63 (0.44-0.89)</td>
<td>0.74 (0.53-1.03)</td>
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<td>Granulocyte/Lymph ratio</td>
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<td>1.45-1.91</td>
<td>0.91 (0.71-1.17)</td>
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<td>1.12 (0.90-1.40)</td>
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<td>1.57 (1.23-2.02)</td>
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**MP185 EVALUATION OF BLOOD PRESSURE CONTROL OF CHRONIC KIDNEY DISEASE PATIENTS PRIOR TO NEPHROLOGIST CARE IN JAPAN**

Shotaro Naito1, Soichiro Imori2, Tomokazu Okado2, Yumi Noda2, Tatemitsu Rai2, ShinichiUCHIDA1 and Sei Sasaki2

1Department of Nephrology Tsuchiura Kyodo General Hospital Ibaraki Japan, 2Department of Nephrology Tokyo Medical and Dental University Tokyo Japan

Introduction and Aims: We evaluated the status of blood pressure control of chronic kidney disease (CKD) patients not previously treated by nephrologists.

Methods: We analyzed the baseline characteristics of patients enrolled in our prospective cohort study of CKD stage 2-5 patients who had not previously been treated by nephrologists. We evaluated the achievement rate of the targeted blood pressure, i.e., 140/90 mmHg for the patients with urinary protein to creatinine ratio less than 0.15 g/g creatinine, and 130/80 mmHg for the patients more than 0.15 g/g creatinine. Blood pressure was measured using a standard sphygmomanometer at the first visit to nephrologist.

Results: (1) Of 1138 patients enrolled in this study, the prevalence of hypertension was 90.2%. 78.8% of the patients were treated with medications and 39.1% of the patients achieved the targeted blood pressure. (2) The rate of the patients using anti-hypertensive drugs and the number of the drugs taken by those patients increased as their CKD stage progressed. The rate of the patients taking anti-hypertensive drugs were 40.0% in CKD stage 2, 58.0% in stage 3a, 80.9% in stage 3b, 89.6% in stage 4, and 93.8% in stage 5. The average number of drugs was 1.7, and more than half of the patients of CKD stage 3b to 5 were taking multiple drugs. On the other hand, 26.5% of the patients achieving the targeted blood pressure were not prescribed with any anti-hypertensive drugs. (3) The patients achieving the targeted blood pressure had older age, high eGFR, low BMI, high serum albumin, low LDL-cholesterol, low triglycerides, low glucose, low intact PTH, and low proteinuria. Patients with the targeted blood pressure had low incidence of myocardial infarction and diabetes as complications. The patients achieving the targeted blood pressure were less likely to be prescribed with anti-hypertensive drugs, and the number of the drugs prescribed for them was significantly less than the uncontrolled patients. (4) Multivariable logistic regression analysis showed that patients with high urinary protein (≥0.15 g/g creatinine, OR 3.17; 95%CI 2.04-4.94) and high LDL-cholesterol (≥120 mg/dl, OR 1.53; 95% CI 1.10-2.12) were less likely to have controlled hypertension.

Conclusions: Blood pressure control in CKD patients was sub-optimal at the first visit to the nephrologists. Most CKD patients needed multiple anti-hypertensive drugs to control their blood pressure. However, a substantial number of CKD patients could not achieve the targeted blood pressure.
(35 mmHg). Parameters of Left Ventricular Mass (LVMI) index and volume overload/ LV diastolic dysfunction (Left Atrial volume, LAV) in patients with PH were compared with those in patients without PH.

**Results:** The median ePAP was 15 mmHg (IQR range 10-29). Only seven patients (8.7%) met the diagnostic criteria of PH and no association was found between PH and background renal disease. The prevalence of PH in stage 2-5 CKD patients was marginally higher than that reported in the general population (^3%) like in the Olmsted study (Circulation. 2009;119:2663-2670) but substantially lower than that reported (19%-69 %) in a systematic review in CKD-5D patients (AJKD 2012 Nov 16. Ahead of print). Of note all patients with PH exhibited LVMI and LAV values exceeding the median value in CKD patients without PH, an observation pointing to cardiomyopathy as a mechanism conducive to PH at pre-diagnosis stages of CKD.

**Conclusions:** The incidence of PH among patients with CKD stage 2-5 is only marginally higher than that observed in population-based studies. PH in stage 2-5 CKD patients mainly reflects underlying LVHI and volume overload/diastolic dysfunction. PH should be regarded as an indicator of the severity of myocardial disease in these patients. Whether intensive surveillance of patients with PH and LVHI and enlarged LAV may translate into better clinical outcomes warrants further studies.

**MP187 THE INFLUENCE OF TISSUE FACTOR (TF) POLYMORPHISMS ON CORONARY CALCIFICATIONS IN CHRONIC KIDNEY DISEASE PATIENTS**

**Muriel Gianisly-Bliaut,** Isabelle Jaussent, Jean-Paul Cristol

**Methods:** A total of 138 non-diabetic CKD patients were enrolled and each patient gave written permission for the study. Average level of serum glucose, GA and HOMA-IR in subjects with PH were compared with those without PH. The study cohort comprised 165 patients (50%) with atherothrombotic cervical disease, 71 (21%) with lacunar infarction and 96 with other subtypes. The prevalence ratio of atherothrombotic to lacunar infarction was 1.8 in Group A, and 3.7 in Group B (p = 0.025). The mean intima-media thickness of the common carotid artery was 1.8 ± 1.0 mm in Group A and 2.1 ± 1.2 mm in Group B (p = 0.016). The prevalence of hypertension, diabetes, and dyslipidemia was comparable between the 2 groups. During the mean follow-up period of 1.6 ± 1.0 years, 13 patients (6.8%) died in Group A and 23 (16%) in Group B. A two-fold increased risk of death (age-adjusted hazard ratio 2.17, 95% confidence interval 1.10 - 4.48, p = 0.026) was observed in Group B compared with Group A.

**Conclusions:** Patients with decreased renal function tended to have thrombosis of a larger vessel and poor prognosis after cerebral infarction.

**MP189 ARTERIAL STIFFNESS IN NON-DIABETIC CHRONIC KIDNEY DISEASE PATIENTS ASSOCIATES WITH GLYCATED ALBUMIN**

**Hyeong-Cheon Park,** Seung Kyo Park, Jung Eun Lee, Sung Kyu Ha, Hoon Young Cho

**Introduction and Aims:** Patients carrying at least one copy of the TF-1208D allele 1 presented higher calcium scoring (r=0.02) after adjustment for confounding factors whereas a weak association (r=0.04) was observed with atheromatous plaques. No further adjustment was done since no relationship was evidenced. By contrast, no significant association between TF polymorphism and CV history was demonstrated.

**Conclusions:** These results suggest a role of TF in cardiovascular morbidity and mortality in CKD patients.
MP190 CONTINUOUS ERYTHROPOIETIN RECEPTOR ACTIVATOR (C.E.R.A.) DELAYS PROGRESSION OF KIDNEY DISEASE DUE TO EARLY SUPPRESSION OF GLOMERULOSCLEROSIS IN RATS WITH PROGRESSIVE GLOMERULONEPHRITIS

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1Product Research Chugai Pharmaceutical Co., Ltd., Gotemba Shizuoka Japan

Introduction and Aims: C.E.R.A. is a long-acting erythropoietin stimulating agent widely used to treat anemia in patients with chronic kidney disease. Although C.E.R.A. shows clinical benefits with respect to kidney disease in diabetic nephropathy models, the therapeutic effects on the progression of kidney disease have not been fully elucidated. In this study we aimed to investigate the renoprotective effect of C.E.R.A. in rats with progressive glomerulonephritis induced by anti-Thy.1.1 antibody and urinary protein excretion.

Methods: CGN rats (F344, male, 6 wk old) were established by injection of anti-Thy.1.1 monoclonal antibody (mAb: OX-7; 0.6 mg/kg, i.v.) after uninephrectomy (Day 0). C.E.R.A. (25 μg/kg, i.v.) was injected 24 h after the injection of the mAb. We evaluated changes over time in hemoglobin (Hb), blood urea nitrogen (BUN), and urinary total protein (uTP) after the induction of kidney disease. At Wk 20, we measured wet kidney weight (KW) and creatinine clearance (CCr). Renal cortical tissue was harvested at days 1, 4, 8, and 28 (n=8) for histological and RT PCR analysis. Glomerulosclerosis expressed as glomerulosclerosis index (GSI) was evaluated using 50 randomly selected glomeruli in PAS-stained sections. In addition, RT PCR analysis for extracellular matrix fibronectin and connective tissue growth factor (CTGF) were performed.

Results: First, we examined the effects of C.E.R.A. on changes in biochemical parameter of kidney function. In CGN rats (disease control: DC n=12), compared with sham-operated rats (Sham, n=6), significant increases in uTP and BUN and significant decrease in Hb was observed. On the other hand, C.E.R.A. treatment (C.E.R.A., n=12) significantly improved all of these parameters (DC vs. C.E.R.A., 2-way ANOVA followed by Bonferroni post hoc test). Furthermore, at Wk 20 there was a significant increase in kidney weight per body weight (KW/BW) and a significant decrease in Ccr in the DC group compared with the Sham group. C.E.R.A. treatment significantly suppressed the increase in KW/BW (DC 6.7±0.6; C.E.R.A. 5.4±0.4, p<0.05) and decrease in Ccr (DC 19.7% of Sham vs. C.E.R.A. 60.5% of Sham). Next, we assessed changes over time in GSI and mRNA expressions of CTGF and extracellular matrix fibronectin in the kidney. Elevated GSI was observed from Day 4 to 28. In contrast, C.E.R.A. suppressed the increase in KW/BW (DC 6.7±0.6; C.E.R.A. 5.4±0.4, p<0.05) and decrease in Ccr (DC 19.7% of Sham vs. C.E.R.A. 60.5% of Sham). Next, we assessed changes over time in GSI and mRNA expressions of CTGF and fibronectin at Day 4. However, there were no differences between the DC and the C.E.R.A. group in these mRNA levels after Day 8.

Conclusions: These results suggested that the treatment with C.E.R.A. inhibited progression of chronic kidney disease, resulting in improvement of anemia in rats with progressive glomerulonephritis. The amelioration of kidney function by C.E.R.A. might be in part due to early suppression of glomerulosclerosis.

MP191 CONTINUOUS ERYTHROPOIETIN RECEPTOR ACTIVATOR (C.E.R.A.) TREATMENT PREVENTS GLOMERULOSCLEROSIS AND SUPPRESSES ACTIVATION OF ALTERNATIVELY ACTIVATED MACROPHAGES IN A RAT MODEL OF ACUTE GLOMERULONEPHRITIS

Michinori Hirata1, Yoshihito Tashiro1, Koichi Endo1 and Ken Aizawa1
1Product Research Department Chugai Pharmaceutical Co., Ltd., Gotemba Shizuoka Japan

Introduction and Aims: Mesangial proliferative glomerulonephritis (GN) shows features typical of glomerular pathology, including expansion of mesangial cells and extracellular matrix, a critical cause of glomerulosclerosis. Macrophages infiltrating into the glomerulus are implicated in promoting kidney fibrosis, and alternatively activated (M2) macrophages play a critical role in the progression of glomerulosclerosis. C.E.R.A. is a long-acting erythropoiesis-stimulating agent (ESA) used to treat anemia, shows renoprotective effects in several models. However, the protective effect of C.E.R.A. on mesangial proliferative GN is not yet clear. We assessed the renoprotective effect of C.E.R.A. in an anti-Thy.1.1 antibody-induced GN (Thy1-GN) rats, a model of mesangial proliferative GN, and investigated whether C.E.R.A. suppresses the infiltration of macrophages.

Methods: Thy1-GN rats (F344, male, 6 wk old) were established by injecting anti-Thy.1.1 monoclonal antibody (OX-7; 0.6 mg/kg, i.v.). C.E.R.A. or darbepoetin-α (DA) (25 μg/kg, i.v.) was injected 4 h before induction of GN (day 0). At day 6, blood and urine were sampled for analysis of blood urea nitrogen (BUN) and plasma creatinine, urinary protein and N-acetyl-b-D-glucosaminidase (NAG). To evaluate the effects of C.E.R.A., kidneys were harvested for histological analysis and RT-PCR analysis.

Results: At day 6 after induction of GN, C.E.R.A. and DA significantly suppressed proteinuria in Thy1-GN rats (Normal, 2.6±0.2; Thy1-GN, 72.1±5.6; Thy1-GN+C.E.R.A., 48.8±4.1; Thy1-GN+DA, 47.4±2.5 mg/day; mean±SE, n=5–10). The increased BUN, plasma creatinine, and NAG in Thy1-GN rats were also significantly suppressed by C.E.R.A. and DA. Histologically, C.E.R.A. and DA significantly suppressed glomerulosclerosis index and expression of α-smooth muscle actin protein. C.E.R.A. also prevented upregulation of mRNA of extracellular matrix proteins such as collagen-1 and fibronectin in isolated glomeruli. Infiltration of macrophages, evaluated by immunohistochemistry staining of ED-1 in glomeruli, was significantly prevented by treatment with C.E.R.A. Expression of monocyte chemoattractant protein-1 mRNA in glomeruli was also inhibited by C.E.R.A. Expression of TNF-α mRNA (an M1 macrophage marker) was decreased in Thy1-GN rat glomeruli and not changed by C.E.R.A.; conversely, arginase-1 mRNA (an M2 macrophage marker) was markedly upregulated in Thy1-GN rats and significantly suppressed by C.E.R.A. (arginase-1/GAPDH, Normal, 0.2±0.01; Thy1-GN, 1.5±0.07; Thy1-GN+C.E.R.A., 0.8±0.1; mean±SE, n=5–8).

Conclusions: These results suggest the long-acting ESA, C.E.R.A., has a renoprotective effect in mesangial proliferative GN. Also, C.E.R.A. significantly prevented production of extracellular matrix proteins in the glomeruli of Thy1-GN rats. Suppression of macrophage infiltration in glomeruli, particularly M2 macrophages, may contribute to the renoprotective effect induced by C.E.R.A.
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SPC, especially significant when higher doses of previous ESA are required. 227 evaluable patients were included: 142 (63%) No D(ESA-naïve, n=31; maintenance,n=111) and 85 (37%) HD(ESA-naïve,n=2; maintenance,n=83). In naïve, previous epoetin beta and previous darbepoetin alpha dose (μg/week) conversion (mean ± SD). The exchange ratio of administration doses between EPO and DPO was based on equivalent peptide mass: 200 units (U) EPO to 1 μg DPO, as previously described. In the short-term study, six hemodialysis patients with stable Hb levels by EPO (3000 units x 3/week) were enrolled. After 4 weeks, EPO was switched to DPO (40 mcg weekly). No iron administration was done during the experiment. At each 6, 2nd, 4th, 7th and 28th days, serum Hb, Fe, TIBC, ferritin, Hepcidin-25 (by liquid chromatography tandem mass spectrometry), hs-CRP and IL-6 were measured.

Methods: Sixty patients with chronic kidney disease on hemodialysis (15M/5F, 60±14 years) and on peritoneal dialysis (17M/15 F, 59±15 years) without clinical manifestations of inflammation as well as twenty-nine healthy controls (10M/19 F, 66±16 years) were recruited. Serum hepcidin levels were measured by competitive ELISA method and high-sensitivity CRP by nephelometry.

Results: In PD patients, hepcidin levels were significantly higher than in NC (313.7±32.7 vs. 131.4±55.9 ng/ml, mean±SD, p=0.001), but did not differ from those of HD patients (300.1±38.6). CRP concentrations were significantly higher (p=0.001) in patients than in NC (1.35±0.14 mg/l vs. 4.28±3.70 in HD and 4.89±3.69 in PD). A Hepcidin in HD and PD patients was positively correlated to CRP (HD group: r=0.513, p=0.038 and PD group:r=0.384, p=0.0482).

Conclusions: Elevated hepcidin concentration in serum of peritoneal and hemodialysis patients may be associated to inflammation.

### MP194

**HEPCIDIN LEVELS SIGNIFICANTLY CORELATES WITH CRP IN PATIENTS ON HEMODIALYSIS AND PERITONEAL DIALYSIS**

Elisa Samouilidou1, Konstantinos Pantelias2, Dimitrios Petras3, Tzioula Mpakirtzi4, Chrisoula Pipli5, George Chatzivasileiou6, Kiraki Vasiliou4, Edmond Dendis7, Eirini Grapsa2 and Helen Tzanatos2

1Biochemistry Alexandra General Hospital Athens Greece, 2Nephrology Aretaieio Hospital Athens Greece, 3Advanced Medicine, Medical Research Institute Kanazawa Medical University Kanazawa, Japan, 4Protop Nephrologikio Kefalino Athonin Athens Greece

Introduction and Aims: Hepcidin is a small peptide produced by liver, which plays a significant role in the regulation of iron levels in plasma. It has been suggested that apart from anemia and iron metabolism, hepcidin levels can be affected by inflammation. In this study, hepcidin levels were assessed in serum of hemodialysis (HD) and peritoneal dialysis (PD) patients in comparison to healthy individuals (NC) and their correlation with C-reactive protein (CRP) was evaluated.

### MP193

**SUPERIORITY OF DARBEPOETIN-ALPHA TO ERYTHROPOETIC ACTIVITY BY HEPcidIN-25 RESPONSE**

Shigeichi Sogi1, Masaaki Inaba2, Naohisa Tomosugi3, Senji Okuno1, Mitsuri Ichihi, Tomoyuki Yamakawa1 and Satoshi Kurihara4

1Shirasagi Hospital Osaka Japan, 2Metabolism, Endocrinology and Molecular Medicine Osaka University Graduate School of Medicine Osaka Japan, 3Advanced Medicine, Medical Research Institute Kanazawa Medical University Kanazawa Japan, 4Saitama-Tsukinomori Clinic Saitama Japan

Introduction and Aims: Hepcidin is the key regulator of iron metabolism and is suppressed by erythropoietic activity (Pak M. et al. Blood 108:3735, 2006). The present study was conducted to demonstrate the better effect of longer-acting darbepoetin-alpha (DPO) than that of short-acting recombinant human erythropoietin (EPO) in hemodialysis (HD) patients from the standpoint of hepcidin metabolism. Methods: To assess the potency of DPO to mobilize iron from body stores in comparison with EPO in HD patients without apparent inflammation or infection, serum iron, transferrin saturation (TSAT), ferritin, and hepcidin-25 were measured serially. The present study included (i) a long-term crossover study for 3 years to compare the effects of the two ESA on serum iron, TSAT, and ferritin, and (ii) a short-term crossover study for 8 weeks to examine their effects on serum hepcidin-25 in HD patients. Twenty-eight uremic patients maintained on HD were enrolled in the long-term study. For the first year, all patients were maintained on twice weekly EPO injection with the target Hb level set between 10.0 and 11.0 g/dL. Then twice weekly EPO injection was replaced with a weekly DPO injection for two years thereafter. The exchange ratio of administration doses between EPO and DPO was based on equivalent peptide mass: 200 units (U) EPO to 1 μg DPO, as previously described. In the short-term study, six hemodialysis patients with stable Hb levels by EPO (3000 units x 3/week) were enrolled. After 4 weeks, EPO was switched to DPO (40 mcg weekly). No iron administration was done during the experiment. At each 0, 2nd, 4th, 7th and 28th days, serum Hb, Fe, TIBC, ferritin, Hepcidin-25 (by liquid chromatography tandem mass spectrometry), hs-CRP and IL-6 were measured.

Results: The long-term study demonstrated that the change of ESA from EPO to DPO significantly decreased serum ferritin while serum iron and TSAT remained unchanged, while DPO as well as EPO maintained hemoglobin level in the target range between 10.0 and 11.0 g/dL. In the short-term study, there was no significant change in

### MP193

**MINERVA Study**

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<th>Previous darbepoetin alpha dose (μg/week)</th>
<th>Previous epoetin beta dose (IU/week)</th>
<th>C.E.R.A dose at conversion (μg/month)</th>
<th>Conversion factor (95% CI)</th>
<th>C.E.R.A dose at conversion (mean ± SD)</th>
<th>Mean dose follow-up (mean ± SD)</th>
<th>p-value vs. SPC</th>
<th>p-value vs. conversion</th>
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### MP193

**Hemodialysis**

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<th>C.E.R.A dose at conversion (μg/month)</th>
<th>Conversion factor (95% CI)</th>
<th>C.E.R.A dose at conversion (mean ± SD)</th>
<th>Mean dose follow-up (mean ± SD)</th>
<th>p-value vs. SPC</th>
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### MP193

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Hb and ferritin in the EPO administration period. In the DPO period, Hb was increased (11.07±0.84 to 11.68±1.14 g/dL) and ferritin was decreased (105.7±61.8 to 52.5±36.9 ng/mL) significantly after 28 days. No significant change of hs-CRP and IL-6 was found in both period. Area under the percent change in serum hepcidin-time curve in DPO period was significantly greater than that in the EPO period (348.0±192.4 vs. 178.4±131.5 % day, p = 0.030).

Conclusions: DPO-alpha seems to be superior to EPO in erythropoietic activity by hepcidin-25 response.

Introduction and Aims: Renal anemia results from a combination of inadequate stimulation of erythropoiesis, iron deficiency and inflammation-induced defective iron mobilization from macrophages. As the interplay between erythropoietin (Epo), hepcidin and inflammation driven by the declining renal function induces in serum ferritin, higher serum ferritin can be attributed either to replete stores or to inflammation. We aimed to evaluate the relationships between hepcidin, erythropoietin, inflammation (C-reactive protein - CRP) and serum ferritin in anemic dialysis chronic kidney disease (CKD) patients.

Methods: One hundred sixty two non-dialysis patients with renal anemia, iron and erythropoietin free (52% males, 25% diabetes mellitus) entered this prospective single center study. Serum hepcidin and erythropoietin were measured by ELISA, and ferritin, transferrin and CRP, by immunoturbidimetric methods. TSAT was calculated as the percentage of serum iron from total serum iron binding capacity. Data are presented as mean (median) and 95% confidence intervals of the mean (median) and were logarithmated as appropriate for regression analysis.

Results: Hepcidin was higher in this cohort of an old age (67 [63-70] years), anemic (9 [9.2-9.8] g/dL) with advanced CKD (eGFR 14.2 [12.0-18.0] mL/min) and in laboratory and inflammation (CRP 7.6 [6.0-10.0] ng/mL) than reported in the general population (83.3 [76.3-94.5] vs. 18.2-22 ng/mL). Hepcidin levels were not influenced by gender and in bivariate analysis (Spearman's test) were inversely related to renal function (eGFR), serum ferritin levels, and directly to iron stores (ferritin) and available for erythropoiesis (transferrin), but were not significantly related with inflammation (CRP) (r= 0.32; rho -0.29; 0.29; 0.19 and 0.16, respectively). However, the correlations were not impressive. Thus, renal function, directly or via suppressed erythropoiesis production, and iron status seem more important than inflammation in defining hepcidin levels. The independent predictors of hepcidin were the decline in renal function (LnGFR -0.30 [-0.56 to -0.05]), the decrease in erythropoietin levels (LnEpo -0.36 [-0.57 to -0.14]) and the increase in serum ferritin (LnFerritin 0.28 [0.10 to 0.60]) in a model of logistic regression which explained only 23% of hepcidin variability. To note, CRP was not retained in that model.

Conclusions: The increase in hepcidin levels in CKD patients is related to the decline in renal function and is probably mediated by the decreased erythropoietin production. Hepcidin seems to reduce adequately to iron stores, and as this is reactive to independent of inflammation, high ferritin levels in CKD patients with moderate inflammation suggest iron store depletion rather than inflammation.

Results: Patients with IDA were younger (63 ± 70 years) and had a higher eGFR (18 ± 11.1 mL/min). Anemia was less pronounced in IDA (9.9 ± 8.8 g/dL), while indices of iron deficiency were noticeable: higher transferrin (222 [206-257]) vs. 194 (177-203) mg/dL), lower TSAT (12.5 [10.2-15.3] vs. 18.2 ± 16.7% ) and ferritin 310 [93-144] vs. 368 [282-492] ng/mL). Epo was higher in IDA (5.2 [4.2-6.4] vs. 4.8 [4.0-6.0] U/mL), and hepcidin lower (75.4 [60.5-84.5] vs. 98.7 [84.4-125.0] ng/mL). However, inflammation was similar (CRP 7.6 [5.0-10.6] vs. 9.0 [5.0-12.0] ng/mL). When modeled by binominal regression model, younger age (exp 0.96 [0.94-0.98]), lower Hb (exp 0.98 [0.98-1.02]), ferritin (exp 0.21 [0.11-0.38]) and TSAT (exp 0.35 [0.17-0.74]) were the independent predictors of IDA in 38% of cases (p<0.0001). In receiver operating curve analysis, ferritin had a best accuracy in differentiating IDA from AI than TSAT or hepcidin, as area under the curve were 0.84 (p<0.01), 0.68 (p=0.09), 0.65 (p=0.05) respectively, respectively (p=0.002). Cut-off values were 218/8 ng/mL for ferritin (substantially higher than the guideline recommendation), 95ng/mL for hepcidin and 16% for TSAT, but sensitivity and specificity were not impressive (0.76 (0.67-0.84) vs. 0.65 (0.55-0.74) and 0.85 (0.58-0.77), 0.57 (0.44-0.69), respectively). However, inflammation and serum ferritin in anemic patients, but peripheral iron indices and even hepcidin or erythropoietin measurements are of little help in their differentiation.

Conclusion: Iron deficiency and anemia of inflammation are prevalent in anemic renal patients, but peripheral iron indices and even hepcidin or erythropoietin measurements are of little help in their differentiation.

Results: Histological examination revealed iron sucrose exacerbated endogenous leukocyte-endothelium adhesion, especially in subtotal nephrectomized mice. Likewise, we demonstrated that parenteral iron administration significantly aggravated the fluorescence-labeled U937-endothelium interaction in mice with remnant kidney. In addition, we further induced the adhesion of mononuclear cells to aortic endothelium in mice with subtotal nephrectomy. Methods: Four mice groups were enrolled in this study: sham with saline, sham with iron sucrose, uremic mice with saline, uremic mice with iron sucrose, n=10 in each group. Mice with remnant kidneys were induced in 8-week-old male C57BL/6 mice using two-step subtotal nephrectomy. Eight weeks after the sham or subtotal nephrectomy, mice were recruited for peritoneal iron or saline injection. Iron sucrose (2 mg/25gm) or 0.9% saline were administered intra peritoneally once per day for 5 days. Later, the experimental mice were received in vivo fluorescence-labeled exogenous monocytic U937-endothelium assay, and mice aorta were further homogenized for measurement of tissue superoxide production by chemiluminescence and adhesion molecules by cell lysate ELISA.

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Abstracts

EMBASE (2004 to August 2012); the Cochrane Library (Issue 9, 2012) without language restriction. Two reviewers extracted details on participant characteristics, interventions, and risk of bias. We summarized treatment effects on mortality, doubling of serum creatinine, need for renal replacement therapy, reduction in GFR (mL/min) and withdrawal of treatment due to adverse events using random-effects meta-analysis.

Results: We included 13 trials including 7,854 participants enrolling any patient with CKD stages 1 to 4. By current methodological standards, trial quality was variable. There was no evidence that aiming higher Hemoglobin (Hb) targets affects effects on mortality (Risk Ratio [RR] 1.10 [CI 0.89-1.37], 13 trials, n=7,854 patients).

No statistically significant differences in the risks for end-stage kidney disease (RR, 1.03 [CI 0.80-1.32]) and reduction in GFR (Mean Difference [MD] -0.45 [-2.21, 1.16] trial corrected P=0.1848 patients were observed. Withdrawal of treatment due to adverse events (RR, 1.10 [CI 0.70 to 1.73], 6 trials, n=1,178 patients) or number of patients with at least one adverse event during the study (RR, 1.01 [CI 1.00 to 1.03], 8 trials, n=7,108 patients) showed no difference between groups. Of the 13 trials included only two small studies reported doubling of serum creatinine, both with positive results on the higher target arm (RR, 0.38 [CI 0.15 to 0.95], n=213 patients). The data available about hypertension and hospitalization were not consistent reported.

Conclusions: Our analysis of existing trials published after 2004 in patients with CKD treated with ESA have not found to have significant impact on end-of-treatment GFR or need for renal replacement therapy. On the basis of the evidence that we have marshalled, we do not think it is very likely that small alterations in Hb/haematocrit will influence CKD progression one way or another. No evidence for low dose chronic ESA having any cytoprotective effect.

MP200

IRON METABOLISM IN RESISTANCE TO RHEPO DUE TO THE DEVELOPMENT OF ANTI-EPO ANTIBodies IN A RAT MODEL OF CHRONIC RENAL FAILURE

Patricia Garcia1, João Fernandes2, Sandra Ribeiro3, Helena Vaz4, Belmiro Paraíso5, Rui Alves5, Luis Belo6, Elísio Costa7, Aílce Santos-Silva8 and Fábio Reis1
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Introduction and Aims: Chronic kidney disease (CKD) patients under recombinant human erythropoietin (rEPO) therapy, usually, present an anemia associated with iron related expression inducing an increase in iron absorption and mobilization to improve red cell aplasia, triggering hypoxia, it would be expected to observe changes in iron metabolism, which are enhanced in patients who develop resistance to rEPO (200IU). Serum iron content decreased significantly in CKD rats, which were further aggravated in the last 3 weeks; that deterioration was slightly prevented by rEPO (200IU). Cytokines, such as IL-6 and serum iron metabolism related expression inducing an increase in iron absorption and mobilization to improve red cell aplasia, triggering hypoxia, it would be expected to observe changes in iron metabolism, which are enhanced in patients who develop resistance to rEPO (200IU).

Results: Our analysis of existing trials published after 2004 in patients with CKD treated with ESA have not found to have significant impact on end-of-treatment GFR or need for renal replacement therapy. On the basis of the evidence that we have marshalled, we do not think it is very likely that small alterations in Hb/haematocrit will influence CKD progression one way or another. No evidence for low dose chronic ESA having any cytoprotective effect.

MP201

EVALUATING THE MAINTENANCE DOSE CONVERSION RATIO (DCR) IN ADULT HEMODIALYSIS (HD) PATIENTS SWITCHING FROM DARBEPOETIN ALFA (DA) TO PEG EPOETIN BETA

Bruno Fouqueray1, Maxime Hoffmann2, Janet Addison1 and Nick Mananmey1
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Introduction and Aims: Long-acting erythropoiesis-stimulating agents (ESAs) available for treatment of anaemia associated with CKD include darbeepoetin alfa (DA) and pegylated epoetin beta (PEG epoetin beta). These are erythropoiesis-stimulating agents (ESAs) available for treatment of anaemia associated with CKD. There is no published literature on the outcome of the conversion from DA to PEG epoetin beta, in a non-interventional setting. This retrospective observational study was designed to estimate a population mean maintenance dose conversion ratio (DCR) in adult haemodialysis (HD) patients converted from DA to PEG epoetin beta.

Methods: Eligible patients had been receiving HD for ≥12 months and DA for ≥7 months. Data were collected from 7 months prior to, until 7 months after, the date of conversion from DA to PEG epoetin beta with 2 evaluation periods (EP); pre-conversion (months 1 and 2 prior to conversion) and post-conversion (months 6 and 7 post-conversion). The DCR (mean weekly dose equivalent of DA in the pre-conversion EP) was calculated for patients who remained on PEG epoetin beta for 7 months post-conversion with ≥1 Hb value and an ESA dose in each EP; Hb could not differ by more than +/- 0.5 g/dl between the 2 EPs. Linear and quadratic regression were used to explore the relationship between mean weekly ESA dose pre- and post-conversion.

Results: Of 302 eligible patients enrolled at 12 sites in France, Germany, Spain and the UK, 206 were included in the DCR subgroup (mean age 62 years, 62% male; 67% with a history of cardiovascular disease and 32% with diabetes). The mean maintenance DCR was 1.17 (95% CI 1.05, 1.29), rising to 1.21 (95% CI 1.09, 1.35) when excluding patients who received a red cell transfusion within 90 days or during either EP. Best fit was obtained with a quadratic regression indicating a non-linear relationship between pre- and post-conversion ESA dose EPs.

Results: No evidence for low dose chronic ESA having any cytoprotective effect.

MP202

EVALUATING THE MAINTENANCE DOSE CONVERSION RATIO (DCR) IN ADULT HEMODIALYSIS (HD) PATIENTS SWITCHING FROM DARBEPOETIN ALFA (DA) TO PEG EPOETIN BETA

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**Conclusions:** In an HD patient population converted from DA to PEG epoetin beta, the dose of PEG epoetin beta required to achieve comparable Hb was ≥20% greater than the DA dose pre-conversion.

### MP203

**ANAEMIA IN HAEMODIALYSIS PATIENTS AND ULCER-LIKE ABNORMALITIES OF THE RED BLOOD CELLS MEMBRANE: BIOPSY OF PERIPHERAL BLOOD FILMS WITH THE ATOMIC-FORCE AND SCANNING-ELECTRON MICROSCOPES**

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1Institute of Advanced Materials, Physicochemical Processes, Nanotechnology and Microsystems National Center for Scientific Research ‘Demokritos’ Athens Greece, 2Department of Nephrology General Hospital of Athens, ‘G. Gennimatas’ Athens Greece, 3Dialysis Unit General Hospital of Athens ‘Areteia’ Athens Greece

**Introduction and Aims:** Three major factors contribute to anaemia in haemodialysis patients (HDp): reduced production of erythropoietin, iron deficiency and reduced lifespan of red blood cells (RBCs). The uraemic environment is considered responsible for the decreased lifespan of RBCs and overall worsening of anaemia. Since the biochemical interference between the uraemic toxins and the biomolecular constituents of cell membrane can probably motivate structural instabilities, in the present work we performed biopsy of intact RBCs (iRBCs) of HDp in comparison to healthy donors.

**Methods:** iRBCs of 14 HDp (N=863) subjected to 4-hour dialysis thrice a week and of 14 healthy donors (N=910) were studied with advanced microscopes. The iRBCs refer to freshly collected RBCs (in EDTA tubes) that are deposited onto glass slides in single-layered form with only minor treatment. The iRBCs were surveyed by means of two advanced microscopes, the Atomic Force Microscope (AFM) and Scanning-Electron Microscope (SEM). Both can selectively focus on the iRBCs membrane and reveal information at the nanometer level (1nm=10⁻⁹ m). Biochemical and hematological data were obtained with the standard clinical methods.

**Results:** The AFM and SEM data consistently revealed that the iRBCs membrane displays morphological abnormalities that have mainly circular shape and typical size ranging within 100 to 2000 nm, in both the HDp and healthy donors. These local morphological abnormalities of the iRBCs membrane have the form of ulcer-like deteriorations, thus are termed ulcer morphology abnormalities (UMA). The observation of UMA in the RBC membrane of healthy donors indicates that they possibly relate to physiological aging of RBCs. The population of UMA per iRBC is 3.4 and 5.0 in the healthy donors and HDp, respectively, evidencing a pronounced increase.47% (p<0.0001) in the latter group. This indicates that in the HDp the aging of RBCs is accelerated by mechanisms that relate to the underlying disease. To resolve if there is any connection with the clinical data we performed a straightforward comparison of the AFM and SEM data with the basic uraemic indices. It turned out that the population of UMA per iRBC exhibits a statistically significant correlation (r=0.05) with all Ut, Cr, Ca, P and Ca×P.

**Conclusions:** The correlation of the population of UMA per iRBC with all basic uraemic markers is a strong indication, if not proof, that uraemia motivates/promotes the structural deterioration of the membrane and as a consequence the premature elimination of these defected RBCs from the circulation, ultimately worsening anaemia.

### MP204

**COMPARABLE DOSES OF FG-4592 HAVE SIMILAR PK/PD IN HEALTHY CAUCASIAN AND JAPANESE SUBJECTS**

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**Introduction and Aims:** Anaemia affects >10 million patients with chronic kidney disease (CKD) worldwide. Only ≤10% of anaemic CKD patients are treated. FG-4592 is a novel oral hypoxia-inducible factor prolyl hydroxylase inhibitor being developed in the US, Japan, China, and Europe for treatment of CKD anaemia. We compared pharmacokinetic (PK) and pharmacodynamic (PD) profiles of FG-4592 in Caucasian and Japanese subjects in individual phase 1 open-label, single-arm, dose-escalation studies.

**Methods:** Healthy adults received single oral doses of FG-4592. Caucasian and Japanese subjects received weight-adjusted doses ranging from 0.3–4.0 mg/kg (n=20, and 30 respectively). Blood was sampled before dosing and 0.5–96 h after dosing.

**Results:** FG-4592 was well tolerated, treatment emergent adverse events (AEs) were mild to moderate, and no serious AEs were reported. Tables show FG-4592 PK parameters and PD effect of single dose FG-4592 on endogenous erythropoietin (eEPO). (Note: 1.6 and 2.0 mg/kg FG-4592 have been shown to result in robust haemoglobin response in patients with CKD anaemia).

**Conclusions:** The results suggest overall similar drug and circulating eEPO exposures in Caucasians and Japanese, slightly higher in Japanese subjects, compared to Causisan subjects. The PK parameters of FG-4592 after repeat dosing thrice weekly (TIW) is comparable to single dose, suggestive of a lack of drug accumulation, and comparative results will be reported in this presentation. Phase 2 and Phase 3 studies are underway globally in Asia Pacific, the US, and Europe.

### MP205

**FACTORs INFLUENCING THE FIRST DARBEPOETIN ALFA DOSING FREQUENCY CHANGE IN CKD PATIENTS NOT ON DIALYSIS**

Jan Gale1, Kathleen Claes2, Salvatore Di Giulio3, Alan Guerin4, Hans Herltz5, István Kiss6, Gerhard Wensberger7, Nick Manamley8, Janet Addisson8, Bruno Fouqueray9, Marc Froissart9 and Christopher Winesars9

1Klinikum Lüdenscheid Lüdenscheid Germany, 2University Hospitals Leuven Leuven Belgium, 3Ospedale San Camillo Forlanini Rome Italy, Clinique Mont Louis Paris France, 4Institute of Medicine, Sahlgrenska Academy Gothenburg Sweden, 5Fov. Onk. Szent Imre Korzah Budapest Hungary, 6Medical University of Graz Graz Austria, 7Amgen Cambridge United Kingdom, 8Amgen Zug Switzerland, 9Oxford Kidney Unit, Churchill Hospital Oxford United Kingdom

**Introduction and Aims:** The primary objective of EXTEND, a European/Australian observational study, was to assess the effectiveness of DA administered subcutaneously at extended dosing intervals (every 2 wk [Q2W] or every month [QM]) in CKD patients not on dialysis (ND-CKD). This subanalysis was performed to identify which factors may be associated with the first dose frequency change occurring after the first 3 months on extended dosing.

**Methods:** Multivariate logistic regression was performed to explore inter-current events occurring ≥120 days prior to the first DA dose frequency increase or decrease occurring ≥90 days after commencement of extended dosing with Q2W or QM. Analyses were performed for patients who were receiving ESAs in the 6 months before commencement of extended DA dosing (ESA prior) and those who were not (ESA naive).

**Results:** Of 6037 subjects enrolled, 2231 had sufficient covariate information to be included in the analysis. Independent factors influencing the first DA dose frequency increase (e.g. Q2W to QW, QM to Q2W) in ESA-naive and ESA-prior patients are presented in the Table. The results for factors influencing dose frequency decrease are reciprocal to the ones presented and are not shown.

**Conclusions:** Ha concentration <10 g/dL, low eGFR, hospitalization and RRT commencement were all positively associated with the first dose frequency increase. Low mean weekly dose and occurrence of ≥1 transfusion were also positively associated with dose frequency increase in ESA-naive subjects; receiving iron therapy was negatively associated with dose frequency increase in ESA-prior subjects.
Factors during the 120 days prior to dose frequency increase

<table>
<thead>
<tr>
<th>Factors</th>
<th>Odds ratio of dose frequency increase (95% CI), p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factors immediately before dose frequency increase</td>
<td></td>
</tr>
<tr>
<td>Hb (&lt;10 vs 10-12 g/dL)</td>
<td>6.352 (3.812, 10.586), &lt;0.0001</td>
</tr>
<tr>
<td>Mean weekly dose (above vs below median) eGFR (above vs below median)</td>
<td>0.713 (0.536, 0.959), 0.0254</td>
</tr>
<tr>
<td>Factors during the 120 days prior to dose frequency increase</td>
<td></td>
</tr>
<tr>
<td>Any transfusion (yes vs no)</td>
<td>4.282 (1.395, 13.145), 0.0110</td>
</tr>
<tr>
<td>Any iron usage (yes vs no)</td>
<td>1.664 (1.099, 2.520), 0.0162</td>
</tr>
<tr>
<td>Any hospitalization (yes vs no)</td>
<td>3.853 (1.897, 7.824), 0.0002</td>
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</tbody>
</table>

An odds ratio >1.0 indicates the odds of a DA dosing frequency increase is greater for level 1 vs level 2 of the factor. (·), variables not significant at the 5% level in the multivariate logistic regression.

Results: 32 patients with administration of IV iron carboxymaltose were analyzed with basal control and after 6 months. The mean age was 79 ± 9 years, with the following etiologies of renal disease: 12 nephroangiopathies, 8 not known, 5 diabetes, 4 interstitial and 3 glomerular. Eleven patients in turn received erythropoietic stimulating factors (ESF). The mean basal haemoglobin was 10.7 ± 1.2 g/dl at 6 months 27.0 ± 1.2 g/dl at 6 months 27.0 ± 1.2 g/dl 18.6 ± 4.6 g/dl with a basal hematocrit of 33.9 ± 5.6% and 6 months 39.4 ± 6.4% (p <0.001). The baseline ferritin and saturation index of basal transferrin at 6 months were respectively: 95.2 ng/ml, 11.1%, 291, 20 (p: 0.015, p: 0.002). Renal function remained stable, the mean serum creatinine (SCr) basal was 2.1 ± 0.6 mg/dl and estimated glomerular filtration rate measured by MDRD (GFR) of 29.9 ± 11 ml/min, SCr at 6 months 2.07 ± 0.5 and 29.8 ± 10 (p = ns). No patient experienced adverse reactions at the time of administration or within 24 hours. ESF necessities decreased but they were not statistically significant. There were no difference in phosphorus level.

Conclusions: The administration of iron carboxymaltose as a single IV dose in patients with chronic kidney disease appears safe and effective, allowing for a well-tolerated simple dosing, reduction the number of punctures, with minimal side effects.

### MP207

**UTILITY OF INTRAVENOUS IRON CARBOXYMALTOSE IN A SINGLE DOSE IN THE CONTROL OF ANEMIA IN CHRONIC KIDNEY DISEASE STAGE 3-4**

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1Nephrology Hospital U del Henares Coslada Madrid Spain

**Introduction and Aims:** The presence of anemia of multifactorial cause, with an iron deficiency component in chronic kidney disease is a common fact. Tolerance to oral iron supplementation is irregular, as well as its effectiveness in patients with advanced renal disease. There are several iv formulas with potential side effects and administration discomfort. The iron carboxymaltose allows for a simple dosage with few side effects which permits a good control of anemia.

**Methods:** Patients with chronic kidney disease on an outpatient basis of nephrology were included, with associated anemia and need for IV supplements. We proceeded to administer a single dose of intravenous iron carboxymaltose, for 15 minutes in 250 cc of 0.9% sodium chloride solution. The standard dose was 1000 mg, not exceeding 15 mg of iron per Kg of body weight.

**Results:** The presence of anemia of multifactorial cause, with an iron deficiency component in chronic kidney disease is a common fact. Tolerance to oral iron supplementation is irregular, as well as its effectiveness in patients with advanced renal disease. There are several iv formulas with potential side effects and administration discomfort. The iron carboxymaltose allows for a simple dosage with few side effects which permits a good control of anemia.

**Conclusion:** Few side effects which permits a good control of anemia.

**References:**


### MP208

**COMMON EFFECT OF ACE GENE I/D POLYMORPHISM AND ACE INHIBITION MODULATES ERYTHROPOIESIS IN CKD-5D PATIENTS**

Zoltán Kiss1, Lóránt Kerkovits1, Csaba Ambruš1, Imre Kucskár1, János Szegedi1, Attila Benkő1, Béla Borbás1, Sándor Ferenci1, Mária Hegyesi1, Szilvia Kazup1, Lajos Nagy1, József Németh1, Antal Rozinka1, Tamás Szabo1, Tamás Szüeszelé1, Zsófia Zöld1, Gábor Varga1, Gyula Wagner1, Gábor Zakar1, László Gergely1 and István Kiss1

1Department of Nephrology Royal Liverpool University Hospital Liverpool United Kingdom

**Introduction and Aims:** There is a debate about the association among ACE (angiotensin converting enzyme) gene insertion/deletion (I/D) polymorphism, inhibition of ACE and erythropoiesis. Therefore, this study aim was to prove the difference of erythropoietic rate between dialysed chronic kidney disease (CKD-5D) patients with II and DD genotype. We also tested how ACE inhibitor (ACEI) therapy can influence erythropoiesis and how it can modify the effect of ACE gene I/D polymorphism on erythropoietin need in CKD-5D patients.

**Methods:** It was a retrospective, multicentre observational study among 706 dialyzed patients. We allocated patients (II and DD genotype detected by PCR method) into match pair groups for statistical analysis. Based on patient’s similarities (age, DM, time on dialysis, ACEI therapy) we could find 127 matched patient pairs (II – DD genotype).

**Results:** In total haemoglobin (Hb) level was higher (p=0.197) in patients with DD genotype and without ACEI therapy (98.8±12.5 vs 95.6±14.1 g/l). Patients with DD genotype on ACEI therapy the Hb level was (p=0.011) significantly lower (92.7±12.5 vs 98.2±11.8 g/l), however, total median erythropoietin dose was similar (p=0.214). In erythropoietin and ACEI treated dialysed patients with DD genotype the Hb level (91.9±11.6 vs 97.8±12.3 g/l) was lower (p<0.01) and the median erythropoietin resistance index (204.1±175.1) value was higher (p>0.05) than in patients with II genotype. In erythropoietin treated patients without ACEI therapy these associations between subgroups were not significant.

**Conclusion:** ACEI therapy may be an erythropoietin resistance factor in CKD-5D patients with ACE gene DD genotype. This study was supported by Hungarian Scientific Research Fund T023977.
Introduction and Aims: Anemia is a known complication of advanced chronic kidney disease (CKD). In recent years, there has been a growing interest in optimizing iron management for the treatment of renal anemia, in order to reduce the high cost of erythropoiesis stimulating agents (ESAs) in comparison to iron therapy. Furthermore, in a significant proportion of pre-dialysis CKD patients iron therapy is undertaken as the primary treatment of anemia [1]. Intravenous (IV) iron sucrose (IS) is the agent of choice in most hospitals for the treatment of renal anemia. However, IV IS must be administered over 5 minutes, thereby multiplying multiple visits. As a suitable alternative, we introduce IV Ferric carboxymaltose (FC) as a single dose agent for the treatment (Rx) of renal anemia with multiple advantages including reduced hospital visits, patient satisfaction and cost-effectiveness.

Methods: We modified our local renal anemia management policy according to National Institute of Clinical Excellence guideline (NICE CG114, UK) using single dose IV FC. All cases that were classed as CKD renal anemia received IV FC were included in this audit over a 6 month period. The cohort also included patients on ESAs. Data was collected prospectively, including pre and post haemoglobin (6 weeks post IV FC Rx), iron studies and clinical information regarding pre and post blood pressure (BP) monitoring and adverse effects.

Results: A total of 245 patients with renal anemia (not on dialysis) were identified and results obtained pre and post IV FC infusion. Among them, 42% of patients were on ESAs. Mean age 71(24-95) with M:F ratio 119:126. There is a mean increase of Hb level >1 gm/dl with single dose IV FC (mean Hb 10.1 g/dl vs. Hb 11.3 g/dl post treatment). There was also a significant improvement of the iron profile (Table 1). Median BP pre 144/77 mmHg and post 133/47 mmHg. In patients on ESAs (n=104), 26% (1 in 4) either had their ESA dose reduced or stopped following IV FC infusion. Only 17% (n=41) of the total patient cohort required 2nd dose of IV FC as it did not achieve the target iron profile. No reported incidence of any serious adverse effect. Table 1: Pre and Post treatment (Rx) Ib and Iron profile with IV FC.

Conclusions: Single dose IV FC was associated with significant improvements in Hb and iron profile and was relatively safe. Other pathways involved multiple hospital visits, reduced interruption in lifestyle and improved patient experience. Furthermore, single dose IV iron replacement with FC has been associated with reduced ESA usage and therefore, overall cost efficient.


**Table 1: Pre and Post treatment (Rx) Ib and Iron profile with IV FC.**

<table>
<thead>
<tr>
<th></th>
<th>Pre Rx (mean)</th>
<th>Post Rx (mean)</th>
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</thead>
<tbody>
<tr>
<td>Hb (g/dL)</td>
<td>10.1</td>
<td>11.3</td>
</tr>
<tr>
<td>Serum iron (μmol/L)</td>
<td>7.86</td>
<td>12.03</td>
</tr>
<tr>
<td>% Iron saturation</td>
<td>15.33</td>
<td>26.92</td>
</tr>
<tr>
<td>Ferritin (μg/mL)</td>
<td>170.32</td>
<td>480.37</td>
</tr>
</tbody>
</table>

**Conclusion:** Single dose IV FC was associated with significant improvements in Hb and iron profile and was relatively safe. Other pathways involved multiple hospital visits, reduced interruption in lifestyle and improved patient experience. Furthermore, single dose IV iron replacement with FC has been associated with reduced ESA usage and therefore, overall cost efficient.

Dr. Constantin Capusa1,2, Raluca Oprican2, Ana Stanciu2, Mariana Lipan2, Simona Stanciu2, Bogdan Chirulescu2 and Gabriel Mirculescu1,2,3

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**Introduction and Aims:** Anemia is common in chronic kidney disease (CKD) and iron deficiency is an important contributor to its pathogenesis. Diagnosis and therapy are based on hemoglobin, transferrin and ferritin levels, all of which are dependent on the hydration status. Accordingly, we thought to evaluate the relationship between these parameters and the hydration status in CKD patients not on dialysis.

**Methods:** 129 clinically stable non-dialysis CKD patients (60 male; 60 [47-71] years; median eGFR 31 [17-43] mL/min/26 with diabetes mellitus) entered this prospective, observational, cross-sectional study. All subjects were erythropoietin and iron therapy naive. Patients with anemia of identifiable cause were excluded. Serum hemoglobin (Hb), ferritin, transferrin saturation (TSAT), albumin and C-reactive protein (CRP) were measured. The hydration status was assessed by bioimpedance spectroscopy with a portable body composition monitor device (BCM Body Composition MonitorTM). The overhydration parameter (OH) provided by BCM describes the fluid located almost exclusively in the extracellular space and is used to characterize hydration status.

**Results:** Median serum Hb was 12.4 [11.3-13.7] g/dL. The prevalence of anemia (Hb <11 g/dL) increased along CKD stages 2 to 5 from 0% to 1%, 3%, 5% and 4%, respectively (p=0.008). Higher percentages of overhydration (OH >1 liter) and lower serum albumin levels (<3.5 g/dL) were seen in stage 5 as compared to stage 2 CKD (50% vs. 10%, p=0.002, and 25% vs. 1.7%, p=0.01, respectively), suggesting a potential additional decrease in serum proteins. In the group of decreased iron stores (ferritin <100 mg/mL and iron availability for erythropoiesis (ferritin 100-400 mg/mL and TSAT <20%) were 17% and 24%, respectively, without differences across CKD stages. In univariate analysis, Hb correlated directly with eGFR (r=0.47, p<0.001). TSAT was inversely correlated (r= -0.21, p=0.03), and inversely with hydration status (r=-0.40, p<0.001), but not with serum ferritin and CRP. Overhydration (t ratio = -2.5, p<0.01) along with eGFR (t ratio = 5.23, p<0.001) and serum albumin (t ratio = 2.06, p=0.04) were the independent predictors of anemia in a model of multiple linear regression which explained 35% of hemoglobin variation.

**Conclusions:** As overhydration is a common denominator for hemoglobin and TSAT levels, and is closely related to the reduction in GFR, it should indeed be considered in the management of renal anemia, at least in advanced CKD.

**Table 1:**

<table>
<thead>
<tr>
<th>Hb (g/dL)</th>
<th>Serum iron (μmol/L)</th>
<th>% Iron saturation</th>
<th>Ferritin(μg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre Rx</td>
<td>10.1</td>
<td>7.86</td>
<td>15.33</td>
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<tr>
<td>Post Rx</td>
<td>11.3</td>
<td>12.03</td>
<td>26.92</td>
</tr>
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</table>

**MP211 DARBEPETOIN ALFA, ONCE MONTHLY DOSING, CORRECTS ANEMIA IN CHRONIC KIDNEY DISEASE PATIENTS NOT ON DIALYSIS: A RANDOMIZED PHASE III STUDY**

Sándor Ferenzi1, Simon Roger2, Robert Malecki2, Mourad Farouk2, Frank Dellanna2, Mark Thomas1, and Nick Mankarious2

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Introduction and Aims: While darbepoetin alfa (DA) can be administered once monthly to maintain hemoglobin (Hb) levels in anemia patients with chronic kidney disease not on dialysis (CKD-ND), the monthly use of DA in patients with CKD-ND anemia was not previously investigated in interventional studies.

**Methods:** In this randomized double-blind, non-inferiority, active-controlled, phase III study, adult patients diagnosed with CKD-ND stage 3-4 and Hb levels ≤10 g/dL who had not been treated with an erythropoiesis-stimulating agent were randomized in 1:1 ratio to receive DA every 2 weeks (Q2W) or once monthly for 33 weeks (QM) with initial doses of 0.75 μg/kg Q2W or 1.5 μg/kg QM. Patients were treated to target Hb levels of 10-12 g/dL and a 1 g/dL increase from baseline. The primary endpoint was Hb change between baseline and the evaluation period (weeks 29-33), the non-inferiority margin being 0.5 g/dL. Additional endpoints included the proportion of subjects and time to achieve Hb level ≥10.0 g/dL and ≥11.0 g/dL increase in Hb from baseline, da doses over the duration of the study, and safety.

**Results:** 115 patients were enrolled (Q2W: n=57, QM: n=58). Of these, n=114 (Q2W) and n=115 (QM) had ≥1 Hb during the evaluation period. The mean change (95% CI) from baseline was Hb 2.16 g/dL (1.98, 2.33) for the Q2W group and 1.97 g/dL (1.80, 2.14) for the QM group. The mean (95% CI) difference in Hb change (Q2W-QM) was -0.19 (-0.43, 0.05) g/dL. The majority of subjects (97.9% Q2W, 98.1% QM) achieved both a Hb level ≥10.0 g/dL and ≥11.0 g/dL increase in Hb from baseline; median (Q1, Q3) time to this event was 5 (3, 7) weeks for the Q2W arm and 5 (3, 9) weeks for the QM arm. The mean (SD) weight-adjusted weekly equivalent dose was Q2W 752 (232) μg/kg/week for the Q2W group and QM 677 (306) μg/kg/week for the QM group. Safety profiles were similar between groups.

**Conclusions:** The results of our study indicate that QM dosing was non-inferior to Q2W dosing for correction of anemia with similar safety profiles in CKD-ND patients.
(14.9%), spaced (40.9%) or dose decreased (44.2%). In case of infection, attitudes of FN
are highly variable to adapt the treatment. In case of surgery or hemorrhage,
maintenance of ESA is consensual (94%).

Introduction and Aims: This study in CKD ND patients shows that the impact of recent anemia
tests is significant: the Hb target is lower and Hb overshooting leads to space or lower
ESA doses. Iron treatment is given by oral route predominantly. The maximum of F
levels is not consensual. This study provide a representative picture of french medical
practices before KDIGO recommendations.

Results: A total of 34 patients with CKD 3-5 stage not on dialysis (eGFR <60 ml/min/ 1.73 m²) and anemia (Hb 10-12.5 g/dl) were enrolled. Patients with iron deficiency
(ferritin <100ng/ml; transferrin saturation <20%), severe hyperparathyroidism (PTH
>300 pg/ml) and inflammation (C-reactive protein >1mg/dl) were excluded. The
enrolled patients were randomly 1:1 assigned to receive either paricalcitol (CASE) or
native vitamin D/calcitriol (CONTROL) for 6 months. The initial paricalcitol dose was
1 mcg/die. Dose adjustments were based on laboratory results for PTH, Calcium and
Phosphorus, according to KDIGO guidelines. The primary end point was the
difference in Hb levels from the basal after 6 months of treatment (T3) in the two
groups.

Conclusions: Both groups had similar characteristics at baseline and follow up. The patients
(PT) of the case group (n=17) showed a significant increase in Hb levels after 6 months
of therapy (12.02 g/dl vs 12.96 g/dl respectively at T0 and T3, p=0.03). In control
group (n=17: 8 pt in treatment with calcitriol and 9 with native vitamin D), Hb
progressively decreased (12.03 g/dl vs 11.31 g/dl respectively at T0 and T3, p=0.01).
Moreover, after only 2 months (T1) the difference in Hb levels between the groups was
significant (Hb12.43 g/dl vs 11.75 g/dl respectively in case and in control group,
p=0.012), and remained stable until the end of the study (12.96 g/dl vs 11.31 g/dl at
T3, p=0.015).In case group, 1 pt stopped the therapy with eritropoietin (epo); 1
reduced the epo dose; 1 stopped iron therapy. No significant change was reported in
PTH and Cr-reactive protein levels. No change was made in paricalcitol dose.

Conclusions: Oral paricalcitol could improve anemia in CKD patients. The increase in
Hb levels is likely due to a direct stimulation of erythroid precursors as reported in
vitro for calcitriol and it could be no related to hyperparathyroidism correction.
**MP215**

**TRANSCATHETER AORTIC VALVE REPLACEMENT IN PATIENTS WITH CHRONIC KIDNEY DISEASE**

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**Introduction and Aims:** Transcatheter aortic valve replacement (TAVR) is an established percutaneous technique for the management of patients with severe symptomatic aortic stenosis at high operative risk with or without chronic kidney disease (CKD). Sineo contrast administration, rapid cardiac pacing and use of large core catheters in putative calcified arteries are among the most important drawbacks of TAVR, especially in CKD patients. The aim of the study was to examine the outcome of TAVR in CKD patients compared to no apparent CKD patients and to evaluate the parameters influencing renal function, in the whole cohort, during hospitalization.

**Methods:** During the last two years TAVR was performed in 116 patients, 59 men and 57 women, of mean age 79±8.7 years. The mean logistic EuroSCORE was 25.8±12.1, the mean STS mortality was 6.4±3.7 and the mean STS morbidity & mortality was 28.1±10.5. Echocardiographic parameters were assessed pre- and post-TAVR. GMR (MDRD) and its changes (delta-GFR) were assessed at admission, 2nd and 4th day, respectively.

**Results:** According to admitted GFR patients were divided in two groups: group A (GFR<60ml/min) 73 patients and group B (GFR≥60ml/min) 43 patients. Pre-TAVR NYHA status II, III and IV were estimated in 10 (8.6%), 86 (74.2%) and 20 (17.2%) patients, respectively. TAVR was performed successfully transfemorally in 100 (86%), transeosophageally in 7 (6%) and transaortically in 8 (7%) and through subclavian access in 1 (1%) patients. Balloon expandable Sapien-XT was implanted in 79 (68%) patients and self expandable CoreValve in 37 (32%) patients. The mean volume of iodinated x-ray contrast agent was 131±10.6, the mean ICU stay was 10.6±0.7 days and the mean hospital stay was 5±1.4 days. The effective aortic valve area was increased from 0.67±0.15cm² to 1.83±0.48cm² (p<0.001) and the mean transvalvular pressure gradient was declined from 81.4±20mmHg to 16.5±7mmHg, (p<0.001). The renal function was decreased (delta-eGFR>−25%) in 18 patients (15.5%), improved (delta-eGFR<−25%) in 16 patients (14%) and remained constant (−25%≤delta-eGFR<25%) in 82 (70.5%) patients. Both groups showed similar improvement, after TAVR, in all clinical and echocardiographic parameters. The change of renal function was not correlated with the estimated parameters, and interestingly, nor with the contrast volume. In our discriminate analysis none of the measured parameters determined the renal outcome.

**Conclusions:** In our data CKD was not an adverse factor for TAVR success. In addition, renal function was not influenced by invasive-contrast administration.

**MP216**

**ARTERIAL STIFFNESS IN NON-DIALYSIS STAGE 4 CHRONIC KIDNEY DISEASE (NDCKD) PATIENTS: ONE YEAR FOLLOW-UP**

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**Introduction and Aims:** The relationship between renal function and arterial stiffness (AS) a marker/factor of increased risk mortality remains, until now, a subject to debate. Moreover, factors determined AS deterioration in NDCKD has not been determined.

**Methods:** We prospectively investigated AS with the use of pulse wave velocity (PWV) and augmentation index (AI) in 49 NDCKD stage 4 (mean age 64±13 ys) consecutive patients (45.2% men, 24.3% diabetics) at baseline and after 1 year of follow-up. All patients were on drug therapy: 57.5% of them were receiving RAS inhibitors, 32.9% statins, 32.9% vitamin D analogs and 79% EPO agents.

**Results:** Mean peripheral systolic/diastolic/pulse blood pressure (PSBP/DPBP/PPP) levels, mean central systolic/diastolic/pulse (CSBP/DDBP/CPP) levels, mean estimated glomerular filtration rate (eGFR) at baseline and at the end of the study are shown in the table: Both AS indices were also increased significantly at the end of FU. Serum calcium (Ca++) and phosphorus (PO43−) levels remained within the target in 97-98% of the patients while Parathormone levels increased (176 vs 204, pg/ml, p=0.08). Furthermore, Hb levels were 11.59 and 11.7 g/dl (p=ns) at the onset and latest FU.

**Conclusions:** During the FU, lipid parameters were also improved significantly (total cholesterol, p<0.05, triglycerides, p=0.05, HDL-cholesterol, p<0.001 and LDL-cholesterol, p=0.05). Moreover, medial values of proteinuria at baseline and at the end of the study were 1.300 and 775 mg/24h respectively (p=0.01). Factors associated with increased PWV were age, diabetes mellitus, total-cholesterol, (p=0.001) male sex, (p=0.05) and smoking (p=0.05). Factors associated with increased AI were PSBP (p=0.05), CSBP (p=0.05), serum PO4 levels (p=0.04) and proteinuria levels (p=0.04).

**MP217**

**META-ANALYSIS OF THE IMPACT OF VITAMIN D RECEPTOR ACTIVATORS FOR REDUCTION OF PROTEINURIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMISED CONTROLLED TRIALS**

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**Introduction and Aims:** Renin-angiotensin-aldoosterone system (RAAS) blockers protect against chronic kidney disease (CKD) progression and cardiovascular complications by reducing proteinuria and blood pressure. However, RAAS blockade is limited by drug side-effects, and residual proteinuria, a key determinant of future renal and cardiovascular complications. Recent small-to-medium-sized randomised clinical trials (RCTs) addressed whether vitamin D receptor activators (VDRAs) reduce residual proteinuria, but results have been inconsistent. Therefore we undertook the first systematic review and meta-analysis of all RCTs examining the effect of VDRA on residual proteinuria in CKD.

**Methods:** We systematically searched Medline, Embase, and Cochrane Library databases for CKD RCTs featuring VDRA use published between 1950-September 2012, extracting standardized data. We included all studies with any type of VDRA that reported proteinuria or albuminuria as outcome. Primary endpoint was the total reduction in proteinuria from baseline to last follow, while secondary endpoint was the total number of patients with >15% reduction in proteinuria from baseline to last follow up. Our meta-analysis included a sub-analysis of the PRIMO study with only patients that had albuminuria at baseline. Meta-analysis was performed using random effects models.

**Results:** We included eight trials, six with paricalcitol, two with calcitriol, providing data on 732 patients. Most patients (84%) received RAAS blockers throughout. VDRA’s reduced residual proteinuria (weighted mean difference from baseline to last measurement -17% [95% confidence interval [-1% -21%] compared with controls (+2% [95% CI -5% to +8%], p=0.0003) (Figure 1). Proteinuria reduction was achieved more often in VDRA-treated patients (220/416 patients) than in control patients (92/316 patients, OR 2.78 [95% CI 1.74 to 4.46]; p<0.0001). The effect was comparable for calcitriol and paricalcitol, and in diabetic or non-diabetic CKD.

**Conclusions:** VDRAs effectively target residual proteinuria in CKD patients, in addition to concurrent RAAS-blockade based therapy. The 17% reduction in proteinuria is clinically equivalent to the addition of a further RAAS Blocker. Future studies should address whether VDRAs can also arrest CKD progression.
During median follow-up of 3.8 (range, 0.1 to 5) years, 64 of 185 participants had cardiovascular death in relation to renal arteries diameter (low reference diameter or minimal luminal diameter in 185 participants with RAS). Cardiovascular disease events (myocardial infarction, heart failure, stroke or cardiovascular death) in relation to renal arteries diameter (low reference diameter or minimal luminal diameter) in 185 participants with RAS were analyzed. The degree of stenosis and major confounders were taking advantage of the cohort of the RAS-CAD trial to test whether the renal artery diameter impact the prognosis of patients with ischemic heart disease and non-significant renal artery stenosis.

**Introduction and Aims:** Recently, our group reported for the first time that small renal arteries, defined by a low reference diameter or minimal luminal diameter, are independently associated with low GFR and resistant hypertension, independent of the degree of stenosis and major confounders. In the present report we taking advantage of the cohort of the RAS-CAD trial to test whether the renal artery diameter impact the prognosis of patients with ischemic heart disease and non-significant renal artery stenosis.

**Methods:** We used proportional hazards models to analyze first-onset major cardiovascular disease events (myocardial infarction, heart failure, stroke or cardiovascular death) in relation to renal arteries diameter (low reference diameter [RD] or minimal luminal diameter [MLD, see Fig.1.]) in 185 participants with RAS. 10-70% (mean age, 67 years; 32% women) of the RAS-CAD study.

**Results:** During median follow-up of 3.8 (range, 0.1 to 5) years, 64 of 185 participants (34.6%) experienced an event. In multivariable models adjusted for age, sex, smoking, and presence of dyslipidemia, hypertension, diabetes mellitus, chronic kidney disease stage 3-4 and bi or three coronary artery disease, lower MLD was associated with a 1.04% increase in cardiovascular disease risk (90% confidence interval, 1.17 to 3.57; P<0.01; Fig. 2). After that low MLD was added to a standard risk factor model, integrated discrimination improvement was 2.3% (from 71.3% to 73.6%).

**Conclusions:** In patients with ischemic heart disease and non-significant renal artery stenosis (RAS 10-70%), lower MLD is associated with increased risk for a first cardiovascular event. MLD improves risk prediction of cardiovascular events when added to standard risk factors and may represent a valuable biomarker of cardiovascular disease risk in patients with ischemic heart disease and non-significant renal artery stenosis.
aorta in these donors was calculated with a mean AAC severity score of 0.98 ± 0.56. In kidney donors > 50 years of age there was significantly more AAC than in those < 50: 2.47±1.56 vs. 0.31±0.29, p<0.001. There was no relationship between the presence or severity of aortic AAC and serum FGF-23, systolic blood pressure, pulse pressure, calcium-phosphate product or smoking.

Conclusions: AAC prevalence, patterns and severity in this important donor population have not previously been described in the literature. There was relatively little VC in what can be regarded as a “healthy” donor population - present in about a third of patients. VC was more common with age, but the other possible risk factors for the presence or severity of VC did not impact on overall AACS scores. VC did not influence vascular stiffness as represented by pulse pressure. Following the evolution of AAC over time in those who have donated a kidney, and lost some global renal function as a consequence, would be of considerable interest.

**MP221**

THE EFFECT OF DIETARY PHOSPHATE ON FGF-23 SECRETION IN PATIENTS WITH DIABETIC AND NON-DIABETIC MODERATE TO ADVANCED CHRONIC KIDNEY DISEASE

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Introduction and Aims: An increased serum concentration of fibroblast growth factor 23 (FGF-23) has been linked to worse prognosis in chronic kidney disease (CKD). It has been recently shown that the responses of both FGF-23 and PTH to an increased oral phosphate intake are impaired in type 2 diabetes mellitus. The aim of this study was to assess the effect of increased phosphate on serum FGF-23 and other parameters of calcium-phosphate metabolism in CKD patients with moderate to severe renal function impairment with and without diabetes.

Methods: 26 patients with CKD (age 64±14 yrs) were included. 15 patients had diabetic kidney disease (DM) and 11 patients non-diabetic nephropathies (non-DM). Mean GFR was 30.3±12.9 mL/min in DM and 32.8±24.3 mL/min in non-DM group (ns). All patients received for 7 days a high-phosphate diet (1000 mg/24h) with additional intake of 90 ml of sodium and potassium phosphate as a solution containing: Na2HPO4/K2HPO4 and NaH2PO4/KH2PO4 in 4:1 ratio (31 mg of phosphate, 0.9 mEq sodium and 0.9 mEq potassium per 5 ml of the solution). At baseline and after 3 days of high phosphate diet serum concentration of FGF-23, Ca, P and 1,25OH2D, was measured and the urine was collected for Ca and PO4.

Results: In diabetic CKD patients serum calcium decreased from 2.21±0.11 mmoL/L at baseline to 2.12±0.14 and 2.08±0.23 mmoL/L on day 3 and 7, respectively (p<0.01). The change of serum calcium was not significant in non-DM CKD patients. Serum phosphorus was 1.28±0.24, 1.41±0.26 and 1.44±0.34 mmoL/L, respectively at baseline and on day 3 and 7 of the study in DM group and 1.15±0.21, 1.31±0.22 and 1.46±0.40 mmoL/L, respectively in non-DM patients (p<0.01). Serum PTH increased from 179±135 to 260±128 and 279±252 pg/ml on day 7 in all patients (p=0.01) and the change of PTH was similar in DM and non-DM patients. 1,25OH2D levels did not change during the study and were 26.4±9.1, 27.2±10.6 and 28.2±12.8 pg/ml in DM and 25.0±10.5, 26.4±11.7 and 27.4±12.6 pg/ml on day 3 and 7 of the study in non-DM patients (p=0.01). The serum 1,25OH2D level in patients with micro-albuminuria had higher BMI (p<0.03), pDBP (0.297, p<0.007) and cSBP (0.362, p<0.001) than those with macro-albuminuria.

Conclusions: Diabetic patients with impaired kidney function are characterized by preserved mechanoregulation of renal phosphate excretion. Increased phosphate intake decreases serum calcium and increases serum phosphorus, PTH and 1,25OH2D in both groups. Patients with macro-albuminuria had higher BMI, pSBP, cSBP and crBP (p<0.001, p<0.001, p<0.001 and p<0.001, respectively) than patients with micro-albuminuria.

**MP222**

UREAEMIC PRURITUS: RELIEF OF ITCHING BY GABAPENTIN AND PREGABALIN IN 85% OF CONSECUTIVELY-TREATED PATIENTS

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Introduction and Aims: Pruritus (skin irritation or itching) is a common symptom in patients with CKD stages 4 and 5. When severe, it is associated with disrupted sleep, reduced quality of life, depression and increased mortality. A video of a patient describing the symptoms is at vimeo.com/49458473. A randomized placebo-controlled crossover trial showed that gabapentin increased skin irritation in severely limited renal function with gabapentin.

Reference: Gunal AI, Ozalp G, Yoldas TK, Gunal SY, Kirciman E, Celiker M.

Conclusions: Gabapentin relieved itching in 46 patients (66%). Most patients reported the effect after the first tablet. A video of a patient describing the effect is at vimeo.com/495976, 26 patients (37%) suffered side-effects from gabapentin: over-sedation (12), dizziness (6), light chest/breathlessness (3), shaking limbs (2), vomiting (2), blotchy rash (2), nightmares (1), cramp (1), hair loss (1), low BP (1), inconvenience (1); some patients had multiple side-effects. 24 (34%) stopped gabapentin: 3 due to lack of effect on itching, 21 due to side-effects. In 7 patients who stopped gabapentin due to side-effects, 16 started pregabalin. Pregabalin relieved itching in 13 patients (81%), 3 stopped pregabalin: 1 due to lack of effect on itching, 2 due to side-effects (over-sedation in both). In total, gabapentin or pregabalin relieved itching in 60 patients (85%), median follow-up 1 month (range 0.25 to 8 months). Median itch severity of 10 reduced from 8 (range 6 - 10) to 1 (range 0 – 5).

Conclusions: Patients with CKD stages 4 and 5 routinely should be asked about skin irritation or itching. Severe itching is usually not associated with elevated serum levels of calcium or phosphate. Gabapentin in pregabalin relieved itching in 85% of 71 consecutively-treated patients. Patients should be advised about the risk of side-effects and the drug started at a low dose. Patients who do not tolerate gabapentin may tolerate pregabalin.

**MP223**

MACRO-ALBUMINURIA AS MARKER FOR WORSENING ARTERIAL STIFFNESS IN CKD STAGE 1-2 HYPERTENSIVE NON-DIABETIC PATIENTS

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Introduction and Aims: Albuminuria is recognized as a marker of vascular dysfunction. Pulse wave velocity (PWV) and augmentation index (AI) are early markers of atherosclerotic vascular changes and aortic stiffness (AS) in chronic kidney disease (CKD). We aimed to assess the association between albuminuria levels and arterial stiffness in CKD stages 1-2 non-diabetic patients with hypertension treated with renin angiotensin blockade (RAS) agents plus other hypotensives when needed.

Methods: One hundred fifteen patients with median age 52 years, (68% males) were consecutively enrolled in the study. For each patient, we recorded: gender, age, BMI, peripheral systolic blood pressure (pSBP), peripheral diastolic blood pressure (pDBP), peripheral pulse pressure (pPP), central systolic blood pressure (cSBP), central diastolic blood pressure (cDBP), central pulse pressure (cPP), hematocrit, hemoglobin, CRP, lipids, calcium, phosphorus, parathormone, serum albumin, and 24 h urine albumin excretion. According to 24-hour urine albumin collection, patients were classified as those with micro (<300 mg/d) and those with macro (>300 mg/d) albuminuria. We considered AS indices (PWV c-f and AI) as outcomes. We explored potential correlation between macro-albuminuria and AS indices using a multiple linear regression model.

Results: Fifth eight patients were included in the micro group and 57 in the macro. Blood pressure measurements of the patients were 138±1/82±1.3 mmHg (systolic /diastolic). There were no significant differences in age, sex, and BP measurements between the two groups. Patients with macro-albuminuria had higher BMI (p<0.03), crBP (p<0.001), and fibrinogen levels (p<0.02) than patients with micro-albuminuria. In multivariate linear regression analysis, macro-albuminuria (β=0.822, p=0.04) and pSBP (β=0.4, p=0.004) remained independent determinants of increased PWV c-f. In addition, macro-albuminuria (β=0.287, p<0.001) and cPP (β=0.362, p<0.04) remained independent determinants of increased AI. No other variables were significantly correlated to AS indices.

Conclusions: These findings demonstrate an independent association between AS in macroalbuminuria and in non-diabetic, hypertensive patients with CKD stages 1-2 treated with RAS blockers.

**MP224**

ECHOCARDIOGRAPHY, PULMONARY HYPERTENSION AND RIGHT HEART FAILURE IN NKF STAGE III CKD PATIENTS

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Introduction and Aims: Pulmonary hypertension and right heart failure are common in CKD patients. TAPSE measurement during echocardiography is a well known measure of right heart systo-diastolic function. Low TAPSE means reduced chronic-cranial-causal exclusion of tricuspid annulus, sign of both reduced ejection fraction and reduced distensibility of right ventricle. It is a good prognostic index for cardiac mortality risk in CHF patients, adding significant prognostic information to NYHA stadia. This datum is probably crucial in vascular access policy.
Methods: 202 patients (56±12 years, 123 females, 79 males), affected by mild chronic renal disease (CKD-Epi estimated GFR between 60 and 15 ml/min) without overt heart disease, underwent conventional mono-, two-dimensional and Doppler echocardiogram, with the use of 7.5 MHz sectorial transducer and harmonic detection. Right Ventricular End Diastolic Diameter was recorded averaging measured on M-mode from parasternal long-axis projection and on B-mode from an apical view. TAPSE measurement was obtained from an apical approach, with a M-mode section of tricuspid annulus, on the external side of atrial floor, measuring the distance (in mm) between the highest and the lowest point of annulus plun excursion.

Results: TAPSE resulted mildly depressed (<18 mm) in 44.5% (99 subjects) of enrolled patients, while it was moderately reduced (<15 mm) only in 10.3% (21 patients) of them. Right ventricular end diastolic diameter > 22 mm was reported in 88 patients (43%), while values >26 mm were reported in 107 patients (52.9%), and values >30 mm only in 6 of them (14.8%). PAPs exceeded 30 mmHg in 28.7% of patients (58 patients), overcoming 40 mmHg in 5% of them (10 patients). Significant inverse correlations were observed between TAPSE and PAPs (β = -0.47, p<0.005) (Figure 1), right ventricular end diastolic volumes (β = -0.19, p<0.005) (Figure 2), Framingham score (β = -0.19, p<0.005). No correlations have been observed between eGFR, PTH, blood pressure levels and TAPSE or PAPs.

Conclusions: TAPSE measurement was obtained from an apical approach, with a M-mode section of tricuspid annulus, on the external side of atrial floor, measuring the distance (in mm) between the highest and the lowest point of annulus plun excursion. It should be stressed that inclusion criteria were selected in a population at low risk of pulmonary hypertension. It can be then assumed that "real" data about the presence of right ventricular dysfunction is even more widespread.

INTRODUCTION AND AIMS: Atherosclerosis is one of the most serious and frequent complications among patients suffering from chronic kidney disease (CKD). Moreover, the risk of cardiovascular events increases with degree of reduced renal function. However, molecular mechanism that enhance the formation of plaque in CKD patients are still unclear. The major goals of these studies was better understanding the relation between CVD and CKD related atherosclerosis, identified by reduced TAPSE and slightly increased PAPs, in a discrete quote of population affected by moderate chronic kidney disease (stage III according to National Kidney Foundation), in the absence of known heart disease.

RESULTS: Significant inverse correlations were observed between TAPSE and PAPs (β = -0.47, p<0.005) (Figure 1), right ventricular end diastolic volumes (β = -0.19, p<0.005) (Figure 2), Framingham score (β = -0.19, p<0.005). No correlations have been observed between eGFR, PTH, blood pressure levels and TAPSE or PAPs.

CONCLUSIONS: TAPSE measurement was obtained from an apical approach, with a M-mode section of tricuspid annulus, on the external side of atrial floor, measuring the distance (in mm) between the highest and the lowest point of annulus plun excursion. It should be stressed that inclusion criteria were selected in a population at low risk of pulmonary hypertension. It can be then assumed that "real" data about the presence of right ventricular dysfunction is even more widespread.

MP227 ASSESSMENT OF RADIAL ARTERY STIFFNESS HELPS TO IDENTIFY SUBCLINICAL CARDIAC DAMAGE AMONG SUBJECTS AFFECTED BY CHRONIC KIDNEY DISEASE

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Introduction and Aims: Arterial stiffness and subclinical cardiac damage are associated with a worse cardiovascular (CV) prognosis and often they coexist. We investigated whether among subjects affected by chronic kidney disease (CKD) evaluation of arterial stiffness may help to identify individuals with subclinical cardiac impairment.

Methods: We evaluated 93 patients (M/F=56/37) affected by CKD (stages 1-4 of the NKF-KDOQI classification) and free from CV events. Renal function was estimated by CKD-EPI (eGFR) formula. Proteinuria was measured as 24 hours collection (ProtU) and as the average of three urinary albumin/creatinine ratios (A/C). Vascular stiffness was assessed using an Omron HEM-9000AI device. Radial Augmentation index (AI) was measured directly whereas central aortic blood pressure (BP) and systolic reflection pressure (SRP) were estimated. Left ventricular mass indexed at height (27LVMI) and E/A ratio (E/A) were assessed by echocardiography. Left ventricular hypertrophy (LVH) was defined as LVMI ≥51 g/m².

Results: 33% of patients had LVH (LVH+). LVMI was correlated with systolic and mean blood pressure (r=0.28 and r=0.08 respectively) and as the average of three urinary albumin/creatinine ratios (A/C). Vascular stiffness was assessed using an Omron HEM-9000AI device. Radial Augmentation index (AI) was measured directly whereas central aortic blood pressure (BP) and systolic reflection pressure (SRP) were estimated. Left ventricular mass indexed at height (27LVMI) and E/A ratio (E/A) were assessed by echocardiography. Left ventricular hypertrophy (LVH) was defined as LVMI ≥51 g/m².

Conclusions: Among subjects affected by CKD the evaluation of radial artery stiffness provides several direct (AI) and indirect (CBP and SRP) indices that are associated with subclinical cardiac damage, thus it may help to stratify their CV risk profile.

MP228 CONTRIBUTION OF UREMIC TOXINS TO BLOOD PRESSURE REGULATION IN CKD PATIENTS

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Introduction and Aims: Patients suffering from chronic renal failure often show further organic disturbances concomitantly. In particular, cardiovascular diseases (CVD) lead to complications of these patients. Accumulations of uremic toxins, which under non-pathophysiologic conditions are removed by the healthy kidney, are the most important factors of genesis of cardiovascular symptoms of chronic renal failure patients. However, the identification of the uremic toxins with the strongest impact on the genesis and/or progression of cardiovascular diseases in chronic renal failure patients is still pending. Since this knowledge is essential for the clarification of the pathophysiology of cardiovascular diseases and for development of innovative therapeutic approaches, we tested the direct vasoconstrictive effects of 74 known uremic mediators within this study. The overall aim of this study was to identify the systematic comparison of previously unknown uremic vasoconstrictive mediators and the classification their pathophysiological effects in patients with chronic renal failure.

METHODS: 202 patients (56±12 years, 123 females, 79 males), affected by mild chronic renal disease (CKD-Epi estimated GFR between 60 and 15 ml/min) without overt heart disease, underwent conventional mono-, two-dimensional and Doppler echocardiogram, with the use of 7.5 MHz sectorial transducer and harmonic detection. Right Ventricular End Diastolic Diameter was recorded averaging measured on M-mode from parasternal long-axis projection and on B-mode from an apical view. TAPSE measurement was obtained from an apical approach, with a M-mode section of tricuspid annulus, on the external side of atrial floor, measuring the distance (in mm) between the highest and the lowest point of annulus plun excursion. It should be stressed that inclusion criteria were selected in a population at low risk of pulmonary hypertension. It can be then assumed that "real" data about the presence of right ventricular dysfunction is even more widespread.

Conclusions: TAPSE measurement was obtained from an apical approach, with a M-mode section of tricuspid annulus, on the external side of atrial floor, measuring the distance (in mm) between the highest and the lowest point of annulus plun excursion. It should be stressed that inclusion criteria were selected in a population at low risk of pulmonary hypertension. It can be then assumed that "real" data about the presence of right ventricular dysfunction is even more widespread.
Methods: For this study the bioassay of the perfused isolated rat kidney was used. Hereby, the known vasocostrictive effects of endothelin-1, methyguanidine-HCl, and neuropeptide Y were confirmed. Additionally, we identified 1-methyl adenosine, phenol, and uridine as strong vasocostrictive mediators, accumulating in CKD patients.

Results: The vasocostrictive effects elicited by 1-methyl adenosine, phenol and uridine were in the physiologic relevant range and the effects of these new vasocostrictors were additive in the bioassay.

Conclusions: 1-methyl adenosine, phenol and uridine are novel strong vasocostrictors, which contribute to hypertension of chronic renal failure patients.

Higher Stage of Chronic Kidney Disease (CKD) Is A Risk Factor for Peptic Ulcer Disease in CKD Patients

Kyungrang Lee1, In Hye Hwang1, Soo Bong Lee1, Dong Won Lee1, Il Young Kim1, Ihm Soo Kwak2, Eun Young Seong2, Min Ji Shin2, Harin Rhee2 and Byeong Yun Yang2

Introduction and Aims: Abnormal G I bleeding (GIB) is a common and potentially serious complication of renal failure. Peptic ulcer disease (PUD) has been reported to account for nearly 60% of upper GIB episodes in CKD patients. The association between PUD and CKD remains unclear yet. Therefore, we investigated endoscopic findings and sought to find out risk factors for PUD in the CKD.

Methods: This study initially included 1,131 patients registered with diagnosis code of CKD stage 3-5 on our hospital administrative database between Jan. 2008 and Dec. 2012. Among them, 375 patients were underwent gastroduodenoscopy examination (GDE). We excluded 73 patients with a history of gastric surgery, cancer involving gastroduodenal area or hospitalized in ICU while the GDE. Finally 302 patients were enrolled in this study. Demographic and clinical parameters and endoscopic findings were reviewed from the electronic medical records. We evaluated drugs which had been used for at least 4 weeks before GDE including PPI, H2RB, steroid, and anti-coagulants such as aspirin, clopidogrel, cloxstazol and warfarin. All subjects did not use NSAIDs.

The study population was divided into 2 subgroups according to the presence of PUD.

Results: According to the gastroduodenoscopy, GERD was most prevalent (174 patients, 57%), followed by atrophic gastritis (126 patients, 41%) and PUD (103 patients, 34%). Erythematous gastritis, erosive gastritis, and hemorrhagic change were seen in 58 patients (19%), 51 patients (16%) and 18 patients (6%), respectively. With regards to PUD, the prevalence of DM is higher in PUD group than non-PUD group. However sex, age, comorbidities except DM, medication history and the percentage of smoking, diastolic blood pressure were different between PUD and non-PUD groups.

Adjusted OR of CKD stage 4 and 5 about PUD were 2.485 (95% CI 1.97–9.99, P=0.003) and 2.763 (95% CI 1.239–6.162, P=0.025), respectively. In the subgroup analysis for CKD stage 5, hemodialysis was not risk factor of PUD.

Conclusions: Two hundred and five patients started dialysis with mean C-G 6.1 ± 1.9 ml/min after 14-month follow up, on average. Multivariate analysis identified higher serum phosphorus, higher proteinuria, lower age and lower C-G values at the entry of the study vasocostrictory mediators accumulating in CKD patients.

Essentials and Safety of Oral Febuxostat in Subjects with Moderate-to-Severe Chronic Kidney Disease (CKD): One-Year Results

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Introduction and Aims: Hyperuricemia is considered an independent cardiovascular risk factor and an important mediator in chronic kidney disease (CKD) development and progression. Febuxostat, a novel non-purine selective xanthine oxidase inhibitor, is more effective than allopurinol and equally safe in the management of chronic hyperuricemia. However, insufficient safety and efficacy data are available for Febuxostat administration to subjects with hyperuricemia and impaired renal function. This study was designed to prospectively evaluate efficacy and safety of oral Febuxostat in hyperuricemic subjects with stages 3–4 CKD.

Methods: Nineteen patients, male/female 12/7, median age 70 (41–86) years with serum uric acid (sUA) ≥ 8.0 mg/dl and serum creatinine (sCr) ≥ 2.0 mg/dl received Febuxostat for one year. Nine out of 19 patients were previously on allopurinol and, due to intolerance or lack of efficacy, were switched to Febuxostat after 15-day washout. Patients with renal transplantation, active liver disease, alcohol abuse or severe, life threatening medical condition were excluded. Febuxostat starting dose was 80 mg orally every other day with creatinine clearance estimated by Cockcroft-Gault formula (eCrCl C-G) ≥ 30 ml/min and every third day with < 30 ml/min. This dose was achieved to adjust target sUA levels of ≤ 6 mg/dl. Hematology, biochemistry and creatinine clearance with 24-hr urine collection (24hr-CrCl) were performed and eCrCl C-G as well as eGFR MDRD2 were calculated at baseline and every other month thereafter. Adverse events were recorded.

Results: sUA was significantly reduced already by month 1 (9.9±1.6 vs. 5.6±1.5 mg/dl, P<0.001). This significant difference remained throughout the study up to month 12 (5.4±0.8 mg/dl, P<0.001). Target sUA at the study end was achieved in 16/19 (84.2%) patients. Renal function, assessed by sCr, 24hr-CrCl and eGFR C-G remained unchanged through month 12 (2.6±1.1 vs. 2.4±1.2 mg/dl, 28.10±9.45 vs. 28.80±10.37 ml/min and 28.60±9.54 vs. 31.80±11.90 ml/min, respectively), whereas eGFR MDRD2 was found significantly higher by the end of follow-up (28.16±8.04 vs. 28.84±10.69 ml/min, p=0.03). No significant differences were observed for the rest of studied parameters, including C-reactive protein (CRP), proteinuria and liver tests. Febuxostat weekly dose variation was similar throughout the study in all patients. No significant differences between males/females, diabetic/no diabetic as well as CKD3/CKD4 patients were observed in Febuxostat sUA lowering effect or in renal function evolution. Gastrointestinal adverse events recorded in 2/19 patients were mild.

Conclusions: Febuxostat, administered over one-year period in significantly reduced dosage, appears to be effective and safe with minimal side effects in the management of chronic hyperuricemia for patients with moderate-to-severe CKD.

Estimation of Body Fluid Volumes by Bioimpedance Spectroscopy in Patients with Hyponatremia Can Replace Physical Exam

Jae Seok Kim1, Byoung Geun Han1, Seung Ok Choi1 and Jae Won Yang1

Introduction and Aims: Current methods to estimate body fluid volumes in hyponatremic patients, including bioimpedance spectroscopy (BIS) and bioimpedance analysis (BIA), suffer from several drawbacks. BIS can be readily performed in patients with low serum sodium concentrations. BIA requires a good contact between the electrodes and the skin in all body regions. We have previously shown that estimation of body fluid volumes by BIS can be used in clinical practice. Therefore, the aim of the present study was to test the applicability of BIS and BIA for estimating body fluid volumes in hyponatremic patients.

Methods: The present study was performed in the University Hospital of the University of Athens, Greece. A total of 100 patients with serum sodium concentrations ≤ 135 mmol/l were included. BIS and BIA were performed in all patients. Body fluid volumes were estimated by BIS and BIA and compared with the values obtained by the standard method of bedside weighing.

Results: The results of the present study showed that BIS and BIA were able to estimate body fluid volumes with high accuracy in hyponatremic patients.

Conclusions: The results of the present study suggest that BIS and BIA can be used as a reliable alternative to the standard method of bedside weighing in hyponatremic patients.
Introduction and Aims: Estimation of body fluid volumes in patients with hypernatremia is useful for diagnosis and therapeutic decision making. Physical exam has been generally used to estimate body fluid volumes, but it depends on physician’s abilities. Bioimpedance spectroscopy (BIS) has been suggested to be a reliable method for the assessment of body fluid volumes. Therefore, this study was intended to investigate whether BIS could replace physical exam in patients with hypernatremia.

Methods: This study included thirty patients with hypernatremia. At the time of the first visit, we took medical and drug use history, and measured laboratory data, including hormones. Body fluid volumes were simultaneously assessed by both physical exam and BIS. In addition, the estimation of body fluid volumes by clinical diagnosis was also carried out, which was retrospectively assuming the body fluid volume that corresponded with most likely cause of hypernatremia (clinical body fluid evaluation).

Results: The results of body fluid volumes estimated by physical exam showed that the patients with hypernatremia were nine, euolemia were thirteen, hypovolemia were eight. The results by BIS showed that hypernatremia were ten, euolemia were fifteen, hypovolemia were five. The degree of agreement between BIS and clinical body fluid evaluation was higher than the other. Conclusion: BIS can be considered as an alternative method to replace physical exam for estimating body fluid volumes in patients with hypernatremia. In addition, BIS may be more objective and correspond with clinical diagnosis than physical exam.

Methods: In this prospective cohort study, 936 consecutive patients with CKD stage 4-5 pre-dialysis were included. Patients with hypokalemia (n=18) were excluded for survival comparisons. Patients were followed for a median of 402 days, and they were treated according to standard CKD care at hospital-based dialysis unit. Correction of metabolic acidosis and anti-angiotensin drugs (ACEIs, ARB or DRI) were considered major therapeutic objectives, and none of patients was treated with potassium restriction diets, potassium-sparing diuretics, digital, or ion-exchange resins. All cause mortality, sudden death and dialysis initiation were the outcome variables.

Results: Hyperkalemia (serum K levels > 5.5 mEq/l with no evidence of hemolysis in the sample) was observed in 255 patients (27%). By multiple logistic regression analysis, diabetes (OR= 1.989, p=0.004), eGFR (OR= 0.963, p=0.03), serum bicarbonate levels (OR= 0.853, p<0.001), and treatment with anti-angiotensin drugs (OR=2.072; p=0.001) were the main determinants of hyperkalemia. During the pre-dialysis follow-up period 191 patients (20%) died. In univariate survival analysis, hyperkalemia was associated, although not significantly, with better overall survival than that of normokalemic patients (84% vs. 78%). On multiple Cox regression analysis, hyperkalemia was not independently associated with mortality. Sudden death was more frequently observed in normokalemic than in hyperkalemic patients (20% vs. 5% of total deaths, not significant). During the study period, a lower percent of hyperkalemic patients survived free of dialysis than that of normokalemic patients (32% vs. 38%, log-rank=14.16; p=0.0001). However, neither hyperkalemia nor serum K levels was independently associated with the probability of dialysis initiation in multiple regression models. Conclusion: Hyperkalemia is highly prevalent in advanced CKD not yet on dialysis. However, hyperkalemia was not associated with worse overall survival or higher incidence of sudden death.

Methods: This study included thirty patients with hyponatremia. At the time of the first visit, we took medical and drug use history, and measured laboratory data, including hormones. Body fluid volumes were simultaneously assessed by both physical exam and BIS. In addition, the estimation of body fluid volumes by clinical diagnosis was also carried out, which was retrospectively assuming the body fluid volume that corresponded with most likely cause of hyponatremia (clinical body fluid evaluation).

Results: The results of body fluid volumes estimated by physical exam showed that the patients with hyponatremia were nine, euolemia were thirteen, hypovolemia were eight. The results by BIS showed that hyponatremia were ten, euolemia were fifteen, hypovolemia were five. The degree of agreement between BIS and clinical body fluid evaluation was higher than the other. Conclusion: BIS can be considered as an alternative method to replace physical exam for estimating body fluid volumes in patients with hyponatremia. In addition, BIS may be more objective and correspond with clinical diagnosis than physical exam.

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Results: We successfully isolated exosomes from human urine. Electron microscopy verified a typical shape of urinary exosome with average size of 65.1±25.9nm and was positively immunogold labelled with anti-CD9 and AQP2. MicroRNAs extracted from the exosomal fraction to RNase digestion. 16S of urine was sufficient for microRNA isolation. Exosome was stable at 4°C 24 hours for shipping before stored at -80°C. Exosomal microRNA was detectable despite 5 freeze-thaw cycles. The detection of microRNAs by quantitative PCR showed high reproducibility (r>94% for intra assay and r>97% for inter assay), high sensitivity (positive call 100% for 15 patients), broad dynamic range (8-log wide) and good linearity for quantification (R²>0.99).

Conclusions: The presence of urinary exosomal microRNA was confirmed for patients with a diversity of chronic kidney disease. The conditions of urine collection, storage and microRNA detection determined in this study may be useful for future biomarker discovery efforts.

**MP237**

**EFFECT OF ROSUVASTATIN WITH OR WITHOUT EZETIMIBE ON RENAL FUNCTION IN PATIENTS UNDERGOING ELECTIVE VASCULAR SURGERY**

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Introduction and Aims: The effects of statin therapy on renal outcomes remain an issue of controversy. We prospectively compared the effects of lipid lowering treatment by statin monotherapy versus intensified by combining statin with ezetimibe on renal function in patients undergoing elective vascular surgery.

Methods: A total of 262 patients participated, 136 on treatment by rosuvastain 10 mg/day (RSV) and 126 by RSV 10 mg/day plus ezetimibe 10 mg/day (RSV/EZT) starting 1 day before surgery. Aliquots of 25 ml blood were drawn at baseline, 6 and 12 months after the procedure.

Results: The patients were classified as mild, moderate or severe CKD-EPI 69.3 ml/min (range 21.2-102.5) were enrolled. We calculated ideal body weight. Moreover, MDRD and CKD-EPI could underrate renal function in obese patients. The predictive models, for example redistribution this ion secretion but determined other mechanisms, for example redistribution this ion excretion but determined other mechanisms, for example redistribution this ion. Moreover, MDRD and CKD-EPI could underrate renal function in obese patients. The predictive models, for example redistribution this ion secretion but determined other mechanisms, for example redistribution this ion excretion but determined other mechanisms, for example redistribution this ion. Moreover, MDRD and CKD-EPI could underrate renal function in obese patients. The predictive models, for example redistribution this ion secretion but determined other mechanisms, for example redistribution this ion excretion but determined other mechanisms, for example redistribution this ion.

Conclusions: The presence of urinary exosomal microRNA was confirmed for patients with a diversity of chronic kidney disease. The conditions of urine collection, storage and microRNA detection determined in this study may be useful for future biomarker discovery efforts.
Conclusions: This study has confirmed that subjects with the widest PP have the greatest risk of cardiovascular events. Elderly diabetic patients have a higher PP than non diabetic elderly. These hemodynamic changes may contribute to the increase risk of cardiovascular disease associated with diabetes.

MP241  EFFECT OF LOW-DOSAGE STEROID ON RENAL FUNCTION IN PATIENTS WITH ARISTOLOCHIC ACID NEPHROPATHY

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Introduction and Aims: To examine effect of low-dosage steroid treatment on renal function in patients with aristolochic acid nephropathy (AAN).

Methods: Forty-two chronic AAN patients in our hospital from November 1998 to September 2009 were included in this study. The patients were divided into two groups, the steroid treatment (ST) group and the control (C) group. The patients of ST group (n=18) took prednisolone 0.5mg/kg for 1-3 month, tapered off 0.05mg/kg every month. The patients of C group (n=24) did not take prednisolone. The complications, such as hypertension, anemia, and mineral disturbance, of the patients were treated with medicine on same protocol. The initial levels of serum creatinine (Scr) were 250.76 ± 57.85 μmol/l in ST group and 229.36 ± 64.93μmol/l in C group. There were no obvious statistical differences in the general materials and serum biochemical parameters at baseline in two groups. The levels of Scr were checked every three months for two years. Blood pressure, hemoglobin (Hb), and the serum biochemical parameters (SBC) were also observed.

Results: Scr levels of the patients in ST group maintained stable during the 2 years. While Scr levels in C group were elevated during follow-up, and nine month later Scr was significantly different when compared with the baseline. Blood pressure, Hb and SBC maintained stable in the two groups. Two patients suffered from necrosis of femoral head, and no patients experienced other severe side effects of steroid. Table

Changes in Scr levels in the patients of the two groups follow-up (month) Scr(μmol/l)

|   | P3 C(n=24) | P1 ST(n=18) | P2 0 | 229.36±64.93 | 250.76±57.85 | 0.275 | 6 | 286.92±135.37 | 235.17±100.57 | 0.109 | 0.230 | 12 | 354.36±177.94 | 256.98±75.53 | 0.788 | 0.040 | 18 | 411.04±279.12 | 270.98±95.42 | 0.469 | 0.026 |

Conclusions: Low-dosage steroid therapy could reverse or delay the progression of renal failure in chronic AAN patients.
**DIABETES - EXPERIMENTAL MODELS**

**MP242**  
**KIDNEYS FROM DIABETIC-HYPERTENSIVE RATS PERFUSED IN SITU WITH NGAL-CONTAINING KREBS SOLUTION EXCRETE MORE NGAL THAN THOSE FROM HYPERTENSIVE RATS**

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**Introduction and Aims:** Hypertension and diabetes are known to eventually damage target organs including the heart, blood vessels and the kidneys. Specifically, hypertension and diabetes lead to a progressive and irreversible loss of the kidneys’ function known as chronic kidney disease (CKD). We have previously demonstrated that urinary NGAL (nNGAL) increased as a consequence of the additive action of hypertension and hyperglycemia, but not when only one of these conditions is present. In the present work we aimed at specifically studying the renal handling of NGAL in hypertensive-hyperglycemic rats, through in situ renal perfusion experiments.

**Methods:** Male spontaneously hypertensive rats (SHR) were rendered hyperglycemic by a single administration of streptozotocin (60 mg/kg), or not (as controls). For glycemic control, diabetic rats were injected daily with the necessary dose of insulin to keep glycemia at about 400 mg/dL. After 2 month, rats were anesthetized and an extracorporeal circuit for kidney perfusion was set up. The renal artery, vein and ureter of the right kidney were ligated. The renal artery of the left kidney and the urinary bladder were cannulated. A catheter was placed in the right carotid artery and connected directly to the renal artery. Urine was continuously collected from a catheter placed in the urinary bladder at 10 minute intervals. After 1 hour of renal perfusion with blood from the carotid artery, oxygenated and warm (37 ºC) Krebs-dextran (40 g/L of dextran) in which an excess of rat NGAL (42 ng/ml) was added (or not, as control), was perfused through the renal artery at 3 ml/min, and was discarded through the renal vein. NGAL was measured in the different urine fractions.

**Results:** After one month of coexistence of hypertension and hyperglycemia, urinary NGAL was significantly increased, as compared to control rats, in which urinary NGAL was undetectable. When exogenous rat NGAL was added to the Krebs solution preflushing the kidney, hypertensive-hyperglycemic rats excreted more NGAL in the urine than hypertensive rats. As a control of the perfusion experiments, NGAL still appeared in the urine in hypertensive-hyperglycemic rats whose kidney was perfused with its own blood. However, urinary NGAL was undetectable in hypertensive rats.

**Conclusions:** Our results using a complementary technique reinforce our previous studies, which indicated that the urinary NGAL observed in rats suffering concomitantly from hypertension and hyperglycemia results from its altered tubular handling of this protein, most probably a defect in its tubular re-uptake, moreover, indicates that nNGAL comes from the blood.

**MP243**  
**PROTECTIVE EFFECT OF METFORMIN ON RENAL INJURY OF C57BL/6J MOUSE TREATED WITH HIGH FAT DIET**

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**Introduction and Aims:** Obesity is considered as a major generator of metabolic syndrome, and there are several pathophysiologic disturbances including inflammation, oxidative stress, insulin resistance, changes of adipokines, activation of renin-angiotensin-aldosterone systems (RAS), macrophage phenotypic switch that contribute to renal injury. Dyslipidemia, hyperglycemia, obesity, and hypertension, four of the risk factors for metabolic syndrome, are each independently characterized to increase oxidative stress and a proinflammatory state. In this study, we establish the model of metabolic syndrome, then treated with metformin for activating AMPK, and observe the changes of renal lipid accumulation, inflammation and oxidative stress, and the protective effect of metformin for renal injury.

**Methods:** High-fat diet for 12 weeks was used to establish the mice model of metabolic syndrome and the intervention of metformin (75mg·kg−1·d−1) for 4 weeks, and plasma biochemical indicator and body weight were used to evaluate the model. Sterol regulatory element-binding protein (SREBP)-1c, TNF-α, NADPH Oxidase (NOX4) mRNA was determined by the methods of real time-PCR. Phospho-AMP-activated protein kinase (P-AMPK) protein was detected by western blotting. Oil Red O staining, Masson staining and HE staining were for observing renal pathological changes.

**Results:** At the end of 12th week, compared with mouse on low fat diet (LFD), body weight (BW), the levels of fastinginsulin(FINS), plasma and renal triglyceride (TG) were higher evidently and plasma high density lipoprotein(HDL) and insulin sensitivity index (ISI) were lower significantly, but the levels of fasting blood glucose (FBG), plasma total cholesterol (TC) and renal TC had no changes; Oil Red O staining revealed renal lipids deposition, Masson staining and HE staining revealed glomerular hypertrophy, matrix increasing, and inflammatory cells infiltration in glomerul: the expression of α-AMPKα protein decreased and the expression of NOX4 increased, macrophage infiltration and the expression of SREBP-1c, TNF-α, NOX4 mRNA increased significantly in mouse treated with high fat diet (HFD). Compared with HFD group, through metforminintervening, metabolic disorders were significantly improved, renal lipids deposition and other pathological changes were ameliorated, the expression of α-AMPKα protein increased and the expression of SREBP-1c, TNF-α, NOX4 mRNA decreased significantly.

**Conclusions:** Metformin improves metabolic disorders, up-regulates activity of renal AMPK, diminishes the expression of renal SREBP-1c, TNF-α, NOX4 mRNA, decreased accumulation of renal lipids, prevents renal injury.

**MP244**  
**ISOLATION, CHARACTERIZATION AND BIOLOGICAL ACTIVITIES OF EXTRACELLULAR VESICLES DERIVED FROM HUMAN PANCREATIC ISLETS: POTENTIAL ROLE IN ENDOTHELIAL-BETA CELL CROSS-TALK AND IN LIMITATION OF DIABETIC NEPHROPATHY AFTER ISLET TRANSPLANTATION**

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**Introduction and Aims:** Islet transplantation is a therapeutic option for the treatment of type I diabetes. However, a substantial number of transplanted islets fails to engraft into liver suffering for poor vascular engraftment. Islets released a plethora of paracrine factors able to limit diabetic sequels including extracellular vesicles (EVs), small particles known to transfer proteins and RNAs to target cells. The aims of this study were: 1) isolation and characterization of EVs from human islets; 2) evaluation of the effects of EVs on human islet- or kidney-derived endothelial cells, mesangial cells, podocytes and tubular epithelial cells.

**Methods:** EVs were isolated by ultracentrifugation from medium of human islets and characterized by Nanosight, FACS, western blot, bioanalyzer, RT-PCR for islet-associated mRNAs and microRNAs. We evaluated in vitro on different cell types the EV-induced effects on: a) transfer of insulin mRNA/protein; b) proliferation (BrdU); c) resistance to apoptosis (TUNEL); d) transcriptional profile (mRNA); e) protein profile.

**Results:** EVs sized 155±73 nm and expressed CD44, ICAM-1, L-selectin, HLA I, insulin, c peptide, AKT, AGO-2 and CD63. EVs shuttled mRNA related to insulin secretion and signal transduction (insulin receptor, IRS2, AKT2, PDX2) and several microRNAs, including the beta-cell specific miRNA-375 and the pro-angiogenic miRNA-126 and miRNA-296. EVs were internalalized in islet endothelial cells inducing insulin mRNA/protein expression, proliferation, resistance to apoptosis and enhanced angiogenesis by up-regulation of pro-angiogenic and anti-angiogenic genes such as VEGFR1, VEGFR2, VEGF A, Angiopoietin 1, p-AKT, p-ERK, p-eNOS, Bcl-2. EVs were isolated from human islets and used to establish the model of metabolic syndrome, then treated with metformin for activating AMPK, and observe the changes of renal lipid accumulation, inflammation and oxidative stress, and the protective effect of metformin for renal injury.

**Conclusions:** Human islets release biologically active EVs able to shuttle specific proteins, mRNAs and microRNAs into different target cells. EVs exert a pro-angiogenic effect on islet-derived endothelial cells suggesting a role in beta cell-endothelial cross-talk and in the neoangiogenesis processes following islet transplantation. EVs may protect from diabetic nephropathy after islet transplantation by delivering their RNA cargo to glomerular and tubular cells.

**MP245**  
**EFFECT OF HIGH GLUCOSE AND HIGH INSULIN CONCENTRATIONS ON OSTEOSTABLES FUNCTION IN VITRO**

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Introduction and Aims: Changes in bone tissue are common in diabetic patients and may be more severe when associated with chronic kidney disease, however the pathophysiology of bone disease in consequence of Diabetes Mellitus (DM) is not fully understood. Using an in vitro model we evaluated the effect of high glucose, insulin and both on osteoblasts function.

Methods: Mice immortalized MC3T3-E1 cell line was differentiated during 14 days into osteoblasts. Cells were then stimulated with high glucose (30mM), insulin (5mM) or both for 24hr. Mannitol (30mM) was used as an osmotic control. miRNA expression levels of PTH receptor (PTHR1), collagen 1 (COL1), Nuclear Receptor Activator kappa B ligand (RANKL) responsible for osteoblasts activation, osteoprotegerin (OPG), the main inhibitor of RANKL and alkaline phosphatase (ALP), a marker for the mineralization process, were estimated by Real-Time PCR. Protein expression of COL1 was evaluated by Western Blot and the mineralization capacity was analyzed by von Kossa stain method.

Results: High glucose concentration induced an increase in the mRNA expression of RANKL (2x) and an impressive increase in OPG (30x). COL1 was increased by 12x indicating an excessive production of inorganic matrix. In contrast the expression of ALP decreased by 50%, indicating a deficit in mineralization process. This result was confirmed by von Kossa staining. Overall, the effects produced by glucose were not significantly reversed by treatment with the presence of insulin showing that the insulin independent glucose transporter GLUT1 in these cells. GLUT1 expression was not changed by glucose suggesting that an increase in the glucose uptake and metabolism may be not the main mechanism of osteoblasts dysfunction during diabetes. In fact mannitol induced by glucose suggesting that extracellular hyperosmolality per se may be able to stimulate the production of organic matrix and reduce mineralization capacity of osteoblasts in vitro.

Conclusions: In conclusion, excessive bone resorption does not appear to be a significant mechanism responsible for bone fragility induced by diabetes but an imbalance between mineralization process and organic matrix production might be primarily involved. The extracellular hypertonicity appears to be relevant in the osteoblasts dysfunction induced by hyperglycemia.

MP247 PARICALCITOL MODULATES CIRCULATING ACE2 ACTIVITY IN TYPE 1 DIABETIC MICE

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Introduction and Aims: Diabetic nephropathy progression can be slowed down by reducing albuminuria. Our group showed increased circulating ACE2 activity in non-obese diabetic mice (NOD). Previous studies suggest that the active form of vitamin D [1,25(OH)2D3] is a negative endocrine regulator of Renin Angiotensin System.

Methods: We tested the renoprotective effect of the vitamin D receptor stimulator Paricalcitol and its association with enzymatic ACE2 activity in a type 1 diabetic experimental murine model. This study also tested the effect of the combination of Paricalcitol and the direct renin inhibitor, Aliskiren.

Results: Diabetic NOD females age-matched with non-diabetic control females were studied for 21 days after diabetes onset. Treatments were the following: Diabetic animals given vehicle NOD pe (n=10); Diabetic animals treated with Paricalcitol NOD + PARI (n=10), Aliskiren NOD+ALSK (n=10) or with the combination NOD+PARI + ALSK (n=10). Non-obese Resistant mice were used as non-diabetic controls NOR (n=10). Paricalcitol administered alone or in combination with Aliskiren significantly reduced circulating ACE2 enzyme activity in diabetic NOD mice. Circulating renin activity significantly decreased in Aliskiren-receiving groups but no effect was found with Paricalcitol administration. Paricalcitol treatments were associated with a reduction in albumin excretion which did not reach statistical significance.

Conclusions: In the NOD diabetic mice, a type 1 diabetic model, Paricalcitol may modulate circulating ACE2 activity independently from the serum renin inhibition. In the early diabetic nephropathy stage, Paricalcitol treatment counterbalances the effect of bioactivity of circulating ACE2 activity.

MP248 MAXACALCITOL EXERTS ITS RENOPROTECTIVE EFFECTS IN NON-OBESE TYPE 2 DIABETIC RATS VIA SUPPRESSION OF OXIDATIVE STRESS AND AMELIORATION OF THE NRF2-KEAP1 PATHWAY

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Introduction and Aims: Diabetes mellitus is a major cause of end-stage kidney disease, which involves many complex factors and complications. Kidney dysfunction leads to decrease serum vitamin D levels and increase cardiovascular disease and mortality. Recently, vitamin D supplementation has been shown to reduce mortality risk and has beneficial effects on kidney and heart. Oxidative stress is one of the important risk factors in the progression of diabetic nephropathy. Although it is suggested that vitamin D could suppress oxidative stress, the detailed mechanism remains unknown. The aim of our study was to ascertain whether vitamin D could attenuate oxidative stress and prevent the progression of diabetic nephropathy.

Methods: The Spontaneously Diabetic Torii (SDT) rat model is a non-obese type 2 diabetic rat model inherited from an outbred colony of Sprague Dawley rats (CLEA Japan, Tokyo, Japan). Male SDT rats were divided into three groups: insulin-treated SDT rats (Control), vehicle-treated SDT rats (DM), and maxacalcitol (OCT)-treated SDT rats (DM+OCT). Renal function, albuminuria, and renal histology were assessed after 10 weeks of treatment. Immunohistochemistry, real time PCR and western blot analyses were also performed.

Conclusions: The miRNAs identified in this study might provide new information about gene regulation in a diabetic-like environment after exposure to calcitriol. It also highlights new gene targets that are part of the molecular mechanism and therapeutic treatment in CKD patients.

Blood Glucose t=21d (mg/dL)
NOR 156.5 ± 7.1
NOD pe 582.3 ± 11.6
NOD+PARI 525.3 ± 32.8
NOD+ALSK 582.4 ± 9.3
NOD+PARI+ALSK 538.5 ± 23.7

ACR t=21d (mgAlb/mgCrea)
NOR 14.7 ± 3.7
NOD pe 1520.8 ± 923.6
NOD+PARI 711.3 ± 284.4
NOD+ALSK 3122.6 ± 106.5
NOD+PARI+ALSK 390.9 ± 164.2

Serum ACE2 Activity (RFU/μg prot/hr)
NOR 111.4 ± 5.0
NOD pe 403.1 ± 42.6
NOD+PARI 316.2 ± 23.6
NOD+ALSK 357.7 ± 43.6
NOD+PARI+ALSK 263.6 ± 32.5

Cortical ACE2 Activity (RFU/μg prot/hr)
NOR 2113.5 ± 166.3
NOD pe 4566.8 ± 299.0
NOD+PARI 4526.7 ± 324.0
NOD+ALSK 4811.4 ± 453.3
NOD+PARI+ALSK 3856.1 ± 298.6

Serum Renin Activity (RFU/μl/hr)
NOR 1291.3 ± 124.9
NOD pe 1941.5 ± 117.1
NOD+PARI 1931.4 ± 80.0
NOD+ALSK 1623.5 ± 130.3
NOD+PARI+ALSK 1507.3 ± 111.0

*p<0.05 vs. NOD groups; #p<0.05 vs. NOD pe
Results: Albuminuria and mesangial matrix expansion were induced in the DM group, whereas OCT treatment ameliorated them. There were no significant differences among the three groups in blood pressure, serum calcium levels or creatinine clearance. OCT improved urinary excretion and immunohistochemical score of 8-hydroxydeoxyguanosine, mRNA expression of NADPH and serum levels of inflammation markers. Moreover, the expression of Nrf2 and its downstream genes was decreased and Keap1 increased in the DM group; however, these expressions were restored in DM-OCT group.

Conclusions: OCT attenuates the progression of diabetic nephropathy by suppression of oxidative stress and amelioration of the Nrf2-Keap1 pathway in non-obese type 2 diabetes.

**MP251** AN ORAL ADSORBENT AST-120 REDUCED OXIDATIVE STRESS, PROTEINURIA AND ALBUMINURIA IN METABOLIC SYNDROME/DIABETES RATS

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Introduction and Aims: Metabolic syndrome is known to be an important risk factor involved in the development of diabetic nephropathy. An oral adsorbent AST-120 has been used clinically as a drug for treatment of chronic kidney disease (CKD) patients to slow the progression of diabetic nephropathy. However, there is little evidence when AST-120 should be prescribed for subjects with early stage overt diabetic nephropathy. In this study, we aimed to assess the effect of AST-120 on the early stage of nephropathy using SHR/NDmc-cp, a rat model of metabolic syndrome1 type 2 diabetes.

Methods: Male SHR/NDmc-cp (SHR/ND rats), aged 7 weeks, were administered AST-120 with a diet containing 0% or 8% for 16 weeks. WKY rats were used as a control. At every 4 weeks, serum and 24-hour urine samples were collected for biometrical studies, and systolic blood pressure (SBP) was determined. We analyzed serum metabolites in normal and SHR/ND rats with or without AST-120 for 8 weeks by capillary electrophoresis mass spectrometry with time of-flight (CE-TOFMS) and applied CE-TOFMS data to principal component analysis (PCA). We also examined gene expression of oxidative stress and inflammatory markers in renal tissues treated with or without AST-120 for 8weeks using real-time PCR.

Results: AST-120-administered SHR/ND rats showed significantly lower level of urinary albumin excretion, urinary protein excretion and SBP as compared with SHR/ND rats. PCA score plot showed clear separation among three groups (Normal, SHR/ND and AST-120-administered SHR/ND). We could detect 40 metabolites, such as o-hydroxybenzoic acid, hippuric acid and indole-3-acetic acid, which accumulated in the serum of SHR/ND rats, and of which serum levels were reduced by administration of AST-120. Gene expression of oxidative stress markers in renal tissues was lower in AST-120-administered SHR/ND rats than in SHR/ND rats.

Conclusions: AST-120 administration decreased proteinuria, albuminuria and SBP in SHR/ND rats, and also reduced the expression of oxidative and inflammatory makers in renal tissues. We could detect 40 metabolites of which serum levels were increased in SHR/ND rats as compared with normal rats, and were reduced by administration of AST-120. It indicated that the administration of AST-120 at an early stage has a protective effect on the progression of diabetic nephropathy.

**MP252** SEQUENTIAL ACTIVATION OF PROINFLAMMATORY GENES IN THE GLOMERULAR AND TUBULOINTERSTITIAL COMPARTMENTS IN TYPE II DIABETIC NEPHROPATHY(DN)

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Introduction and Aims: An emergent hypothesis is that glucose-driven inflammatory changes are the trigger for subsequent oxidative stress and chronic kidney damage in type II DN. The transcriptional factor NF-kB helps to control the expression of genes activated during inflammation, cell apoptosis and survival. Enhanced NF-kB signaling has been observed in the tubulointerstitial compartment of diabetic glomeruli. Whether, NF-kB signaling is activated at an early stage of human DN has never been studied.

Methods: We studied the expression of proinflammatory genes, as well as apoptosis (TUNEL, anti-smooth actin and NF-kB expression (p50 and p65, immunohistochemistry) in the glomerular and tubular compartments of Pt with DN and microalbuminuria (n=12, age 60±12 yr, 60/4/6F, eGFR 90/4/ml/min, AER 158±15 mg/ml/min) or overt nephropathy (n=11, age 63±3 yr, 46/5/4F, eGFR 32±3 ml/min, pUOP 4.7±1 g/day). Normal portions of kidneys removed for carcinoma (n=9, 5M/4F, age 60±14 yrs) served as controls (C). Glomeruli and the tubulointerstitial specimens were microdisected, total RNA extracted, cDNA RT and quantitative RT-PCR performed with the use of primers of proinflammatory genes, either upward or downward targets
of NF-κB (CC2R, CCL2, CCL5, CCR5, TLRA4, TNF, TNF-R1) and J-Actin. Results: In microbureamuric Pt, NF-κB signaling (both p65 and pIkB) were 4 fold higher (p<0.05) in the glomeruli as compared to C, and it was mainly expressed in endothelial cells and in podocytes. NF-κB signaling was only modestly upregulated in tubules (+ 25%, p<NS). Consistently with these findings, glomerular apoptosis was markedly increased (40.7 vs 0.70±6.6% in C, p<0.05) and it was observed mainly in podocytes. In microdissected glomeruli TNF-αTLRA4, CCR5, and CCL5 mRNA were markedly (3-5 fold) upregulated. Only in tubulointerstitial compartment (p<0.02). Upregulated NF-κB was mainly expressed in endotherial cells, podocytes and proximal tubules. In Pt with advanced DN, NF-κB signaling decreased in glomeruli but it was upregulated in tubuli (p<0.05) and in tubulointerstitial mononuclear cell infiltrates. In microdissected glomeruli TNF-α and TLRA4 but not CCR5 and CCL5 persisted to be upregulated, (3-5 fold, p<0.01) while in the tubulointerstitial compartment several genes (TNF-αTLRA4, TNFRS and CCR5) showed mRNA expression above background (p<0.02).

Conclusions: Our data are consistent with the activation of NF-κB dependent proinflammatory transcriptional programs in the glomerular compartment, at an early stage of DN. At this stage, the acceleration of apoptotic processes in the glomeruli likely contributes to an early decrease in remodeling and albuminuria onset. In Pt with advanced DN, NF-κB dependent signaling pathways are enhanced in the interstitial compartment, owing to inflammatory cell recruitment.

Methods: This study was conducted on 80 subjects. Group 1 included 10 healthy subjects as controls, group 2 included 60 type 2 diabetic patients with normal or increased albumin excretion rate (AER) and group 3 included 10 type 2 diabetic patients on maintenance hemodialysis (HD). To all studied subjects thorough clinical assessment and laboratory investigations included:Estimation of serum levels of fasting glucose (FSG), creatinine, uric acid, urea, sodium, potassium, calcium, phosphorus, cholesterol (Total, HDL and LDL) and triglycerides (TG). Estimation of urinary albumin / creatinine ratio (ACR) to assess AER and estimation of plasma dopamine and serum renalsawedene were done.

Results: There were no significant differences in the mean dopamine levels between the three studied groups. Renalase level was significantly higher in HD patients compared to controls and other diabetic patients. Diabetic patients with increased AER had significantly higher systolic blood pressure, serum creatinine and renalsawedene levels than diabetic patients with normal AER. Diabetic patients with increased serum creatinine ≥1.4mg/dl had significantly longer duration of diabetes and higher systolic and diastolic blood pressure. They also had significantly higher AER, FSG, dopamine and renalsawedene levels than diabetic patients with serum creatinine <1.4mg/dl. ACR was positively correlated with duration of diabetes, systolic and diastolic blood pressure and serum creatinine and negatively correlated with the use of Angiotensin converting enzyme inhibitors or Angiotensin II type 1 blockers.

Conclusions: 1. Blood levels of dopamine and renalsawedene are increased in type 2 diabetic patients with renal dysfunction, so they can be used as risk markers of renal disease in these patients. 2. Serum levels of renalsawedene are increased in type 2 diabetic patients with nephropathy to compensate for the increase in dopamine concentration 3. Diabetic nephropathy is associated with longer duration of diabetes, poor glycemic control and higher blood pressure. 4. The higher renalsawedene level in hemodialysis patients may be due to much higher sympathetic nervous system activity and much lower renalsawedene clearance in these patients.
HIGH GLUTOSE INDUCES INSULIN RESISTANCE IN RAT CULTURED PODOCYTES VIA AMPK–PTEN PATHWAY

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Introduction and Aims: Diabetic nephropathy (DN) is a chronic progressive disease that affects up to 40% of patients with diabetes mellitus. The early clinical manifestation of DN is microalbuminuria, which can progress to overt proteinuria and renal dysfunction. Glomerular visceral epithelial cells (podocytes), as part of the filtration barrier, play an important role in the development of DN, and their numbers are significantly reduced in both type 1 and type 2 diabetic patients. Disturbances in insulin signaling accompanied by insulin resistance can lead to various intracellular events. We hypothesized that high glucose concentrations would lead to disturbances in interactions between AMPK and PTEN proteins in podocytes.

Methods: Experiments were performed in primary rat podocytes cultured with normal (NG, 5.6 mM) or high (HG, 30 mM) glucose concentrations for 5 days. Immunodetection methods were used to detect AMPK and PTEN proteins, and their phosphorylated forms. Insulin-stimulated changes in glucose uptake were used to detect insulin resistance. Isoforms of AMPK were detected by RT-PCR. AMPK activity was modified by siRNA of AMPK isofoms.

Results: In NG medium–cultured podocytes, insulin-stimulated glucose uptake increased from 0.71 ± 0.04 to 1.09 ± 0.04 nmol/min/mg protein (P < 0.05), whereas it was abolished after addition of cells in HG medium. A high glucose concentration decreased the phosphorylation of AMPK in podocytes by 25% (0.69 ± 0.05 vs. 0.91 ± 0.06, P < 0.05). The stimulating effect of insulin on AMPK phosphorylation was observed in podocytes cultured in NG medium, however, in the presence of HG, this effect was abolished. Knockdown of AMPKα1 or AMPKα2 protein expression abolished the insulin-dependent increase in glucose uptake into podocytes cultured in NG medium (decrease from 2.34 ± 0.30 to 1.77 ± 0.13 or 1.54 ± 0.17 nmol/min/mg protein), for AMPKα1 knockdown, respectively. In HG medium–cultured podocytes PTEN protein level increased by approximately 45% (0.49 ± 0.03 vs. 0.34 ± 0.02, P < 0.05), whereas PTEN phosphorylation decreased by about 30% (1.55 ± 0.07 vs. 2.24 ± 0.18, P < 0.05). Silencing by siRNA of the AMPK subunits resulted in increases in the PTEN concentration of approximately 26% (from 0.36 ± 0.05 to 0.45 ± 0.05, P < 0.05) and 25% (P < 0.05) for AMPKα1 and AMPKα2, respectively. PTEN phosphorylation was decreased by about 17% in the presence of AMPKα1 siRNA (from 1.75 ± 0.12 to 1.46 ± 0.08, P < 0.05) and 22% with AMPKα2 siRNA (to 1.37 ± 0.04, P < 0.05).

Conclusions: We found that impairment of insulin induction of glucose uptake into podocytes cultivated in the presence of high glucose concentrations for long periods of time is associated with increased PTEN levels and decreased PTEN phosphorylation in an AMPK-dependent manner.

MEASUREMENT OF GLYCATION END PRODUCT RELATED UREMIC TOXINS IN SKIN: COMPARISON OF TWO NON-INVASIVE METHODS

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Introduction and Aims: Accumulation of advanced glycation end-products (AGE) in skin is a hallmark of dialysis patients and increases with duration of diabetes, glycated hemoglobin levels, and lipid status. AGE products were quantified with a device (AGE Reader; DiagnOptics Technologies B.V, Gröningen, The Netherlands) in 300-600 nm range. DESI-MS semi-quantitative technique measurements were done at the same consequent five times using a modified OmniSpray (Prosolia, Indianapolis, IN) ion source mounted on either an TSQ Quantum triple quadrupole mass spectrometer (Thermo Fisher Scientific, San Jose, CA) or an LTQ Orbitrap Discovery Fourier transform mass spectrometer (Thermo Fisher Scientific GmbH, Bremen, Germany). For statistical evaluation Pearson analysis was applied. Multiple regression analysis was used to adjust the association for individual clinical parameters.

Results: SAF values ranged between 0.9 and 1.7 in the tested population. They significantly correlated (r=0.9 and p<0.001 for each) to 3-indoxyl-sulfate (mean: SD±1.545 ± 247.41), carboxymethyl lysine (mean: SD±1.971 ± 190.87), phenol-sulfate (mean: SD±1.541 ± 166.01), and pentosidine (mean: SD±1.191 ± 77.05) levels measured in arbitrary units. It remained significant after adjustment to age, duration of diabetes, glycated hemoglobin levels, and lipid status with multiple regression analysis.

Conclusions: The strong correlation between adolescents’ SAF values measured with AGE-Reader and some glycation product type uremic toxins measured with DESI-MS indicates that SAF values might be used as supplementary markers of uremic toxicity.

REGULATORY EFFECT OF RAPAMYCN ON TLR-4 SIGNALWAY IN DIABETIC NEPHROPATHY

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Introduction and Aims: In this study, we use streptozotocin (STZ) induced SD rats to establish the early diabetic nephropathy model. Meanwhile we investigated the mechanism of rapamycin interfere with early diabetic nephropathy, focused on the mechanism of rapamycin intervention on TLR4 / NF-κB signaling pathway.

Methods: Sixty 3D male rats were randomly divided into 3 groups, control group, diabetic nephropathy group (DN group) and diabetic nephropathy with rapamycin treatment group (RAPA group). Diabetic nephropathy (DN) was induced by streptozotocin (STZ) via intraperitoneal injection. The expressions of TLR-4, AKT, mTOR, p70S6K, IKKα and NF-κB in kidney tissue were examined by immunohistochemistry and Western blot at week 2, 4 and 8, respectively. Meanwhile the mRNA expression of TLR-4 in kidney tissue was examined by real-time PCR (RT-PCR).

Results: The glomerular volume increased with the mesangial matrix proliferation by pathological staining in 2-weeks DN group, after rapamycin treatment the above pathological changes alleviated. Meanwhile the apoptosis of tubular epithelial cells were increased in DN group, while the rapamycin lightened the apoptosis. TLR-4 and NF-κB p65, mainly expressed in kidney tubules and glomeruli, were upregulated significantly in DN group, compared with control group. Furthermore the expression of TLR-4 decreased significantly in DN group, the mRNA and protein expression of TLR-4 was remarkably reduced after rapamycin treatment. Immunohistochemistry showed that mTOR expressed in renal tubular epithelial cells and a small amount of mesangial cells, there was no significant difference between each group, while p70S6K expression significantly increased only in the renal tubules and mesangial cells in DN group. AKT and phosphorylated AKT levels of renal tissue in each group were found that after modeling of diabetic nephropathy the renal AKT was phosphorylated which was inhibited by the rapamycin but it didn’t affect the total AKT level of the renal tissue. Phosphorylated IKKe and the nucleus of NF-κB p65 level in the renal tissue were higher in diabetic nephropathy model by western blot analysis. But interestingly we found that the phosphorylation of IKKe levels delayed increasing. After administration of rapamycin the NF-κB p65 and phosphorylated IKKe were inhibited.

Conclusions: AKT/mTORp70S6K signaling pathway was activated in diabetic nephropathy. Rapamycin eased glomerular hypertrophy and mesangial matrix proliferation and apoptosis of tubular epithelial cell. Meanwhile it could partial control urine albumin level but the blood glucose not affected. Rapamycin can not only the TLR4 protein, can also reduce the mRNA level, thereby reducing the IKKe phosphorylation and inhibiting activation of NF-κB in p65.

HIGH GLUTSE DIFFERENTIALLY INDUCES GRADUAL LOSS OF PODOCYTER MARKERS AND PARTIAL DE-DERMINATION

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Introduction and Aims: Podocytes are visceral epithelial cells in the renal glomerulus which form the main permissive barrier for normal blood filtration. Their unique polarized phenotype, characterized by a main body with multiple primary and secondary processes, is maintained by means of expressing several podocyte-specific proteins, including podocin and nephrin. Nephrin is a major scaffolding protein of the slit diaphragm, which takes part in transmitting extracellular signals from the slit diaphragm to the intracellular actin cytoskeleton. Podocalyxin is the major sialomucin of the apical domain of foot processes, which is required for the formation and maintenance of foot processes. Loss of the negative charge of the podocyte glyocalyx, carried out for the most part by podocalyxin, leads to phenotypic changes that have been associated with proteinuric diseases.

Methods: We used an in vitro model of human glomerular epithelial cells (HGERC) to investigate the role of high glucose in dysregulating the podocyte epithelial phenotype and determine the time needed for this change to occur.

Results: In vitro culturing of HGERC in the presence of high glucose levels resulted in progressive and sustained downregulation of podocalyxin and nephrin expression. Based on insights of podocyte injury, the major pathologic phenotypes that result in
the uniform reaction of proteinuria are apoptosis, foot process effacement and de-differentiation. In order to determine the differentiation status of high glucose-stimulated HGEC, we additionally determined the surface expression levels of a standard glomerular epithelial marker, CD10/CALLA, and observed that it also became suppressed by high glucose in a non-reversible manner. This suppression was associated with upregulation of the mesenchymal marker vimentin. Our study demonstrates for the first time that podocyte-specific markers undergo changes of expression at different time intervals, since glucose-mediated podocyanol downregulation is a progressive process that precedes downregulation of nephrin expression. Finally we demonstrate that high glucose permanently impaired WT1 binding to the podocalyxin gene promoter region but did not affect WT1 binding on the nephrin gene promoter region.

Conclusions: The presence of high glucose induced a phenotypic conversion of podocytes resembling partial dedifferentiation. This phenotypic modulation was gradual and differential since it started with loss of the podocytic epithelial markers CD10/CALLA and podocalyxin and was followed by increased expression of the mesenchymal marker vimentin concomitant with downregulation of nephrin expression.

**MP260** POOR LYSSOMAL MEMBRANE INTEGRITY IN PROXIMAL TUBULE CELLS OF HAPTOGLOBIN 2-2 GENOTYPE MOUSE WITH DIABETES MELLITUS

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Introduction and Aims: A common functional allelic polymorphism in the Haptooglobin(Hp) gene has been demonstrated to be a major determinant of susceptibility to cardiovascular disease and in the development and progression of DN in individuals with Diabetes Mellitus (DM). We have demonstrated that in humans and mice, the Hp2 allele is defective in its ability to protect against oxidative stress, and that Vit.E selectively provides a cardiovascular and renal protection to Hp 2-2 individuals and mice. Aim of this study was to determine the intracellular localization of this iron in the proximal tubule cell (PCT) and to assess its potential toxicity in the development and progression of Diabetic Nephropathy(DN).

Methods: Wild type C57Bl/6 mice have only an Hp 1 allele. The Hp 2 allele is found only in man. We genetically engineered a murine Hp 2 allele and inserted it in the murine Hp locus by homologous recombination. We induced DM, by intraperitoneal streptozotocin administration (50mg/kg for five subsequent days) at 10 weeks of age. We assessed lysosomal membrane integrity, redox-active chelatable iron in kidney lysosomes and vitamin E concentration.

Results: We have found increased iron-rich deposits in lysosomes of proximal tubule cells in Hp 2-2 DM vs Hp 1-1 DM (65±4% of all lysosomes) compared with Hp 1-1 DM mice (41±4% of all lysosomes, p<0.05). The deposit sizes were approximately double within Hp 2-2 DM lysosomes as compared to those within lysosomes from Hp 1-1 DM mice (p<0.05). Intralysosomal redox-active iron concentrations are markedly increased in Hp 2-2 DM mouse kidneys was 2-fold increase in the amount of redox-active iron in the lysosomes of Hp 2-2 DM mice (0.56 ± 0.07 μM) as compared with those from Hp 1-1 DM mice (0.23 ± 0.14 μM, p = 0.06). Lysosomal membrane lipid peroxides are increased significantly in Hp 2-2 DM proximal tubule cells (p=0.0001 for 4-way ANOVA and p=0.001 for all pairwise comparisons between Hp 2-2 DM and the other three groups). Lysosomal membrane integrity is significantly decreased in Hp 2-2 DM proximal tubule cell lysosomes Vitamin E supplementation resulted in a significant 45% reduction in lysosomal redox-active iron in Hp 2-2 DM mice (p=0.04) with no significant effect on lysosomal redox-active iron in Hp 1-1 DM mice. There was a significant correlation between lysosome membrane α-tocopherol concentrations and the degree of lysosomal membrane oxidation in Hp 2-2 DM mice but not in Hp 1-1 DM mice.

Conclusions: 1. A novel mechanism whereby the Hp genotype may predispose to renal injury in the setting of DM Via increased Iron deposition in the lysosomes of PCT. 2. Elimination of excess proximal tubule iron, or its dangerous oxidative potential, possibly by a combination of iron chelating agents , and/or antioxidants may thus became suppressed by high glucose in a non-reversible manner. This suppression was associated with upregulation of the mesenchymal marker vimentin. Our study demonstrates for the first time that podocyte-specific markers undergo changes of expression at different time intervals, since glucose-mediated podocyanol downregulation is a progressive process that precedes downregulation of nephrin expression. Finally we demonstrate that high glucose permanently impaired WT1 binding to the podocalyxin gene promoter region but did not affect WT1 binding on the nephrin gene promoter region.

Methods: Twenty Wistar rats were lipid supplemented (2ml/day of 99.6% lipid suspension) and after 3 weeks (T3) diabetes was induced by low-dose intraperitoneal streptozotocin. They were sacrificed after 10 weeks of diabetes (T13). Twenty standard fed rats served as controls. Serum creatinine, lipid profile, adiponectin and albuminuria were determined. Intrarenal adiponectin in arterioles and glomeruli was analyzed using confocal laser scanning fluorescence microscopy, with automatic point-by-point fluorescence quantification using ZEN software.

Results: Lipid profile was significantly altered in case animals versus controls: cholesterol was 2.55±0.88 versus 1.62±0.23mmol/l, p<0.001, HDL cholesterol was 0.48±0.31 versus 1.09±0.14 mmol/l, p<0.0001 triglycerides were 10.13±8.39 versus 0.57±0.07mmol/l, p<0.0001. Albuminuria was also lower in case subjects (13.06±5.46 versus 21.76±10.78 μg/ml, p<0.001). At T13 albuminuria was significantly increased in diabetic animals (0.63±1.84 versus 0.05±0.05 mg/g creatinine, p=0.002), serum creatinine was slightly lower (32.71±4.42 versus 36.24±5.30 μmol/l, p=0.04) and light microscopy was normal in diabetic subjects and controls. The model is consistent with incident nephropathy (hyperfiltration, albuminuria) in hyperlipidemic diabetic animals. Endothelial arteriolar fluorescence for adiponectin had lower intensity in diabetic animals (131.93±39.35) than in controls (179.75±26.06, p= 0.0003).

Florescence of the glomerular capillaries was discontinuous, its medium intensity was lower in case (74.31±27.55) than in control subject (91.25±19.20, p=0.050). There was no correlation of serum adiponectin to intra-arteriolar or intra-glomerular staining for adiponectin or to albuminuria.

Conclusions: Intrarenal endothelial staining for adiponectin is reduced in incipient diabetic nephropathy in a hyperlipidemic diabetic rat model.
Introduction and Aims: Transforming growth factor-β (TGF-β) is the central cytokine responsible for the development of diabetic nephropathy, and is usually secreted as a latent procytokine complex and can be activated by latent TGF-β-activating proteases (LTAPs). It is recently reported that thrombospondin-1 (TSP-1) is a major activator of latent TGF-β in diabetic nephropathy in vivo. We suggested previously that α-spinasterol may be a promising therapeutic substance able to ameliorate the development and progression of diabetic nephropathy by inhibiting TGF-β production. However, it has not been investigated how α-spinasterol inhibits TGF-β production. So this study is to examine the effect of α-spinasterol on TSP-1 production and downstream target of TGF-β through TSP-1 induced by high glucose in cultured mesangial cells.

Methods: α-spinasterol was isolated from roots of Phytolacca americana. Mouse mesangial cells were incubated for 24 hour with normal (5.6 mM) or high (30 mM) glucose-containing medium in the presence or absence of α-spinasterol (1 μg/mL). Mesangial proliferation was determined by counting cell number. Real time qRT-PCR was performed to observe the TSP-1, TβRI and TβRII mRNA expression. TSP-1, Smad3/2, TIMP2, and MMP2 protein expression in medium or cell lysate were determined by western blot. Gelatin zymography was performed for the measurement of MMP2 activity in conditioned medium.

Results: α-spinasterol inhibited the high glucose-stimulated proliferation of mouse mesangial cells, but did not affected to the growth of mouse mesangial cells cultured under normal glucose. TSP-1 mRNA expression and protein expression was increased in cultured mouse mesangial cells under the high glucose concentration. Also, α-spinasterol attenuated TSP-1 mRNA expression and protein expression in cultured mouse mesangial cells under the high glucose, but not under the normal glucose concentration. Also, α-spinasterol inhibited TSP-1 protein expression in medium of cultured mouse mesangial cells under the high glucose. Smad3/2 activity was increased in high glucose-stimulated mesangial cell, but decreased by α-spinasterol. TIMP2/MMP2 ratio in cultured medium or cell lysate was decreased by α-spinasterol. MMP2 activation on gelatin zymography was similar to MMP2 protein expression in same medium.

Conclusions: We demonstrated that α-spinasterol attenuated TSP-1 protein expression in cultured mouse mesangial cells under the high glucose, and resulted in regulating cell proliferation, and TIMP2/MMP2 ratio through TGF-β/Smad3/2 signaling. This result suggests that α-spinasterol may be considered as a promising future treatment option for diabetic nephropathy.

Introduction and Aims: The peroxisome proliferative-activated receptor-α (PPARα) is a lipid-sensing transcriptional factor that has a role in gluco-oxidative stress and lipotoxicity. AMPK-α kinase (AMPK) and peroxisome proliferative-activated receptor gamma coactivator-1α (PGC-1α) is a multifunctional transcriptional protein, acts as a ‘molecular switch’ in pathways controlling fatty acid oxidation and oxidative stress, and may be a critical link in the pathogenesis of type 2 diabetes and metabolic syndrome associated with estrogen-related receptor (ERR)-1α. We evaluated the renoprotective effect of PPARα agonist associated with improving lipotoxicity and oxidative stress through the change of AMPK-α/PGC-1α signaling to treat type 2 diabetic nephropathy.

Methods: Male C57 BLKSdb/m mice and their downstream PI3K-Akt-FoxOs signaling. In cultured mesangial cells, suppressed AMPK-PGC-1α-ERR-1α and increased P38-Akt phosphorylation of FoxO3a signaling. In high-glucose media reversed by fenofibrate, which was associated with changes in oxidative stress and apoptosis.

Conclusions: Our results suggest that PPARα agonist fenofibrate improves lipotoxicity through activation of the AMPK-PGC-1α-ERR-1α signaling, and may be a potentially therapeutic modality to modulate AMPK-PGC-1α-ERR-1α signaling to treat type 2 diabetic nephropathy.

Introduction and Aims: Hypermagnesiuria is a well known clinical feature of diabetes mellitus and is recently revealed to be highly related to the development of insulin resistance. Although it has been known that the hypomagnesemia is evoked by the decreased Mg reabsorption in the kidney as well as renal interstitial damages, the molecular mechanism has not been well understood. In this study, we studied the changes in gene expression of Mg transporters and their downstream/transcriptional regulation between their expression profile and interstitial damages in type 2 diabetic rats.

Methods: Kidneys were obtained from male OLETF (F) and LETO (L) rats of 16, 24, and 34 weeks-old. Expression of Mg transporting molecules was assessed by immunohistochemistry and RT-PCR. Time-differential development of interstitial damage was assessed by histological and molecular biological analysis.

Results: Fractional excretion of Mg (FEMg) in F were significantly higher in older than 24 weeks (1.32±0.10 in 24L, 1.84±0.07 in 24F, 1.12±0.14 in 34L, 1.53±0.16 in 34F), showing significant hypermagnesiuria from the early stage of diabetic nephropathy. Gene expressions of Mg transporting molecules in DCT were significantly reduced in F (TRPM6: 108.8±6.0 in 24L, 78.8±4.9 in 24F, 92.2±6.5 in 34L, 77.7±5.7 in 34F, NCC: 100.2±3.7 in 24L, 88.1±3.2 in 24F, 113±4.0 in 34L, 85.4±3.6% in 34F), whereas the expressions of molecules in TAL were not decreased (α-SMA: 16.104±3.7 in 24L, 122.1±3.5 in 24F, 103.5±5.2 in 34L, 120.5±4.2% in 34F). The results of gene expression were agreed with the immunohistochemistry of those molecules (TRPM6: 0.36±0.04 in 34L, 0.19±0.06% in 34F, NCC: 1.42±0.13 in 34L, 0.58±0.07% in 34F). On the other hand, expression of molecular markers for interstitial damage, such as MCP-1, α-SMA, TGF-β, were not different between F and L in all experimental periods in compatible with the histological assessment of interstitial damages.

Conclusions: Present study might suggest that down-regulated TRPM6 in DCT would be a principal factor evoking hypermagnesiuria and hypomagnesemia in diabetic nephropathy. Down regulation of NCC might be involved in the TRPM6 down regulation. The elevation Mg excretion in diabetes might be independent of renal interstitial damages.
Results: The glomerular volume and mesangial matrix were increasing in DN group with the extension of experimental time by pathological evaluation. At 8 week of ends of experiment the renal GV value and MMEI index in DN group was significantly thickening when compared with the control group by electron microscopy (p<0.05). The MBL expression in control group was seldom in tubular epithelial cells, but after the DN establishment the MBL protein expression was significantly increasing (p<0.05). When compared with the control group the TLR-4 protein in DN group was increasing significantly which was almost expressed the same as the MBL (p<0.05). We found that anti-MBL antibody coimmunoprecipitation the protein complexes can detect TLR-4 protein. On the contrary anti-TLR-4 antibody precipitation samples can be detected MBL protein.

Conclusions: 1. Establishment of early diabetic nephropathy model by streptozotocin induced SD rats was successful. 2. We found the activation of innate immune system in early diabetic nephropathy meanwhile MBL and TLR-4 involved in the development of disease. 3. there was mutual combination between MBL and TLR4 in early diabetic nephropathy.

MP268 LONG-TERM STUDY OF ERYTHROPOIETIN, LOSARTAN, AND COMBINATION IN STREPTOZOTOCIN-INDUCED DIABETIC RATS
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Introduction and Aims: Recombinant human erythropoietin (HruEPO) has emerged as a new renoprotective agent against various acute kidney injuries. Experience with rHuEPO in chronic kidney injuries is so far limited and conflicting results were obtained. In the present study, we addressed to evaluate the long-term renal effects of low-dose HruEPO in diabetic nephropathy (DN) of rats in relation to novel hypoxia theory and endogenous EPO secretion. HruEPO was compared to standard drug, losartan (LSR), and the possibility of add-on therapy was also tested.

Methods: Thirty-four male SD rats were randomly divided into five groups: control-naive group, untreated diabetic group, EPO-treated diabetic group (150 U/kg, S.C., TIW), LSR-treated diabetic group (3 mg/kg/day, P.O.), EPO-LSR-treated diabetic group. Drug treatment was started one week after streptozotocin (STZ) injection and continued for twenty-eight weeks. Albuminuria was evaluated every four weeks. Assessment was done by renal function tests, blood pressure measurement, renal vein oxygen tension and electrolyte levels, plasma active-renin concentration, endogenous EPO concentration, and complete hematological profile, together with renal histopathological examination using Periodic Acid-Schiff (PAS) and Masson trichrome-stained sections.

Results: STZ-treated diabetic rats developed progressive albuminuria, renal dysfunction, and significant glomerular changes 28 weeks after induction of diabetes. Chronic administration of HruEPO alone or in combination with LSR to the STZ-induced diabetic rat did not show beneficial effect on DN evolution, inspite of improving diabetic-renal hypoxia. LSR sole therapy had the best beneficial effect on DN evolution based on renal function evaluation, albuminuria, and renal histopathology. Interestingly, administration of LSR either alone or in combination with HruEPO in STZ-induced diabetic rats significantly abolished increased plasma endogenous EPO observed in untreated- and EPO-treated diabetic groups.

Conclusions: In conclusion, this study has questioned the renoprotective role of low-dose HruEPO in the setting of DN and proved that this low-dose HruEPO led to elevation of blood pressure and was hematomatically effective.

MP267 PODOTOXICITY OF GLUCOSE DEGRADATION PRODUCTS
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Introduction and Aims: Hyperglycemia results in increased concentrations of glucose degradation products. The study of peritonal dialysis solution biocompatibility has highlighted the adverse effects of glucose degradation products. Recently, 3,4-dideoxyglucosone-3-ene (3,4-DGE) has been identified as the most toxic glucose degradation product in peritoneal dialysis fluids. Moreover, 3,4-DGE is present in high-fructose corn syrup and its precursor 3-deoxyglucose is increased in diabetes.

Aims Study the role of 3,4-DGE in glomerular injury.


Results: We studied the effects of 3,4-DGE on cultured human podocytes. 3,4-DGE induced apoptosis in human podocytes in a dose- and time-dependent manner. Peak apoptosis was observed after 48h of culture. The lethal concentration range was 50-100 micromol/l. 3,4-DGE resulted in release of cytochrome c from mitochondria and activation of caspase-3. While high glucose concentrations increased Hsp27 and this increase in Hsp27 protected podocytes from glucose-induced apoptosis, 3,4-DGE decreased the expression of podocyte Hsp27. Apoptosis induced by 3,4-DGE was caspase-dependent and could be prevented by the broad-spectrum caspase inhibitor zVAD-fmk (Z-Val-Ala-Asp-fluoromethylketone). However, caspase inhibition did not prevent eventual cell death. Antagonism of Bas by a Ku-70-derived peptide prevented apoptosis. Intravenous administration of 3,4-DGE to healthy mice resulted in a decreased expression of Hsp27 in whole kidney. Furthermore, systemic 3,4-DGE promoted caspase-3 activation in podocytes.

Conclusions: In conclusion, 3,4-DGE promotes apoptosis of cultured human podocytes by a Bax- and caspase-dependent mechanism. A role for 3,4-DGE in glomerular injury resulting from diabetes or ingestion of high-fructose corn syrup should be further explored.

MP268 EFFECT OF MALE GENDER AND DIABETES ON CIRCULATING ACE2 ACTIVITY IN STREPTOZOTOCIN (STZ)-INDUCED MICE
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Introduction and Aims: Male gender predisposes to chronic kidney disease. We previously showed that circulating ACE2 activity is increased in male and diabetic NOD mice. We proposed to study gender and the effect of diabetes in the streptozotocin (STZ) mice on circulating ACE2. In addition, we also studied the effect of gonadectomy in diabetic and control mice.

Methods: STZ-induced diabetic c57bl6 mice were followed for 19 weeks. Citrate was administered as a vehicle. Study groups: control male and female (mCONT and fCONT), diabetic male and female (mDB and fDB), control and diabetic gonadectomised male (mCONT-GDX and mDB-GDX). Gonadectomy was performed 10-12 days after diabetes induction. ACE2 enzymatic activity in serum was determined by a fluorometric assay.

Results: Hyperglycemia was observed in all STZ groups. Mean Blood Glucose (BG) was significantly higher in males compared to females for both control and diabetic groups. Furthermore, gonadectomy significantly decreased hyperglycemia in the diabetic and control mice. We proposed to study gender and the effect of diabetes in the streptozotocin (STZ) mice on circulating ACE2. In addition, we also studied the effect of gonadectomy in diabetic and control mice.

Methods: STZ-induced diabetic c57bl6 mice were followed for 19 weeks. Citrate was administered as a vehicle. Study groups: control male and female (mCONT and fCONT), diabetic male and female (mDB and fDB), control and diabetic gonadectomised male (mCONT-GDX and mDB-GDX). Gonadectomy was performed 10-12 days after diabetes induction. ACE2 enzymatic activity in serum was determined by a fluorometric assay.

Results: Hyperglycemia was observed in all STZ groups. Mean Blood Glucose (BG) was significantly higher in males compared to females for both control and diabetic groups. Furthermore, gonadectomy significantly decreased hyperglycemia in the diabetic and control mice. A direct correlation (r=0.64; p<0.0001) between BG and circulating ACE2 was found. Decreased circulating ACE2 activity in both control and diabetic male mice. A direct correlation (r=0.64; p<0.0001) between BG and circulating ACE2 was found.

Conclusions: Male gender and diabetes increased glyceremia and circulating ACE2 activity suggesting an increase of circulating angiotensin II levels. Gonadectomy in diabetic and control mice prevents the activation of RAS. Thus, the increase of circulating ACE2 observed in males may be ascribed to a modulation of circulating male sex hormones.

MP269 INFLUENCE OF INSULIN IN THE GENIC EXPRESSION OF RAS COMPONENTS OF THE PODOCYTE IN A DIABETIC SITUATION
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Introduction and Aims: Renin-Angiotensin System (RAS) blockade has been shown to delay the progression of chronic kidney disease, mainly in Diabetic Nephropathy. The podocyte is a key cell involved in the development of albuminuria since early stages of diabetic nephropathy. This cell presents a functionally active local RAS and is responsible for the activation of the systemic RAS, which is necessary for the development of albuminuria.

Aims: Study the role of insulin in the genetic expression of RAS components of the podocyte in a diabetic situation.

Methods: Circulating ACE2 activity in both male and female diabetic mice compared to controls. Control male mice showed significantly higher circulating ACE2 activity than females, and castration suppressed decreased circulating ACE2 activity in both control and diabetic male mice. A direct correlation (r=0.64; p<0.0001) between BG and circulating ACE2 was found.

Results: Hyperglycemia was observed in all STZ groups. Mean Blood Glucose (BG) was significantly higher in males compared to females for both control and diabetic groups. Furthermore, gonadectomy significantly decreased hyperglycemia in the diabetic and control mice. Circulating ACE2 activity was increased in both male and female diabetic mice compared to their controls. Control male mice showed significantly higher circulating ACE2 activity than females, and castration suppressed decreased circulating ACE2 activity in both control and diabetic male mice. A direct correlation (r=0.64; p<0.0001) between BG and circulating ACE2 was found.

Conclusions: Male gender and diabetes increased glyceremia and circulating ACE2 activity suggesting an increase of circulating angiotensin II levels. Gonadectomy in diabetic and control mice prevents the activation of RAS. Thus, the increase of circulating ACE2 observed in males may be ascribed to a modulation of circulating male sex hormones.
Introduction and Aims: We have previously demonstrated that extracellular ATP, via P2X (P2X and P2Y) receptors, modulates a variety renal function, including renal plasma flow (RPF), glomerular filtration rate (GFR) and urinary sodium excretion. The role of purinergic systems in the intrarenal microcirculation of diabetic kidney is not well established. In the present study we examined cortical (CBF), outer medullary (OMBF) blood flow and GFR in streptozotocin (STZ)-induced diabetes mellitus rats and determined the effect of systemic infusion of P2X receptor inhibitors (pyridoxal Phosphoinositol, 2,4-di-aminooacidic acid, PPD) and stimulator (β-γ-methylene adenosine triphosphate, β-γ-meATP).

Methods: The clearance studies were performed on anesthetized Wistar rats (200-250g) with STZ induced hyperglycemia (blood glucose level, 396±13 mg·dl⁻¹). CBF and OMBF were estimated by using laser-Doppler flux during infusion of P2X receptors antagonist PPD (25 μmol·kg⁻¹) and agonist β-γ-meATP (2 mmol·kg⁻¹ bw +20 mmol·kg⁻¹ bw·min). GFR was measured as clearance of [(¹⁹)H]-inulin and RPF as clearance of p-aminohippurate. During all experiments mean arterial blood pressure (MAP) was monitored.

Results: Ten days after STZ injection basal value of GFR (0.96±0.09 ml·min⁻¹) and CBF (574±19 PU) were significantly lower (p<0.001) in STZ-rats (n=17) compared with control rats (GFR, 1.24±0.06, CBF, 655±24 PU, n=16). OMBF tended to be lower in STZ rats, p<0.05. Infusion of PPD decreased CBF (15%) and GFR (28%) in STZ rats (p<0.01; n=5) and in control group (CBF, -13%; GFR, -26%; p<0.01; n=5). In contrast infusion of β-γ-meATP increased CBF (19%; p<0.001) and decreased GFR (28% p<0.01) in control group (n=6). In STZ rats, however, β-γ-meATP did not change GFR, CBF and OMBF. There were no significant changes in MAP during infusion PPD or β-γ-meATP in STZ and control rats.

Conclusions: This results show that the response of renal cortical microcirculation to stimulation of P2X receptors is attenuated in diabetic kidney.
nephropathy. However, CCR5 δ32 gene polymorphism was not studied in diabetic nephropathy patients. We aim to study the association between polymorphisms of both, the PPARγ Pro12Ala and CCR5 δ32 genes with the presence of diabetic nephropathy in Egyptian type 2 diabetic patients.

Methods: We included 51 patients diagnosed with type 2 diabetes at least 5 years duration. They were all normotensive patients with no other clinically identifiable risk factor for kidney disease from the out-patient clinic. Genotype detection for PPARγ Pro 12Ala and CCR5 δ32 gene polymorphisms were carried out by PCR. Clinical data, HbA1c, lipid profile, fasting and postprandial blood sugar were recorded. Serum creatinine and urinary albumin/creatinine ratio were measured to stratify the participants according to presence or absence of diabetic nephropathy.

Results: Age, gender, body mass index, HbA1c and duration of diabetes were not significantly different among those with and those without diabetic nephropathy. Diabetic nephropathy patients had higher urinary albumin/creatinine ratio and lower eGFR (p<0.0001). Homozygotes for the PPARγ Pro12Ala and CCR5 δ32 gene polymorphisms were recruited for this case-controlled study. A statistical analysis evaluated the frequency of those alleles as markers in determining the genetic predisposition to the disease. Genotyping was accomplished via the PCR-RFLP technique. This is the first report demonstrating the presence of the Pro12Ala and CCR5 δ32 polymorphism in Egyptian type 2 diabetic patients. The relationship between urinary albumin/creatinine and genetic profiles was measured using Student's t-test and chi-square test.

Conclusions: Polymorphisms of PPARγ Pro12Ala and CCR5 δ32 genotype showed no association.
affected at 200mM. On MP, 10 nM BPA induced hypertrophy and the upregulation of p27kip1, the TGF-β system and collagen IV in a similar fashion that high glucose (HG), while diminished the expression of both nephrin and podocin. BPA-injected mice display an increased both proteinuria (controls (C) \(2.31 \pm 1.4\) mg/24h vs BPH 5.13 \(\pm 1.5\), \(p<0.05\)) and in the creatinine clearance (C 0.05 ml/min vs BPH 0.08, \(p<0.05\)). These animals also display an increased in both systolic and diastolic blood pressure (C 79.75\(\pm 1.15\) mmHg vs BPH 88.75\(\pm 1.14\), \(p<0.05\)) and (C 65.27\(\pm 1.33\) mmHg vs BFA 69.32 \(\pm 1.14\), \(p<0.05\)) respectively. BPA-injected mice display the renal protein upregulation of p27Kip1, the TGF-β1 system as well as in collagen IV. Moreover, the renal histology of these mice showed mesangial expansion, podocytopenia as well as broadening of foot processes.

**Conclusions:** On podocytes, BPA is able to induce apoptosis, hypertrophy and the upregulation of p27kip1, TGF-β1 and collagen IV in a similar fashion than HG. BPA-injected animals develop hypertension, hyperfiltration, proteinuria, mesangial expansion, podocytopenia as well as broadening of foot processes. Further studies are needed to clarify the potential role of BPA in the pathogenesis of renal diseases, particularly in diabetic patients.
ACID-BASE / ELECTROLYTES / NEPHROLITHIASIS

**MP279**

**CORRECTION SPEED LIMITS FOR CHRONIC HYponatraemia: A SYSTEMATIC REVIEW OF OBSERVATIONAL DATA**

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**Introduction and Aims:** Osmotic demyelination syndrome (ODS) is a rare but dramatic complication that occurs in chronic hyponatraemia when sodium concentrations ([Na]) are corrected too rapidly. During the past ten years, researchers have advocated lowering the traditional limits of 12 and 18 mmol/L in 24 and 48h to minimize the risk of ODS. ERBP aimed to identify the evidence for stricter limits.

**Methods:** We searched MEDLINE from 1997 to September 2012 without language restriction and included all observational studies reporting cases of ODS and corresponding [Na] correction speeds. Two authors assessed studies for eligibility, extracted all data, and judged whether it was reasonable to assume the ODS was caused by the speed of increase in [Na]. Data are presented descriptively as percentages and absolute numbers for count data and medians with interquartile ranges (IQR) for continuous data. Sparse and heterogeneous data precluded informative formal meta-analysis.

**Results:** We identified 54 cases of ODS (45 case-reports and 3 case-series including a total of 9 patients); 63% were female with a median age of 45 years (IQR 45-59 years). In 96% (52/54), the diagnosis of ODS was based on MRI. Important details such as onset and cause of hyponatraemia, initial symptoms and their evolution, presence of other risk factors for ODS, and timing of ODS symptoms to the increase in sodium concentration were generally poorly reported. In 6% (3/54), data were insufficient to allow estimation of the 24h and/or 48h correction speed. In 87% (47/54) of cases, [Na] increased ≥12 mmol/L during the first 24h or ≥20 mmol/L during the first 48h. Only 7% (4/54) developed ODS at lower correction speeds: 2 of these patients developed ODS with [Na] increases of 10 to <12 mmol/L (24h) and 18 mmol/L (48h). Both men had a history of heavy drinking as a risk factor for ODS, but it was unclear whether the neurologic condition was caused by the speed of [Na] correction. One woman, with a history of alcohol abuse and hypokalaemia, developed ODS with a [Na] increase limited to even 2 mmol/L (24h) and 4 mmol/L (48h). Finally, one woman developed ODS after [Na] increased with 15 mmol/L during the first 48h; the 48h limit could not be calculated and reporting was too vague to allow a reasonable assumption of causality.

**Conclusions:** Systematic review of the cases of ODS published during the past 15 years generally supports current limits of <12 mmol/L/24h and <18 mmol/L/48h in [Na] increase. However, four cases were reported with correction speeds below these limits. Unfortunately, case-based data do not allow estimation of true ODS incidence, and recommendations need to consider the potential harms and benefits of treatment to re-locate the [Na] limits when exceeded.

**MP280**

**SIGNIFICANT HYponatraemia in THyroid cancer PATIENTS undergoing low IOdine DiET and Radioactive IOdine therAPy**

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**Introduction and Aims:** High risk thyroid carcinoma patients are usually treated with post-operative radioactive iodine (RAI) therapy. These patients are given low-iodine diet along with levothyroxine withdrawal to optimize RAI uptake by thyroid tissues and patients experience mild hyponatraemia during this short-term hypothyroid state. Some patients, however, develop life threatening severe hyponatraemia. Aim of the study was to assess risk factors for developing significant hyponatraemia during low iodine diet and RAI therapy in thyroid cancer patients.

**Methods:** Data for patients with thyroid carcinoma who underwent total thyroidectomy and RAI therapy from July 2009 to March 2012 at Gangnam Severance hospital was retrospectively collected. Clinical and biochemical parameters including serum sodium and thyroid function tests were assessed along with medication history.

**Results:** Total 2229 patients [female: 1679 (76.3%)] were enrolled and the mean age was 47±11 yrs. The number of patients with serum sodium level less than 130 mEq/L (significant hyponatraemia), 131 to 135 mEq/L, and above 136 mEq/L (normonatraemia) were 44 (2.0%), 263 (11.8%), and 1922 (86.3%), respectively. Three hundred fifty patients (15.7%) were older than 60 years of age, 44 patients (2.0%) used thiazide agents, and 23 patients (1.0%) had lung metastasis. Patients who developed significant hyponatraemia were older (46±11 vs. 81±11, p<0.001) and showed lower mean TSH level (8.2±19.7mcIU/mL vs. 71.3±24.6mcIU/mL, p<0.001) and lower mean serum sodium level measured at the start of RAI therapy (139±2mg/dL vs. 137±4mg/dL, p<0.001). Logistic regression analysis showed that thiazide use (OR 5.4), lung metastasis (OR 5.1), older age (≥ 60 yrs, OR 7.9) were independent risk factors for occurrence of significant hyponatraemia in patients undergoing RAI therapy after total thyroidectomy.

**Conclusions:** Our data suggest that old age, thiazide medication use or presence of lung metastasis are risk factors for developing significant hyponatraemia during RAI therapy after total thyroidectomy.

**MP281**

**UTILITY OF MULTIFREQUENCY BIOIMPEDANCE IN THE STUDY OF HYponatraemic PATIENTS**

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**Introduction and Aims:** Hyponatremia is the most frequent hydremolyctic disorder found in hospitalized patients and it may appear in pipo, normo or hypervolemic patients. Multifrequency Bioimpedance (BIA) allows the detection of changes in intracellular and extracellular fluids, may estimate the total body water and the status of hydration of patients. Our objective was to evaluate the utility of BIA in the diagnosis of the volume status of hyponatremic patients. Also, we analyzed the possible relationship between BIA data and the clinical and biochemical parameters of patients.

**Methods:** We included hospitalized patients with hyponatremia ([Na] < 130 mEq/L) during a 10 month period. Medical history, clinical examination and BIA were performed at diagnosis and after 72 hours of treatment of patients.

**Results:** We studied 104 patients (70.8 ± 14.3 years old, 47 female and 57 male). In 34 patients hyponatremia was diagnosed at admission and the rest during their hospital stay. Mean plasma sodium was 120 ± 4.8 mEq/L. The etiology of hyponatremia was diuretics (55), gastrostomastic losses (17), intravenous hypotonic fluids (28), congestive heart failure (18), chronic hepatic diseases (13) and SAHD (9). In 35 patients we only found one cause of hyponatremia and the rest of patients the cause was multifactorial. In 23 patients kidney failure was also present. BIA results showed that 24 patients had dehydreation (OH < 1). 28 normohydreation (OH between -1 and 1) and 52 were overhydrated (OH > 1). The patients with hyponatremia caused by losses of sodium and water (n=50) had a reduction of the percentage of extracellular volume (% ECW) of -1.5 ± 18 %. Patients with hyponatremia caused by SAHD, inhibitors of serotonin reuptake or lung infection had an increase in % ECW of 1.89 ± 17.27 %. Finally, patients with conditions with provoke hypervolemia had an increase of % ECW of 12.66 ± 13.66 %. The presence of symptoms was correlated with the severity of hyponatremia and with the degree of hydration (p < 0.001). We found correlation between the hydreation degree at diagnosis and the level of plasma sodium (p < 0.013).

**Conclusions:** Our results showed that BIA was a simple method that can help in the diagnosis of hyponatremic patients. This method can establish the degree of hydration and may guide our therapeutic approach.

**MP282**

**HYponatraemia in the hospital setting: interim results from a prospective, observational, multi-center, global registry**

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**Introduction and Aims:** Significant hyponatremia, serum sodium level <120 mEq/L, was identified in 1.4% (11/777) of patients with cancer in a multi-center, prospective registry including 777 patients with cancer from 150 hospitals in 27 countries. The purpose of this exploratory study was to evaluate the frequency and characteristics of significant hyponatremia in patients with cancer and the impact on treatment and outcome. The study was designed to be a prospective, observational, multi-center, global registry.

**Methods:** Significant hyponatremia was defined as serum sodium level <120 mEq/L. Baseline demographic and tumor characteristics, as well as significant hyponatremia, were collected. The primary outcome was death related to cancer or other causes within one year of the diagnosis of significant hyponatremia. This study also evaluated the impact of cancer type, tumor characteristics, and treatment on hyponatremia.

**Results:** A total of 777 patients were enrolled in the study. Significant hyponatremia was observed in 11 patients (1.4%). The frequency and characteristics of significant hyponatremia were similar across the different cancer types. The primary outcome of death related to cancer or other causes within one year of the diagnosis of significant hyponatremia was observed in 5 patients (45.5%). The study also evaluated the impact of cancer type, tumor characteristics, and treatment on hyponatremia.

**Conclusions:** This study is the first to evaluate the frequency and characteristics of significant hyponatremia in patients with cancer and the impact on treatment and outcome. The study also evaluated the impact of cancer type, tumor characteristics, and treatment on hyponatremia. The results of this study will provide insights into the management of significant hyponatremia in patients with cancer and the impact on treatment and outcome.
Introduction and Aims: Hyponatremia (HN) is the leading electrolyte abnormality in hospitalized patients (pts), and an independent predictor of increased mortality in pts with cirrhosis, heart failure, and neurologic disorders as well as hospitalized pts in general. The registry is designed to observe currently utilized management modalities for HN, characterize their relative efficacy, and assess their impact on hospital resource utilization.

Methods: After informed consent or waiver, medical records of pts meeting the registry entry criteria, principally age ≥18 years, and euvoletic (US & EU) or hypervolemic (US only) HN (serum sodium ([Na]) ≤130 mmol/L) were abstracted. Approximately 98% of the planned 5,000 pts have been enrolled. Pt data are summarized by sample size (n) and percentage (%) for categorical data, and mean ± SD for continuous data.

Results: A total of 3795 of the 4909 pts enrolled between study initiation in Sept 2010 and Jan 2013 at 160 US and 93 EU sites had sufficient data for analysis. The mean entry and hospital discharge [Na] values were 124.2±5.8 mmol/L, and 131.7±4.9 mmol/L, respectively. The average length of stay was 10.1±9.3 days.

Conclusions: HN is often chronic and/or recurrent, and pts are frequently discharged with persistent HN. One quarter of the pts received no specific tx for HN, suggesting poor clinical insight to this disorder. Analysis of monotherapy episodes, which permits evaluation of the effect of individual maneuvers, indicates that hypertonic saline and tolvaptan resulted in the most rapid increase in [Na]. T former was most likely to result in overrapid correction. Rate of correction with fluid restriction was similar to the rate with no tx at all. This registry is the largest study on HN, and its complete analysis will disclose relevant aspects of the therapeutic approach of hospitalized patients with HN.

MP284 SEVERE HYPONATREMIC PATIENTS: WHO ARE THEY AND HOW ARE THEY MANAGED?
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Introduction and Aims: Hyponatremia is the most common electrolyte disorder in hospitalized patients; however, physicians feel often insecure with its differential diagnosis and treatment. We aimed to evaluate the frequency, clinical characteristics, as well as diagnostic and therapeutic behaviour in severe hyponatremia.

Methods: We extracted from the laboratory data base all cases with serum sodium <126 mmol/L presenting in the emergency department and in the wards of a 224 bed hospital serving a population of 235,000 inhabitants. The observation lasted 200 days. Hospital records were audited and underlying causes, management and in-hospital outcomes were registered.

Results: The frequency of severe hyponatremia was 0.3% of the patients admitted to the emergency department and submitted to laboratory tests and 0.5% of patients in hospital wards. Clinical and laboratory data are reported in the following table. Main etiologies were diuretics (43%), hypovolemia (28%), SIADH (13%), heart/liver failure (8%), surgery/hypotonic fluids (4%), hyperglycemia (4%). Hypovolemia was more frequent in patients admitted to the emergency department (34% vs 17%). In most patients multiple causal factors were present. A fall was recorded in 14% of cases. Only in 4 cases (5%) urinary Na and K concentrations were available, and in no cases serum and urine osmolality. Treatments given were: slightly hypertonic (348 mOsm/Kg) in 4 cases (5%) urinary Na and K concentrations were available, and in no cases serum and urine osmolality. Treatments given were: slightly hypertonic (348 mOsm/Kg) saline infusion (44%), isotonic saline infusion (34%), offending drug withdrawal (9%), oral sodium supplements (3%), fluid restriction (3%), extracorporeal hemodialifirion/ hemodiafiltration (4%, one case of heart failure and two with CKD5, respectively), no treatment (3%). The rate of correction of serum Na was high (>1 mmol/h) only in two cases of spurious hyponatremia due to hyperglycemia. In-hospital mortality rate was 5%. No cases of myelinolysis were observed.

Conclusions: Severe hyponatremia was common in this unslected population observed in the emergency department and wards of a urban hospital. The most common phenotype was a very elerly woman. Diuretics, hypovolemia and SIADH were
the conditions more commonly underlying hyponatremia. The frequency of adequate laboratory diagnostic testing was very low.

Abstracts

Introdução e Objetivos: A depresão é uma das principais causas de morbidade e mortalidade em países desenvolvidos. Sua importância se amplia, pois pode ser uma manifestação de doenças como doenças mentais mentais, doenças de origem orgânica e doenças de base genética. O objetivo da presente revisão é discutir as fontes de erro que podem levar à malferente na prática clínica.

Métodos: Sendo que a literatura científica é vasta e acessível, os aspectos metodológicos da revisão foram fundamentais para sua concretização. Foram realizadas buscas em base de dados datenacional e internacional, utilizando palavras-chave específicas. O resultado final foi uma síntese de informações com base em evidências científicas.

Resultados: Os resultados da pesquisa demonstraram que a depressão é uma doença complexa e multifatorial, cujas causas podem ser ambientais, genéticas e psicológicas. Apesar disso, a presença de depressão deve ser levada em consideração na prática clínica.

Conclusões: A depressão é uma doença importante e complexa, com múltiplas causas e consequências negativas. É fundamental que os profissionais de saúde estejam preparados para identificá-la e orientá-la de forma eficaz.

MP286

EFFICACY AND SAFETY OF TOLVAPTAN IN TREATING SEVERE HYPONATREMIA DUE TO SYNDROME OF INAPPROPRIATE SECRETION OF ANTIDIURETIC HORMONE (SIADH)

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Introduction and Aims: Tolvaptan is an oral antagonist of V2-receptors for ADH that has been demonstrated to be really efficient in treating hyponatremia due to SIADH. Its safety and efficacy, however, have been validated only for mild degrees of hyponatremia and there is still uncertainty about its use in more severe degrees, where hyponatremia is extremely symptomatic and the infusion of hypertonic solution remains the mainstay of treatment. Aim of this study is to analyze our experience in treating such patients with tolvaptan.

Methods: We retrospectively analyzed clinical and biochemical data following the administration of Tolvaptan in three patients with severe hyponatremia. All patients were euclidean and had elevated natriuresis without signs of adrenal or thyroid dysfunction, all criteria consistent with diagnosis of SIADH. In all patients hyponatremia proved to be resistant to the infusion of hypertonic solution before the administration of Tolvaptan. The administered daily dose of 15 mg was continued for several months in order to prevent relapses.

Results: Serum sodium increased by 5, 12 and 6 meq/L in 24 hours, in each patient respectively. All clinical and laboratory data are listed in Table 1. Correction of serum sodium led to remission of symptoms in all patients and all the weaning attempts from the drug resulted in symptoms relapse. Therefore, it has been a long period since these patients have started this therapy, and during this time it appeared to be both necessary for the control of natremia and well tolerated. The only side effect reported was a slight decompensation of the already known diabetes mellitus in patient #2, which is a known side effect reported by the manufacturer.

Conclusions: To our knowledge, this is the first report of a long-standing therapy with Tolvaptan in patients who were symptomatic for severe hyponatremia due to SIADH. Treatment of severe hyponatremia is challenging for the risk of myelolysis and the most cautious method is the infusion of hypertonic solution with continuous monitoring of sodium levels. Drawbacks of oral therapy with Tolvaptan are a hypothetical uncontrolled increase of natremia and the yet undiscovered long-term safety. In our series, however, the dose chosen allowed to increase sodium concentration in a safe way (i.e. less than 12 meq/L in 24 hours) and appeared to be well tolerated in the long-term, with a marked improvement in quality of life. Our experience should be confirmed by larger and randomized studies.
histrnomorphometric parameters and bone immunostaining. FGF-23 immunostaining did not correlate with any histomorphometric parameter. Eroded surfaces (ES/BS) was positively correlated with both VDR and SOST bone expression; osteoid thickness (O. Th) was also correlated with both VDR and SOST immunostaining.

Conclusions: Present findings did not implicate FGF-23 in the bone alterations normally seen in IH. Current data suggest that VDR and SOST may be upregulated in bone tissue of IH patients with high bone resorption and may contribute to the delayed mineralization, as evidenced by the positive correlation with osteoid thickness.

**MP288**

**NEPHROCALCINOSIS IN AN ADULT PATIENT WITH IDIOPATHIC INFANTILE HYPERCALCIURIA AND A NOVEL CYP24A1 MUTATION**

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Introduction and Aims: Idiopathic infantile hypercalciemia is a rare autosomal recessively inherited disease, presenting in the first year of life with severe hypercalciuria and difficulty to thrive, usually precipitated by vitamin D supplementation. Recently loss-of-function mutations in the CYP24A1 gene encoding 24-hydroxylase, an enzyme that inactivates vitamin D metabolites, have been found in these patients.

Methods: An investigation of calcium and phosphate metabolism including vitamin D metabolites and FGF23 measurement was done in a patient, who had suffered from idiopathic infantile hypercalciuria and presented with nephrocalcinosis, and his family members. Additionally, sequence analysis of the CYP24A1 gene was performed.

Results: We hereby describe a young man homozygous for a novel missense mutation (c.628T>C) of the CYP24A1 gene. In silico analysis predicted that the W210R mutation is damaging to the protein. The mutation was not found in 514 controls. The patient had suffered from severe hypercalciuria in early childhood. At age 29 years he presented with medullary nephrocalcinosis, chronic kidney disease stage 2, microalbuminuria, mild hypertension and nephrogenic diabetes insipidus. He had mild hypercalcemia and moderate hypercalciumuria and hyperphosphaturia. Serum 24,25(OH) vitamin D3 was reduced (0.6 ng/mL), 25(OH) vitamin D3 (28 ng/mL) and calcitriol (41 ng/L) were normal, parathyroid hormone (13 pg/mL) suppressed and total calcium (10.3 mmol/L) were normal, whereas phosphate (1.8 mmol/L) was elevated.

Conclusions: Confirmatory in-vitro experiments were performed with LLC-PK1 cells. Results: Renal tissue histology revealed decreased crystal depositions under all treatment modalities in the order SC > SS > STS when compared to EG. STS treatment preserved renal function and SOD enzyme activity, whereas SC and SS did not. This indicates that the renal protective effect of STS is related to its antioxidative effects. Confirming this notion, STS treatment of oxalate-exposed LLC-PK1 cells showed a dose-response effect and dramatically reduced H2O2 within the cells. Cell-free experiments confirmed the potential of STS to directly quench H2O2.

Conclusions: STS reduces oxidative stress and preserves renal function in an animal model of chronic ethylene glycol exposure. Given its favorable toxicity profile, the therapeutic use of STS in disease states characterized by the generation of oxidative stress should be given consideration.
Abstracts

Nephrolithiasis and Accelerated Vascular Calcification (VC) - A Common Underlying Patho-Mechanism for These Ectopic Calcification Syndromes?

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Introduction and Aims: Nephrolithiasis (NL) is a common condition with a lifetime risk exceeding 6.3% in men and 4.1% in women in the USA. The prevalence of NL has increased in both genders and all ethnic groups recently, and is known to be associated with osteoporosis, fractures and increased prevalence of CV disease. VC (especially aortic calcification) is also common, and is both a marker and a cause of increased cardiovascular (CV) disease. Underlying both NL and VC there may well be a common factor: a lack of calcification inhibitors. We wanted to study the prevalence of VC, and examine VC-associated risk factors, in an NL population. To do this, we studied, for the first time, the severity of aortic calcification (AAC) in a population with an extensive renal stone burden.

Methods: NL study subjects who had undergone a percutaneous nephrolithotomy in 2011 underwent a manual scoring assessment for AAC using CT KUB-derived abdominal aorta imaging to calculate total AAC load. We gathered data on age, gender, GIS stone burden and stone type. The prevalence, severity and associations of AAC were then analysed.

Results: 51/93 stone formers were male, the mean (+/-SD) age was 51.1±3.2 years and they had a mean eGFR of 80.2±16.13 ml/min/1.73m²; 68 patients were idiopathic stone formers (51.9±3.8 years), had an anatomical cause (50.4±10.8 years) and 13 a metabolic cause (45±2.7 years), n=NS for all. 19.22±0.06% of the whole group’s abdominal aortas was calcified, with a total AAC score of 4.19±1.83. In patients > 50 years of age there was significantly more AAC than in those < 50 (5.89±3.0 vs. 0.53±0.0, P<0.01). A positive correlation was found with severity (R²=0.1932, P=0.05), see figure 1, whereas eGFR failed to show any significant correlation (R²=0.0154, P=NS). VC was not more common nor more severe in bilateral vs. unilateral stone formers (16±36 vs. 30/57; 4.8±2.3±2 vs. 3.79±2.21, P=NS, both). The AAC score was significantly lower in metabolic vs idiopathic NL (idiopathic 4.37±2.19, anatomical 9.50±9.54, metabolic 1.09±1.23; p=0.013) but not for any other comparison.

Conclusions: This type of study has not been undertaken previously. We found that VC was both common and severe in NL subjects. AAC severity scores showed a positive correlation with advancing age but other factors, including renal function, failed to show any convincing association. The lower AAC score in metabolic as opposed to the other stone forming groups is intriguing. Further studies are needed in failed to show any convincing association. The lower AAC score in metabolic as opposed to the other stone forming groups is intriguing. Further studies are needed in

Gender- and Age-Related Profiles of Vitamin D Metabolites in Patients with Kidney Stone Disease

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Introduction and Aims: Vitamin D can increase intestinal absorption and urinary excretion of calcium, thereby influencing both bone turnover and risk of kidney stone formation. In this paper we investigated on plasma profiles of vitamin D metabolites in a large cohort of patients with calcium nephrolithiasis, matched for age and sex.

Methods: N=745 stone formers (364 males (M), aged 47±15; 381 females (F), aged 51±16), who had been submitted to our extended study protocol for mineral metabolism during the entire study period for mineral metabolism and urine supersaturation 2009 through 2012, were considered for this study. According to age, both M and F were further classified as subgroups: (A) 18-45 yrs; (B) 46-55 yrs; (C) 56-70 yrs; (D) over 70 yrs. Then, both plasma levels of 25OHVitD3(25D3) and 1.25(OH)2VitD3(1.25D3) profiles were analyzed according to this classification. Results: 25D3 was significantly related to 25D3, in M and F (p<0.01) and independent of BMI (p=ns). A positive correlation was significantly found in M and F, whereas it was independent of PTH in both genders (p=ns). On the contrary, a negative correlation was found in both genders (p<0.01).

Results: In F, 25D3 was significantly related to Body Mass Index (BMI), (R²=0.03, p<0.01), but not to CDCR. In M, 25D3 was significantly related to CDCR (R²=0.02, p<0.01) and independent of BMI (p=ns). 1.25D3 was significantly related to 25D3, in both F and M (p<0.01 for both), whereas it was independent of PTH in both genders (p=ns). uCa was significantly related to 1.25D3, in both F and M (p<0.01 for both).

Main data referred to subgroups are reported in the tables below. In M, neither the averaged 25D3 nor the prevalence of subjects with VitD deficiency varied significantly according to age. The averaged 25D3 was significantly lower in post-menopausal (C+D) than in pre-menopausal (A+B) F and prevalence of VitD deficiency was lower in the latter (p<0.01). In M, 1.25D3 was independent of age, whereas it was lower in post-menopausal compared to pre-menopausal F (p<0.01). Within each subgroup of
age, 1.25D3 did not differ significantly between genders. In group C, 25D3 was significantly lower in females (*)..

Conclusions: There is a high prevalence of vitamin D deficiency in stone forming patients (the higher percentage being observed in postmenopausal women) and its detrimental effects on calcium balance and bone mineral content are probably still underestimated.

### MP294

**RENAIL MANIFESTATIONS IN INFLAMMATORY BOWEL DISEASE - LITHOGENIC FACTORS AND TUBULOINTERSTITIAL INVOLVEMENT**

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**Introduction and Aims:** Renal involvement in patients with inflammatory bowel disease (IBD) can occur either as an extra-intestinal manifestation of disease or as a side-effect of the therapies used, mainly 5-aminosalicylate drugs, often in those with severe, long-standing disease. The most common manifestation in these patients is kidney stones, but tubulointerstitial abnormalities are being reported more frequently and are not uncommon in autopsy studies. Tubulointerstitial involvement, once thought to represent a consequence of therapy, is now being pointed as a consequence of disease. The aim of this study was to evaluate patients with the diagnosis of IBD with respect to the prevalence of nephrolithiasis, lithogenic factors and tubular dysfunction, using an early marker of tubular injury, N-acetyl-beta-D-glycosaminidase (beta-NAG).

**Methods:** A point prevalence study was performed in 45 consecutive outpatients with IBD. Clinical and laboratory data including routine indices of kidney function (serum urea and creatinine, creatinine clearance, urinary protein excretion, pH, density and electrolytes), as well as urinary concentration of beta-NAG. History of kidney stones, exposure to 5-aminosalicylate drugs and severity of disease were assessed by questionnaire and clinical file consultation.

**Results:** Thirty-five patients had IBD diagnosis (23% with UC and 77% with CD). The prevalence of nephrolithiasis was 26% (n=12), and was not different between genders. The most common manifestation in these patients is kidney stones, but tubulointerstitial abnormalities are being reported more frequently and are not uncommon in autopsy studies. Tubulointerstitial involvement, once thought to represent a consequence of therapy, is now being pointed as a consequence of disease. The aim of this study was to evaluate patients with the diagnosis of IBD with respect to the prevalence of nephrolithiasis, lithogenic factors and tubular dysfunction, using an early marker of tubular injury, N-acetyl-beta-D-glycosaminidase (beta-NAG).

**Conclusions:** No significant difference in the prevalence of nephrolithiasis was found between genders, and no relationship was found with 5-aminosalicylate therapy, type of IBD or disease severity. Elevated levels of beta-NAG were detected in 4 patients (9%) and no relationship was found with 5-aminosalicylate therapy, type of IBD or disease severity.

### MP295

**ASSOCIATION OF URINE pH AND CHRONIC USE OF PROTON PUMP INHIBITOR**

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**Introduction and Aims:** Renal involvement in patients with inflammatory bowel disease (IBD) can occur either as an extra-intestinal manifestation of disease or as a side-effect of the therapies used, mainly 5-aminosalicylate drugs, often in those with severe, long-standing disease. The most common manifestation in these patients is kidney stones, but tubulointerstitial abnormalities are being reported more frequently and are not uncommon in autopsy studies. Tubulointerstitial involvement, once thought to represent a consequence of therapy, is now being pointed as a consequence of disease. The aim of this study was to evaluate patients with the diagnosis of IBD with respect to the prevalence of nephrolithiasis, lithogenic factors and tubular dysfunction, using an early marker of tubular injury, N-acetyl-beta-D-glycosaminidase (beta-NAG).

**Methods:** A point prevalence study was performed in 45 consecutive outpatients with IBD. Clinical and laboratory data including routine indices of kidney function (serum urea and creatinine, creatinine clearance, urinary protein excretion, pH, density and electrolytes), as well as urinary concentration of beta-NAG. History of kidney stones, exposure to 5-aminosalicylate drugs and severity of disease were assessed by questionnaire and clinical file consultation.

**Results:** Forty-five patients were analysed – 38% males, mean age 43±15 years, mean time of disease 9.5±6.8 years, 67% with Crohn disease (CD). The prevalence of nephrolithiasis was 20% (n=9), and occurred more frequently in patients with CD compared to patients with ulcerative colitis (23% vs 13%, p=0.29). The occurrence of nephrolithiasis was significantly more prevalent in patients with ileal involvement (33% vs 8%, p=0.03). In male patients with nephrolithiasis, there was a trend for higher urinary excretion of oxalate compared to the patients without history of lithiasis (0.63 ±0.21 vs 0.44±0.15 mmol/24h, p=0.086); on the other hand, female patients with nephrolithiasis had a trend for lower urinary citrate (1.2±1.4 vs 2.4±1.6 mmol/24h, p=0.116). Elevated levels of beta-NAG were detected in 4 patients (9%) and no relationship was found with 5-aminosalicylate therapy, type of IBD or disease severity.

**Conclusions:** As previously reported, ileal involvement in IBD has a significant relationship with the occurrence of nephrolithiasis. Elevated levels of urinary oxalate and low levels of urinary citrate are potential lithogenic factors, and we found an interesting gender difference in our study population considering these parameters. Beta-NAG was elevated in a small number of patients and was not related to any interesting gender difference in our study population considering these parameters.

### MP295bis

**SPONTANEOUS CALCIFICATION PROCESS IN CULTURED RENAL CELLS OF A PATIENT WITH MEDULLARY SPONGE KIDNEY: ROLE OF THE DOWN REGULATION OF GDNF GENE**

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**Introduction and Aims:** Medullary sponge kidney (MSK) is a malformative renal condition associated with a high risk of nephrocalcinosis. We found that GDNF gene rare variants are associated with MSK in a subgroup of patients. The removal of renal cell carcinoma in a MSK patient with a GDNF variant allowed us to observe that cultured renal papillary cells, whose GDNF expression was downregulated, can spontaneously differentiate into osteoblast-like cells producing typical bone matrix proteins and CaPO4 deposits. To understand if GDNF down regulation could trigger the observed phenomenon, we conducted a study of GDNF silencing in HK-2 cells.
Methods: To obtain stably GDNF silenced HK-2 cell lines, 5 shRNAs targeting human GDNF were used. As a negative control (-), we used HK-2 transfected with an empty vector. Clones were grown in medium DMEM F12 10% FBS. GDNF silencing was evaluated at mRNA and protein level by RT-qPCR and by immunocytochemistry. Efficiently HK-2 silenced clones, control (-) and WT cells were cultured in commercially supplied osteogenic media for 15 days. Scanning electron microscopy (SEM) and Von Kossa staining were used to analyze crystal deposition. Gene expression analysis was performed by RT-qPCR to evaluate osteogenic activation (Osteopontin and Osteonectin) and apoptosis (Bax, Bcl-2 and Caspase-3).

Results: The presence of Ca$_2$PO$_4$ was demonstrated by Von Kossa and SEM analysis in the silenced HK-2 cells cultured under osteogenic conditions at 15 days; significantly lower number of deposits were seen in control (-). No Ca$_2$PO$_4$ deposits were observed in control (-) and WT cells as well as in silenced clones cultured in normal conditions. In silenced HK-2 cells, time-course RT-qPCR experiments showed at 15 days, when Ca$_2$PO$_4$ deposits were evident, increased osteonectin/osteopontin ratio. Moreover, apoptosis was activated as early as 5 days, as evidenced by the ratio Bax/Bcl-2 and lowered at 15 days. The crucial role of GDNF silencing in the process was also highlighted by the higher Bax/Bcl-2 ratio in silenced clone in respect to control (-) both in normal and osteogenic conditions.

Conclusions: The silencing of GDNF gene in HK-2 cells induces a biomineralization process similar to that spontaneously occurred in primary papillary cells obtained from a patient with MSK and GDNF mutation. We hypothesize that apoptosis, determined by GDNF down regulation, may be one of the triggering events of the calcification process in our model. This is in agreement with the notion that apoptotic nuclei may trigger Ca$_2$PO$_4$ deposition calcifying vascular cells. GDNF is confirmed as adaptive survival factor whose alteration appears to play a key role in the process of nephrocalcinosis.
CLINICAL NEPHROLOGY - MISCELLANEOUS

INFLUENCE OF A FUNCTIONAL POLYMORPHISM OF ALDOSTERONE SYNTHASE GENE ON CHRONIC GLOMERULONEPHRITIS: A CLINICOPATHOLOGIC STUDY

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Introduction and Aims: In the last years aldosterone has been identified as an important mediator of renal injury. In the present study we evaluated the influence of the C-344T polymorphism of aldosterone synthase (CYP11B2) gene, associated with serum aldosterone levels and the development of arterial hypertension, on the clinical course of chronic primary glomerulonephritis.

Methods: We studied n=283 patients with biopsy proven primary glomerulonephritis (IgA nephropathy: n=143, focal segmental glomerulosclerosis: n=81, membranous glomerulonephritis: n=59) followed up for 7.0±5.7 years. According to the slope of the curve of reciprocal serum creatinine against time (2 or < -0.1 dl * mg-1 * year-1) group A (slow progressors, n=192) and group B (fast progressors, n=91) were defined. One hundred healthy volunteers were analysed as controls. Aldosterone synthase gene C-344T polymorphism was determined by PCR amplification. Aldosterone serum levels were determined in n=57 of our patients at the time of renal biopsy. The biopsies of 157 patients were analysed by the same pathologist. The degree of glomerular sclerosis, tubulointerstitial fibrosis and vascular hypertrophy was evaluated.

Results: The aldosterone synthase genotype correlated to the aldosterone serum levels (CC/CT: 107±70, TT 243±323 pg/ml, p<0.05). The genotype distribution did not differ significantly between our study and control populations (patients: CC/CT genotypes: 72.1%, TT 27.9%; controls: CC/CT: 69%, TT 31%, ns). Age, initial renal function, proteinuria, blood pressure under treatment and number of antihypertensive agents were similar among patients with different genotypes (ns). Furthermore, there was no significant difference in the degree of glomerular sclerosis, tubulointerstitial fibrosis or vascular hypertrophy between patients with different genotypes (ns). The C-344T polymorphism was associated with the progression of primary glomerulonephritis as shown by the genotype frequencies in group A (slow progressors, CC/CT: 66.7%, TT: 33.3%) and group B (fast progressors, CC/CT: 83.5%, TT: 16.5%, p<0.003). There was also a significant difference in the actual rate of progression as estimated by the slope of the curve of reciprocal serum creatinine (CC/CT: 0.169±0.43, TT 0.067±0.10 dl * mg-1 * year-1, p<0.002).

Conclusions: Our results indicate that the functional C-344T polymorphism of the aldosterone synthase gene is an important marker of progression in patients with chronic primary glomerulonephritis.

EPIDEMIOLOGY OF PRIMARY GLOMERULONEPHRITIS IN MOROCCO

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Introduction and Aims: Primary glomerulonephritis (GN) is a common kidney disease, with variable incidence and prevalence rates worldwide. In Morocco, we don’t have an accurate insight of the epidemiology of this disease, since we lack a national registry for primary GN. Thus, data is only limited to single center studies. The aim of our study was to determine the epidemiological profile and outcome of primary GN in our country.

Methods: We performed a multicentric retrospective study, including all cases of primary GN in Morocco from January 2007 to December 2012. Primary GN with end-stage renal disease (ESRD) were ruled out of the study. Demographic, clinical and paraclinical features were determined as well as therapeutic protocols and outcome.

We also analysed renal and overall survival, ESRD and mortality risk factors. We used SPSS 17.0 for statistical analyses.

Results: Our study included 915 cases of primary GN. The mean age of our patients was 36.6 ±15.4 years. Sex ratio displayed a male predominance. Nephrotic syndrome and acute renal failure were the main indications for renal biopsy in our study in respectively 47% and 21% of the cases. Whereas, asymptomatic urinalysis abnormalities accounted for less than 4% of our biopsy indications. Primary GN represented 29% of all the renal biopsies performed during the study period. The incidence of this disease was 1.1·100000 inhabitants/year. Focal segmental glomerulosclerosis (FSGS) was the most frequent primary GN in our country, since it was noted in 32% of the cases, followed by membranous nephropathy (MN) in 23%, minimal change disease (MCD) in 19% of the cases. IgA nephropathy (IgAN) was encountered in 10% of the cases. Postinfectious glomerulonephritis (PIGN), Membranoproliferative glomerulonephritis (MPGN) and Crescentic glomerulonephritis (CGN) were observed in 9%, 6% and 2% respectively. After a mean follow-up of 19.7± 5.5 months, remission occurred in 54% of the cases. Relapse was observed in 17% of the cases. ESRD and death were noted in 2.02% et 4.06% respectively. The percentage of sclerotic, membranous, and tubulointerstitial atrophy were predictors of progression to ESRD in both FSGS and MN (p<0.01; p<0.002), whereas, the lack of achieving remission was significantly linked to ESRD in PIGN (p<0.013). Moreover, dialysis requirement or oliguria at presentation predicted the evolution to ESRD in CGN (p<0.012; p<0.012).

Conclusions: This is the first multicentric study regarding the epidemiology of primary GN in Morocco. It represents a first step in the epidemiological knowledge of this disease in our country. However, further large scale multicentric studies are required as well as the establishment of a national registry for primary GN in order to get accurate data regarding this disease.

CIRCULATING SERUM LEVELS OF GELATINASE-B AND VASCULAR ENDOTHELIAL GROWTH FACTOR-A ARE ASSOCIATED WITH ATHEROSCLEROSIS IN PATIENTS WITH EARLY STAGES OF CHRONIC KIDNEY DISEASE AND PRIMARY CHRONIC GLOMERULONEPHRITIS

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Introduction and Aims: Gelatines-B, reported also as matrix metalloproteinase-9 (MMP-9), is a proteolytic enzyme that has been implicated in chronic kidney disease (CKD) and cardiovascular disease (CVD). Recent evidence suggests that renal vascular changes contribute to progressive renal disease and that alteration of vascular endothelial growth factor-A (VEGF-A) might play an important role in modulating microvascular loss of macrovascular remodeling in the kidney, as well as in the vessels. It remains controversial the mechanism by which VEGF works in the kidney, as well as in the vessels at least in the early stages of CKD. The aim of the present study was to determine the serum levels of MMP-9 and VEGF-A and to investigate their potential correlation with the atherosclerotic markers and albuminuria in early stages of CKD and primary chronic glomerulonephritis (CGN).

Methods: CKD patients of stages 1 and 2 with CGN (n=30) were included. As controls, there were healthy individuals (n=15). Clearance of creatinine (Clcr) and albumin excretion were examined in the 24h urine. VEGF-A and MMP-9 levels were measured by an ELISA method. Intima media thickness (IMT) of carotid and femoral arteries and atheromatic plaque were evaluated by a high resolution ultrasonography. Statistical analysis was performed with the use of a SPSS system.

Results: The levels of VEGF-A were 646.3±130.5 pg/ml in healthy (p<0.001) and MMP-9 levels in CGN were 938.6±87.9 mg/ml vs 115±22.5 mg/ml in healthy individuals (p<0.001; multivariate analysis). MMP-9 serum levels were strongly correlated with VEGF-A serum levels in the group of CGN (pearson correlation 0.52, p<0.001). There were statistically significant correlations between levels of VEGF-A, MMP-9 and albuminuria (p<0.0001). Further, VEGF-A and MMP-9 levels were independently correlated with IMT and atheromatic plaque (p<0.001).

Conclusions: Our study suggests that serum levels of VEGF-A and MMP-9 might present independent risk factors of atherosclerosis and albuminuria, at least in the early stages of CKD and CGN to the progression of CKD.

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Incidence of Glomerular Diseases in the Czech Registry of Renal Biopsies in the Years 1994–2011

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Introduction and Aims: We describe data gathered by the Czech Registry of Renal Biopsies, which includes 10,472 renal biopsies performed over a period of 18 years.

 Methods: We assessed the main demographic and histological data of RB of native kidneys performed in 31 centres in Czech Republic over the period 1994–2011.

 Results: We evaluated 10,472 RBs (males 57.8%, children <15 years 13.6%, elderly >60 years 19.1%). The most frequent renal diseases were primary (55.7%) and secondary (29.1%) glomerulonephritis (GN). Tubulo-interstitial nephritis (TIN) was observed in 3.4% and vascular diseases in 4.1%. The samples were non-diagnostic in 4.2%. Among primary GN the most frequent diagnoses were IgA nephropathy (IgAN) 37.4%, membranous GN (MGN) 13%, focal segmental glomerulosclerosis (FSGS) 12.6%, minimal change disease (MCD) 11.1% and membranoproliferative GN (MPGN) 8%. Among secondary GN, systemic lupus erythematosus (SLE) represented 23.2%, hereditary diseases 19.8%, necrotizing vasculitis (NV) 19.4%, dysmorphic nephropathy (DN) 15.5%, diabetic nephropathy with diabetic nephropathy 13.4%, microhaemaertrea was present in 65.6%, microhaemaertrea in 9.1%. Nephrotic proteinuria (>3 g/24 h) is 39.8% and low-grade proteinuria (<3.5 g/24 h) in 53.7%. Among adults, arterial hypertension was present in 59%, mild renal insufficiency in 27.4% (Scr 110–200 μmol/l), advanced renal insufficiency in 13.8% (Scr >200 μmol/l), and diabetic nephropathy was common in patients with nephropenic proteinuria (MDR 39.7%). Among children, Scr >300 μmol/l was the most common in patients with advanced renal insufficiency. The mean annual incidence per million population was primary GN 39.7, secondary GN 18.1, IgAN 11.6, MGN 0.3, FSGS 0.3, MCD 1.4, NV 13.2, TIN 0.9. The frequency of serious complications (symptomatic haematuria, gross haematuria, blood transfusion) ranged around 3.2%.

 Conclusions: This report provides representative population-based data on native biopsy-proven renal diseases in Czech Republic.
Results: In all post-transplant recurrent cases, foot process effacement was observed in specimens obtained one hour after reperfusion and progressed further for several days. These changes were not observed in non-recurrent cases. Expression pattern of nephrin, SIB1, and CD2AP, ezrin, synaptophysin, and PKCzeta protein expression in the kidney allografts did not change from neither the recurrent nor the non-recurrent cases. However, staining pattern of podocin altered from linear pattern at foot processes to granular pattern on podocyte cytoplasm several days after reperfusion, and the alteration did not accompany changes in nephrin staining. These cytoplasmic podocin signals are partially localized in golgi apparatus. The number of podocytes did not change during the phase.

Conclusions: FP effacement is the earliest event in graft kidney –post-transplant FSGS recurrence, observed within one hour after exposure to FSGS sera, indicating that primary target of circulating factors are the cytoskeleton of podocytes. After several days, podocin, and not the other slit diaphragm proteins, translocates from slit diaphragm to cytoplasm, and this might be associated with defect in intracellular trafficking, or in the formation of slit diaphragm complex. These events represent the sequential changes that underlie in the pathogenesis of FSGS.

Impact of Body Mass Index on the Clinical Course of Chronic Glomerulonephritis

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Introduction and Aims: Obesity is progressively recognised as an important modifiable risk factor for progression in chronic kidney disease. In the present study we evaluated the influence of body mass index (BMI) on clinical course of chronic glomerulonephritis.

Methods: We studied n=329 patients with biopsy proven primary glomerulonephritis (IgA nephropathy: n=178, focal segmental glomerulosclerosis: n=76, membranous glomerulonephritis: n=75) followed up for 6.5 ± 5.9 years. The rate of deterioration of renal function was estimated by the slope of the curve of reciprocal serum creatinine concentration against time. According to the BMI at the time of renal biopsy, patients were divided into the following groups: normal BMI (<25, n=179), overweight (25-29.9, n=103) and obese (≥30, n=47).

Results: Initial renal function was similar among normal, overweight and obese patients (ns). As expected, overweight patients were older (p<0.001). They also presented with higher levels of proteinuria (p<0.040) and tended to have higher blood pressure values under treatment (p=0.101) and to require a higher number of antihypertensive agents (p=0.136). The rate of progression differed significantly between patients with normal BMI (0.087 ± 0.113), overweight (0.161 ± 0.291) and obese patients (0.213 ± 0.177 mg*dl-1*year-1, p=0.007). Similarly, BMI as a continuous variable correlated with the rate of deterioration of renal function (r=0.177, p<0.001).

Conclusions: An increased BMI is associated with a faster decline in renal function in patients with chronic glomerulonephritis.

Post Infectious Glomerulonephritis - Is it Benign?

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Introduction and Aims: Post infectious glomerulonephritis (PIGN) is a self-limited disease, especially in children, but long-term follow-up studies indicate persistent low-grade renal abnormalities in a significant proportion of patients. PIGN continues to be a serious public health concern in third world countries. This study compares PIGN in children and adults in an emerging country.

Methods: A retrospective study of 209 patients (140 children and 69 adults) with postinfectious GN identified during January 2005 - December 2011 was conducted. The diagnosis of post-infectious GN was based on the clinical,serological and pathological features. The diagnosis of PIGN required positive testing of recent group A-beta hemolytic Streptococcal infection by either Anti-Streptolysin O antibody (ASO), or throat swab culture. Post non-streptococcal GN was negative for streptococcal serology and included other bacteria or non-bacterial organisms. Renal biopsy was done in cases with renal failure or nephrotic proteinuria. The histological specimens of the patients with renal failure or nephrotic proteinuria were examined for the presence of an immune-complex glomerulonephritis. The patients were treated with antihypertensives, dialysis as and steroids were given for recipients according to the severity of GN.

Results: In children, 87(62%) had post streptococcal GN while in adults 28(40%) had non streptococcal GN. In 13 cases the causative pathogen could not be identified. One case was shunt nephritis, three cases were staphylococcal associated GN, two cases were tuberculosis associated GN, were 14 E coli associated GN, were 14 Enterobacter aerogenes associated GN, were 14 Staphylococcus aureus associated GN, were 14 Klebsiella pneumoniae associated GN, were 14 Pseudomonas aeruginosa associated GN, were 14 Proteus mirabilis associated GN, were 14 Moraxella non-bacterial GN. 100% of the patients with post streptococcal GN (p < 0.05) , 35 (25%) children and 30 (43.4%) adults needed dialysis. 26 (18.5%) children and 22 (31.8%) adults received steroids. The median times to resolution of proteinuria and normalization of serum creatinine were 2 months and 8 months in adults and 2 months and 4 months in children, respectively. 7 (5%) children progressed to CKD while among adults 12 (17.3%) developed CRF. The mean follow up was for 3 years. 1 child and 3 adults succumbed during acute phase.

Conclusions: PIGN continues to be prevalent in developing countries. Post streptococcal GN following throat infection is most common. Prognosis in children is better than adults with 5% children and 17% adults progressing to CKD.

Intravenous Immunoglobulin G in the Treatment of Patients with Idiopathic Glomerulonephritis: Clinical Experience Lasting 25 Years

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Introduction and Aims: Glomerulonephritis (GN) accounts for 10%-20% of the total incident cases of end stage renal disease (ESRD), and is the third most common cause of ESRD after diabetes and hypertension in western countries. The pathogenesis of GN is prevalently immune mediated: humoral and cell-mediated immunity are involved, although the rationale for an etiological treatment is still lacking. In the last fifty years, empirical use of corticosteroids (CS) and anti-inflammatory immunosuppressive drugs has obtained excellent results in improving survival of both the patient and the kidney. In order to improve the prognosis of glomerulonephritis further, newer strategies with better efficacy, but with lower toxicities are necessary.

Methods: We collected data on 174 patients with biopsy proven idiopathic GN who were treated with high doses of Intravenous immunoglobulin G (IVIG). Nephrotic syndrome had been observed in all patients. 58 patients had renal failure and 139 hypertension. 138 patients were previously treated for a long time as induction immunosuppression with CS, immunosuppressors (IS) and antiinflammatory agents without effect. IVIG had been applied in a dose of 85 mg/kg/24 h three times every other day. Depending on the clinical improvement afterwards (in case of therapy resistance or relapse) these boi had been repeated in 149 patients after 1 month (and every 3 months). The maintenance therapy comprised prednisolone (P), IVIG, azathioprine (AZA) or cyclophosphamide (CYC) or mycophenolate mofetil (MMF), in 78 - prednisolone and IVIG, in 25 - prednisolone and AZA or CYC and in 28 – only IVIG. In 39 patients IVIG was part of the initial therapy.

Results: Proteinuria disappeared and full remission occurred in 61 patients. Partial remission was present in 52 patients. 36 patients went into end-stage renal failure and/or died (13 of them of a nonrenal cause). In 37/58 patients with impaired renal function serum creatinine levels go back to normal after treatment. CS-IS-IVIG group showed better relapse-free survival than CS-IVIG group and CS-IS group (78% vs 74% vs 55% respectively at 5 years; 71% vs 65% vs 36% respectively at 10 years; 58% vs 52% vs 24% respectively at 15 years). Patients treated with IVIG for more than 10 years had better relapse-free survival than those treated for CS-IS (60% vs 39% respectively). Ineffective clinical improvement was observed in 113 patients, associated with marked improvements in renal function and reducing necessary CS doses and proteinuria. Most patients with GN tolerated their IVIG therapies.

Conclusions: Long-term treatment with IVIG from induction to maintenance phase in glomerulonephritis patients is associated with relatively favourable long-term outcome. The glomerulonephritis flares are independently associated with an increased risk of deterioration in renal function; prevention of renal flares might, therefore, also decrease long-term morbidity and mortality. Our results suggested that IVIG therapy may be recommended in patients unresponsive to aggressive conventional treatment.

Minimal Change Disease Due to Mercury-Containing Skin Lightening Cream

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Introduction and Aims: To elucidate the clinicopathological characteristics and the treatment of minimal change disease (MCD) due to mercury-containing skin lightening cream.

Methods: Five patients with mercury-induced MCD were enrolled in this study. The feature of mercury toxicity, the concentration of mercury in urine and skin lightening cream, the clinicopathological presentation and the treatment of the kidneys were investigated.

Results: The patients were all female with an average age of 37.6 years old and had a history of continuous use of skin lightening cream. The duration of contact with skin lightening cream ranged from 1 to 20 years. The exposure routes were pasted directly on the skin. The concentration of mercury in the lightening cream of the patients and the control group were 12 μg/g and 3 μg/g respectively (p<0.05). The concentration of mercury in the urine of the patients and the control group were 21 μg/g and 1 μg/g respectively (p<0.05). The clinicopathological characteristics and treatment results of the patients and the control group were shown in Table 1.

Conclusions: Mercury-Containing skin lightening cream may cause MCD. The pathogenesis is not clear, and the incidence is not low. The lightening cream used by the patients is the key to cause mercury poisoning and MCD. The concentration of mercury in the skin lightening cream and urine is a key indicator of whether it can cause mercury poisoning and MCD. The sunlight exposure index and skin color are the basis for lightening cream selection. The skin of our age group is thin, and the absorption of mercury is stronger. Therefore, we should use MCD skin care products in moderation and use them according to the instructions.
mercury containing skin lightening cream ranged from 3–5 months. They had no history of exposure to other suspicious substance containing mercury. (2) All patients had edema of lower extremity, heavy proteinuria (24 hours urinary protein 3.75–6.50 g/d), hyperalbuminemia (albumin 10.80–24.10 g/L) and hyperlipidemia (cholesterol 8.47–14.91 mmol/L), without hematuria. Two patients’ facial skin was whiter than other parts of the body. They had no rash, stomatitis, fingers trembling, nervous breakdown, and so on. (3) Renal biopsy showed no changes of glomeruli on light microscopy. The immunofluorescence was negative. On electron microscopy, there is a characteristic fusion of endothelial foot. They were diagnosed as MCD. Case 5 had renal tubular epithelial cell lysosome increase and some microvilli fall off. Renal tubules and microscopy. The immunofluorescence was negative. On electron microscopy, there is a parts of the body. They had no rashes, stomatitis, fingers trembling, nervous
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P. VIVAX MALARIA AND THROMBOTIC MICROANGIOPATHY - IS THERE ANY DIRECT PATHOGENETIC LINK?

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Abstracts

Introduction and Aims: Acute renal failure (ARF) is reported to occur in 1–3% patients with falciparum malaria but rarely with vivax malaria. The association between renal failure, anemia, thrombocytopenia and jaundice is a recurrent finding in studies on severe malaria and these finding can mimic with thrombotic microangiopathy (TMA). Although relationship of malaria with TMA is not clear till date but there are case reports exist in medical literature about their association mainly in children with P.vivax infection. So we undertook a retrospective search of our hospital record to find out cases of malaria associated acute kidney injury with clinical, laboratory and histopathological evidence of TMA.

Methods: We reviewed data from electronic database of our institute, of cases of malaria, jaundice and acute kidney injury (AKI) who initially admitted and treated as patients with falciparum infection. So we undertook a retrospective search of our hospital record to find out cases of malaria associated acute kidney injury with clinical, laboratory and histopathological evidence of TMA.

Results: A total of 173 patients were recruited to the study. Mean age were 44.9 ± 16.3 in group 1 (n=55), 42.9 ± 16.1 in group 2 (n=53), and 39.75 ± 13.6 in group 3 (n=66) (p>0.05). The higher mean RDW value was found in group 1 patients (13.4 ± 0.7) before treatment (p>0.05). We found significant decrease in RDW value after successful treatment in group 1 and group 2 (p>0.05). In group 3, there was no change in RDW value after treatment (p<0.05). The most of the patients with remission (n=49, 89%) have a baseline RDW values were under 14% (p<0.001, Kendal Tau: -0.86). The most of resistance to treatment was appeared in patients who have RDW level was > 15 % during new diagnose (86.1 %) (p<0.001, Kendal Tau: -0.87).

Conclusions: Our results suggest that pretreatment RDW value may be a useful predictive biomarker for treatment responsiveness in adult patients with nephrotic syndrome due to primary glomerulonephritis.

EDEMA FORMATION AND PROTEINURIA: IS THERE A ROLE FOR ANGIOPOIETIN-2

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Abstracts

Introduction and Aims: The nephrotic syndrome combines proteinuria, hypoalbuminemia, high cholesterol and high triglyceride levels, as well as edema. Pathophysiologically, the degree of edema is thought to be a consequence of low oncotic pressure due to urinary protein loss. However, some individuals with severe edema have relatively low proteinuria indicating that unknown additional mechanisms might be involved. We hypothesized that Angiopoietin-2 (Angpt-2), an antagonist of the endothelium-stabilizing receptor Tie-2 secreted by endothelium, contributes to the formation of peripheral edema in proteinuric patients.

Methods: We measured Angpt-2 with an Enzyme-linked Immunosorbent Assay (ELISA) in sera from 20 proteinuric patients and 20 healthy controls and analyzed the association with proteinuria, degree of edema (semi-quantitative score: 1 - mild, 2 - moderate, 3 - severe), gain of body weight (BW) and underlying glomerular pathology.

Results: Overall circulating levels of Angpt-2 were significantly increased in nephrotic patient compared to controls (4.26 ± 4.93 vs. 0.79 ± 0.49 ng/mL p<0.0001). Moreover, Angpt-2 levels increased with raising gain of BW groups (0.5-kg: 1.86 ± 0.88 ng/mL; 5-10kg: 3.28 ± 1.4 ng/mL; >10kg: 7.3 ± 7.5 ng/mL) with proteinuria (<1g/d: 1.77 ± 1.0 ng/mL; 1-3 g/d: 3.1 ± 0.6 ng/mL; >3g/d: 5.6 ± 6.0 ng/mL) and a clinical score of edema (0 ± 1.3 ± 0.3; 1 ± 4.97 ± 5.1; 2 ± 5.61 ± 6.6; 3 ± 3.71 ± 4.0 ng/mL). Interestingly, the increase of Angpt-2 was only detectable in those glomerular diseases involving endothelial cells, but not in diseases with primary podocyte involvement.

Conclusions: In conclusion, circulating Angpt-2 might be involved in the pathogenesis of vascular permeability and thereby in the formation of peripheral edema. Further studies are desirable to test if Angpt-2 might serve as circulating biomarker to distinguish pure podocyte pathologies from glomerular endothelial diseases.

MP311

MP312

MP313
follow-up was 1.14 ±0.32. Renal function remained stable in 6 (37.5%) patients and showed a slow decline in the 10 (62.5%) patients remaining. Scr at the end of follow-up was 1.31 ±0.71 mg/dl and eGFR 64.34 ± 89.77. Six (37.5%) patients showed a final eGFR <60 ml/min/1.73m2, three (18.75%) eGFR 60-90 ml/min/1.73m2, two (12.5) 45-60 ml/min/1.73m2 and until five (31.25%) patients had an eGFR <45 ml/min/1.73m2. Mean rate of renal function loss was 1.13 ml/min/year. No significant correlations between the rate of renal function loss and baseline renal function, blood pressure or mean proteinuria during follow-up were found. Kidney size was normal in all the cases, but 9 patients (56%) showed numerous bilateral renal cysts, whose size ranged from 1 mm to 70 mm. No correlations between the presence of renal cysts and renal function at baseline, rate of renal function loss or the amount of proteinuria were detected.

Conclusions: Patients with TBMD and proteinuria >0.5 g/24hr can exhibit a slowly progressive renal function decline. A significant proportion (≥50%) exhibit bilateral renal cysts, whose possible genetic basis and influence on renal outcomes require further investigations.

Introduction and Aims: In 2009 a collaborative multihospitalary task-force was established in Castilla la Mancha (Spain) in order to investigate and compare the renal progression and outcome of the more frequently biopsied GN between 1994 and 2008 and followed up to 06/30/2011. The five categories selected accounts for 60% of total adult renal biopsies.

Methods: We included 852 adult patients with histologically proven selected GN in the five hospitals covering the renal care of 2.1 million population:179 focal and segmental glomerulosclerosis (FSGS),177 membranous nephropathy (MN),204 IgA nephropathy (IgAN),155 lupus nephritis (LN),and 137 crescentic type III glomerulonephritis (CGNIII). Renal and patient outcome were estimated by survival analysis methods. Events of interest considered for renal survival were dialysis because ESRD or death predialysis.Death before or after renal replacement therapy (RT) was event considered for patient survival. The median follow-up from biopsy to predefined renal and patient events, were 5.80 (mean 6.45) and 6.89 (mean 7.34)years respectively (range 0.01-17.5). Kaplan-Meier estimates were used to compare crude survival between diagnostic categories (Log rank) and Cox regression to analyze adjusted influence in survival of age (four strata), sex, GN type (initial eGFR<MDRD4, four levels) and proteinuria in g/ 24h (three levels).

Results: Cumulative (5±SE) renal survival (alive and free of RT) after 5 and 10 years was: 75.3±5.4 in FSGS; 83.3±7.4 in MN; 76.3±6.4 in IgAN; 93.2±9.0 in LN ; 55.5±5.3 in CGNIII. These differences were statistically significant (p<0.0001). The differences across all categories excepted for age, sex, initial eGFR, proteinuria, and some histological diagnosis (LN vs CGNIII as reference category) Cumulative (5±SE) patient survival (alive in out in ESRD) after 5 and 10 years was 96.2±4.5 and 86±4 in FSGS; 91.3±4.3 and 83.4±14 in MN; 95.2±9.2 and 92.3±16 in IgAN; 96.2±10 and 93.3±17 in LN ; 90.5±5 and 57±6 in CGNIII.Log rank test showed CGNIII as the worse (significantly different vs all categories ) followed by RT,being LN the best prognostic diagnosis. After Cox regression adjustment, only age, sex and initial eGFR show independent predictive influence leaving it the diagnostic categories and initial proteinuria.

Conclusions: The observed figures are not different from those reported in recent modern literature except for a worse renal survival in IgAN which could be attributed to a selection bias due to restrictive biopsy indication criteria for this condition in our context.

Introduction and Aims: Due to multiple abnormalities in haemostasis and coagulation system occurring in these patients the nephrotic syndrome (NS) is generally associated with glomerulopathies. Only a few types of primary glomerulonephritis associated with Hashimoto's thyroiditis have been reported in medical literature, the most frequent being membranous nephropathy.

Methods: We performed a prospective observational study including consecutive adult patients with idiopathic NS admitted in a 2 years period. The diagnosis of NS was confirmed by the presence of daily protein excretion greater than 3.5 g. Clinical and biological data, including coagulation and haemostasis-related parameters, were obtained every 6 months during follow-up. Occurrence of VTE was the primary study outcome.

Results: We enrolled 65 patients (44±13 years, 45% men) with a median follow-up period of 24 [IQR 18-42] months. The baseline proteinuria was 7.5 ± 1.9 g/day and baseline serum albumin was 2.4 ± 0.8 g/l. During follow-up, 6 (9.2%) VTE occurred, 67% during the first 6 months, and the median time to VTE was 6.0 [IQR 3-12.75] months. The incidence rate was 4.4 (95%CI 3.2-5.7) 100 patient years. Serum albumin, total blood plasminogen activator (tPA) levels and antithrombin III (ATIII) activity at baseline were independently associated with VTE in Cox modelling. The same parameters, remained independently associated to the VTE risk, when proteinuria and serum albumin were introduced as time-dependent variables in further models.

Conclusions: In this prospective study the risk of VTE was higher in the first 6 months of follow-up. Severe hypoaalbuminemia at baseline, and among the haemostasis-related parameters, only tisular plasminogen activator (tPA) levels and antithrombin III (ATIII) activity at baseline emerged as VTE independent risk factors in idiopathic nephrotic syndrome patients.

Introduction and Aims: In 2009 a collaborative multihospitalary task-force was established in Castilla la Mancha (Spain) in order to investigate and compare the renal progression and outcome of the more frequently biopsied GN between 1994 and 2008 and followed up to 06/30/2011. The five categories selected accounts for 60% of total adult renal biopsies.

Methods: We included 852 adult patients with histologically proven selected GN in the five hospitals covering the renal care of 2.1 million population:179 focal and segmental glomerulosclerosis (FSGS),177 membranous nephropathy (MN),204 IgA nephropathy (IgAN),155 lupus nephritis (LN),and 137 crescentic type III glomerulonephritis (CGNIII). Renal and patient outcome were estimated by survival analysis methods. Events of interest considered for renal survival were dialysis because ESRD or death predialysis.Death before or after renal replacement therapy (RT) was event considered for patient survival. The median follow-up from biopsy to predefined renal and patient events, were 5.80 (mean 6.45) and 6.89 (mean 7.34)years respectively (range 0.01-17.5). Kaplan-Meier estimates were used to compare crude survival between diagnostic categories (Log rank) and Cox regression to analyze adjusted influence in survival of age (four strata), sex, GN type (initial eGFR<MDRD4, four levels) and proteinuria in g/ 24h (three levels).

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Conclusions: The observed figures are not different from those reported in recent modern literature except for a worse renal survival in IgAN which could be attributed to a selection bias due to restrictive biopsy indication criteria for this condition in our context.
**Methods:** In order to confirm the effective rare association between CAT and glomerular diseases we studied prospectively in our Nephrology Centre 550 patients (334 M, 216 F) affected by primary glomerulonephritis in our Nephrology Centre from June 2002 to November 2012. 188 focal segmental glomerulosclerosis (FSG), 148 membranous nephropathies, 113 IgA nephropathies, 44 membranoproliferative glomerulonephritis, 23 crescentic glomerulonephritis, 13 IgM nephropathies, 10 mesangial glomerulonephritis with C3 in mesangial side or without immunofluorescence deposits, 11 minimal glomerular changes.In all patients we controlled the serum level of tSH, free T4, free T3, anti-thyroglobulin antibodies and anti thyroid peroxidase antibodies by laboratory tests. **Results:** Out of 550 patients with various forms of glomerulonephritis, 39 (7.09%) resulted to be suffering from CAT (8 males, 31 females). In particular the incidence of CAT resulted elevated for IgM nephropathy (38%) and for IgA nephropathy (18%), while the incidence was very low for membranous nephropathy (3.4%), PGS (3.3%), crescentic glomerulonephritis (2%). No patient with MPGN, mesangial glomerulonephritis with C3 in the mesangium and negative immunofluorescence, and minimal glomerular changes proved to be affected by CAT. **Conclusions:** The results of our study indicate that the association between CAT and glomerulonephritis is not a rare event and does not confirm the prevalence of MN. The most frequent histopathological pattern resulted to be IgM nephropathy (5/13 patients) (38%); however since IgM nephropathy is a rare form of primary glomerulonephritis, more interesting appears the association with IgA nephropathy (20/113 Pts) appears to be more interesting(17.6%), considering that IgAN is worldwide and represents 1/3 of total primary GN in humans. Out of 39 Pts with CAT and GN 30, (76.9%) proved to be young women and this datum reflects the prevalence of CAT for the female gender (107/1M). The contemporary presence of two immunological disorders in our patients cannot be interpreted as a fortuitous event, but rather the result of an consequential etiopathogenic relationship.

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**Introduction and Aims:** Rheumatoid Arthritis (RA) is a widespread disease and its renal involvement, relatively common, is clinically significant because worsens course and mortality of the primary disease. There is still no agreement on the prevalence of renal disorders in RA: data analysis originates from different sources, as death certificates, autopsies, clinical and laboratory findings and kidney biopsies, each with its limitations. The aim of this study is to assess the prevalence of microalbuminuria in patients with rheumatoid arthritis and its correlation with disease activity and drug treatment.

**Methods:** We studied 74 patients with rheumatoid arthritis and 81 sex and age matched control persons with generalized osteoarthritis. Patients with hypertension, diabetes mellitus, or evidence of previous renal disease were not included. Disease activity was assessed by the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). A drug history for the year before entry to the study was obtained for each patient.

**Results:** 28 of RA patients were found to have microalbuminuria as a symptom of renal disease. Drug therapy or vasculitis were identified as possible reasons for proteinuria in only 25% of these patients; in most patients (75%), no reason for proteinuria was found. Only 9 patients of the control group exhibited microalbuminuria, which was attributable to nephrotic factors. The median follow up time was 124.3 years. Patients with microalbuminuria had a significantly greater median duration of disease. We found a significant correlation to C-reactive protein as a marker for disease activity. Mortality was significantly increased in the RA population as compared to controls (hazard ratio 1.64 (95% CI 1.31-2.07) for all RA patients and for patients with microalbuminuria hazard ratio 2.63, 1.64-4.58).

**Conclusions:** Microalbuminuria is frequently present in patients with rheumatoid arthritis. Screening for renal disease in RA should not only include creatinine measurement and dipstick examination of urine, but also more sensitive methods to detect microalbuminuria as a marker of tubular and early stages of glomerular damage. We suggest its use in the monitoring of patients with rheumatoid arthritis to detect early subclinical renal dysfunction and drug induced renal damage. Urinary albumin excretion was found to be significantly correlated with CRP and may be a sensitive indicator of disease activity in patients with rheumatoid arthritis.

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**Introduction and Aims:** Controlling hypertension is important to protect renal function and prevent cardiovascular disease in chronic kidney disease (CKD) patients but the implementation of recommendations on hypertension treatment in this population is unknown.

**Methods:** The retrospective, cross-sectional study was performed in 1996, 2001, 2006, and 2011 in year in nondialysis patients with CKD to assess the status of hypertension treatment. 190, 489, 1799 and 1695 medical documents of patients treated chronically in outpatient department of kidney diseases of the Medical University of Gdansk were screened respectively. Age, sex, eGFR, basal nephropathy, cardiovascular diseases, causal blood pressures, types and doses of hypotensive agents were recorded. Hypertension treatment efficacy was assessed as the compliance with the target blood pressure according to the recommendations of JNC Reports for CKD patients as follows: < 130/85 mmHg in 1996; <125/75 mmHg for patients with proteinuria >1g/24h and <130/85 mmHg for all others in 2001; < 130/80 mmHg in 2006 and 2011. **Results:** Of Patients in I-II stadium of CKD, subjects below 65 years and those without cardiovascular complications and diabetes reached target blood pressure more often than other subgroups.

**Conclusions:** The improvement of blood pressure control was observed in CKD patients. The mean number of hypotensive agents used in one patients increased. The most common hypotensive agents used in the treatment of hypertension are diuretics and drugs influencing on renin-angiotensin system.

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**Methods:** In order to confirm the effective rare association between CAT and glomerular diseases we studied prospectively in our Nephrology Centre 550 patients (334 M, 216 F) affected by primary glomerulonephritis in our Nephrology Centre from June 2002 to November 2012. 188 focal segmental glomerulosclerosis (FSG), 148 membranous nephropathies, 113 IgA nephropathies, 44 membranoproliferative glomerulonephritis, 23 crescentic glomerulonephritis, 13 IgM nephropathies, 10 mesangial glomerulonephritis with C3 in mesangial side or without immunofluorescence deposits, 11 minimal glomerular changes. In all patients we controlled the serum level of tSH, free T4, free T3, antithyroglobulin antibodies and anti thyroid peroxidase antibodies by laboratory tests. **Results:** Out of 550 patients with various forms of glomerulonephritis, 39 (7.09%) resulted to be suffering from CAT (8 males, 31 females). In particular the incidence of CAT resulted elevated for IgM nephropathy (38%) and for IgA nephropathy (18%), while the incidence was very low for membranous nephropathy (3.4%), PGS (3.3%), crescentic glomerulonephritis (2%). No patient with MPGN, mesangial glomerulonephritis with C3 in the mesangium and negative immunofluorescence, and minimal glomerular changes proved to be affected by CAT. **Conclusions:** The results of our study indicate that the association between CAT and glomerulonephritis is not a rare event and does not confirm the prevalence of MN. The most frequent histopathological pattern resulted to be IgM nephropathy (5/13 patients) (38%); however since IgM nephropathy is a rare form of primary glomerulonephritis, more interesting appears the association with IgA nephropathy (20/113 Pts) appears to be more interesting (17.6%), considering that IgAN is worldwide and represents 1/3 of total primary GN in humans. Out of 39 Pts with CAT and GN 30, (76.9%) proved to be young women and this datum reflects the prevalence of CAT for the female gender (107/1M). The contemporary presence of two immunological disorders in our patients cannot be interpreted as a fortuitous event, but rather the result of an consequential etiopathogenic relationship.

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**Abstracts**

**MP320**

**RENAL DISEASE IN ADULT PATIENTS WITH CYSTIC FIBROSIS**

Adèle Postorino1, Stefano Costa2, Simona Cristacaro2, Giuseppe Magazzù1,2, Guido Napoli3,4,5,6,7,8,9,10, Vincenzo Santoro2,3,4,5,6,7,8,9,10, Michèle Bueno2 and Domenico Santoro2

1Unit of Nephrology and Dialysis University of Messina Messina Italy, 2Unit of Pediatric Gastroenterology and Cystic Fibrosis University of Messina Italy

**Introduction and Aims:** Cystic fibrosis is the most common autosomal recessive disease affecting the caucasian population, with a birth incidence ranging between 1:2500 and 1:1800. It is caused by mutations in the CFTR [cystic fibrosis transmembrane regulator] gene which is localized on 7 chromosome. Renal disease is reported as a relatively rare complication in adult patient with CF. We evaluated proteinuria (11.7%), and 11 patients (14,28%) with chronic renal failure. Mean age was 1:7. Expectancy due to better management. Moreover patients with proteinuria in the elderly patients with chronic kidney disease (CKD).

**Methods:** A retrospective study was carried out in a referral center for CF at University of Messina in Italy. We identified all patients with renal disease, characterized by proteinuria and/or chronic renal failure (CRF), during the period 2007-2012 and reviewed their medical records. To assess the correlation between genotype and proteinuria, genetic mutations were evaluated.

**Results:** From a population of 77 adult patients with CF, we identified 9 patients with proteinuria, genetic mutations were evaluated.

**Conclusions:** Our study shows an higher prevalence of renal disease in patients with CF, CHF was previously reported. The pathophysiology may be related to a higher prevalence of hypertension and CKD.

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**MP321**

**RE-EVALUATION OF THE CLASSIFICATION OF MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS**

Yimin Lu1, Pingyan Shen1, Yao Li2, Yaowen Xu1, Xiao Li1, Xiaoxia Pan1, Weiming Wang1, Yimin Lu1, Pingyan Shen1, Xiao Li1, Xiaoxia Pan1, Weiming Wang1

1Geriatric Nephrology Chinese PLA General Hospital Beijing China

**Introduction and Aims:** The current clinical classification of membranoproliferative glomerulonephritis (MPGN) based on electron microscopy wasn’t helpful for the differential diagnosis of underlying causes of MPGN. A new classification of MPGN based on immunofluorescence findings was proposed to better understand the underlying pathology and furthermore to guide the treatment. We aim to re-evaluate the new classification in our single-center cohort study.

**Methods:** A single-center cohort of MPGN was retrospectively reviewed and patients were divided into two groups according to new classification:

1. Immunoglobulin-mediated and complement-mediated. Baseline clinical characteristics, laboratory and pathological findings and outcomes of treatment were analyzed.

2. Membranous nephropathy (MN) is the most common cause of glomerulonephritis in adults (80%). More progress was determined by the presence of persistent proteinuria, and extensive tubulointerstitial lesions at initial biopsy. In morphologically different forms of glomerulonephritis enzymes of proximal tubular epithelial cell markers are valuable in the assessment of renal damage, even in patients with normal renal function. Parameters of oxidative stress, as the primary mediators in glomerulonephritis, may represent a non-invasive, early biological markers of renal damage. The aim of the study was to investigate whether markers of renal cell dysfunction (glomerular filtration rate, urinary excretion of protein, ectoenzymes proximal tubular epithelial cells, and oxidative stress) in patients with MN, and point to possible therapeutic modification of the expression as a useful treatment.

**Results:** The study included 28 patients with MN age 59.6 ± 7.4 years. The control group consisted of 30 clinically healthy individuals age 48.7 ± 11.6 years. Addition to basic laboratory studies, the enzyme activity was determined in serum and urine (aminopeptidase N-APN, alkaline phosphodiesterase-PC-1, N-acetyl-β-D-glucosaminidase-NAG and Dipetidylpeptidaza DPP IV-V), as well as parameters of oxidative damage (thiobarbituric acid concentration of substance-responders TBARS, reactive carbonyl derivatives-RCD and the concentration of total sulphydryl-SH group).

**Conclusions:** Kidney damage in membranous nephropathy is accompanied by the release of several tubular enzymes, with potential diagnostic and prognostic significance. The study suggests a possible role of oxidative stress in determining therapeutic importance in preventing impairment as part of future therapies.

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**MP322**

**EFFECTS AND SAFETY OF SULODEXIDE ON PROTEINURIA IN ELDERLY PATIENTS WITH CHRONIC KIDNEY DISEASE**

Qiangguo Ao1, Qiang Mai1, Qing Cheng1, Xiaodan Wang1, Sheng Liu1 and Fujian Zhang1

1Geriatric Nephrology Chinese PLA General Hospital Beijing China

**Introduction and Aims:** To investigate the effects and safety of sulodexide on proteinuria in the elderly patients with chronic kidney disease (CKD). Methods: 122 elderly patients(mean age: 80.21±17.53years)with CKD enrolled this study from June 2008 to December 2009. The entry criteria were as follows: 1. CKD stage 1–3 with proteinuria; 2. There were no uncontrolled hypertension, malignant tumor, heart failure, acute kidney injury, fever and infections in those patients; 3. All the patients didn’t receive the therapy of steroid, immunosuppressant and anticoagulant drugs. The patients were divided into three groups according to the levels of 24h proteinuria: group A (0.3g≤24h proteinuria<1.5g), group B (1.5g≤24h proteinuria<3.5g) and group C (24h proteinuria≥3.5g). All groups were given routine treatment and sulodexide 600 LSI/d injections intravenously for 20 days. 24h proteinuria, serum creatinine (Scr), blood urea nitrogen (BUN), uric acid (UA) and conventional blood coagulate parameters were analyzed in the three groups before and after treatment.

**Results:** In the group A and group B, the levels of 24h proteinuria were decreased significantly at the end of the treatment (P<0.05). There were not changes in Scr, BUN...
and UA after 20 days treatment in all the three groups (P<0.05). The levels of prothrombin time (PT), trombixin time (TT) and activated partial thromboplastin time (APTT) were significantly increased (P<0.01) and fibrinogen (FIB) was decreased (P<0.05) at the end of the treatment in the three groups. However, there were not any bleed events in the patients during the period of this study.

**Conclusions:** Sulodexide can decrease the level of proteinuria in elderly CKD patients without nephrotic range proteinuria. There were no bleed events in the patients after treatment with Sulodexide.

**MP325 PRIMARY GLOMERULAR DISEASES IN TURKEY: MULTICENTER STUDY OF TURKISH SOCIETY OF NEPHROLOGY, GLOMERULAR DISEASES WORKING GROUP**

Savas Cizturk1
1Nephrology Dicle University School of Medicine Diyarbakir Turkey

**Introduction and Aims:** Primary glomerular diseases have major importance in nephrology practice. There has been no sufficient data about primary glomerular diseases in our country till now. Herein, the preliminary results of TSN Glomerular Diseases Working Group, Primary Glomerular Diseases Study, are presented.

**Methods:** In our multicenter study; we recorded renal biopsy data of adult patients with primary glomerular diseases were recorded on a web based study-specific database. The clinical presentation, demographic data and basal laboratory values were recorded also. Among the 1439 patients from 25 centers recorded between May 2009 and July 2012; 1274 patients’ data were found to be suitable for further statistical analyses by SPSS program.

**Results:** Mean age was 40.8± 14.6 (14-92) years. Female/male ratio was 568/706. 2. 94% of the biopsies were performed in nephrology clinics. Indications of biopsies and biochemical data on admission are presented in and. Biopsy indication of 736 patients (57.8%) was nephrotic syndrome. When all patients were included, the most common causes for renal biopsy were membranous nephropathy (367 patients, 28.8%) and FSGS (246 patients, 19.3%) (Figure 2). The most common glomerulonephritides detected in patients with nephrotic syndrome were membranous nephropathy (42.0%) and FSGS (20.4%), also. The total number of glomerulus per biopsy was 9.7. Mean systolic and diastolic blood pressures were 130±20 mmHg and 82±12 mmHg, respectively. Average daily proteinuria was 989±2256 mg, the mean estimated GFR was 107±57 ml/min at baseline measurements.

**Conclusions:** In Turkey, primary glomerulonephritides requiring renal biopsy, present mostly with nephrotic syndrome. Membranous nephropathy is the most frequently glomerulonephritis diagnosed in the biopsy of these patients.

**MP325**

<table>
<thead>
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**MP326**

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<td>Erythrocyte sedimentation rate (mm/h)</td>
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**MP327 CLINICAL AND MORPHOLOGICAL FEATURES OF KIDNEY INVOLVEMENT IN PRIMARY SJOGREN SYNDROME: ABOUT 50 CASES**

Saida Hajri1 and Samia Barbouriche1
1Nephrology Charles Nicole Hospital Tunis Tunisia

**Introduction and Aims:** Quantifying protein in urine is commonly used in the diagnosis of kidney diseases, measuring the efficiency of the treatment and evaluation of prognosis. We aimed to perform a prospective evaluation of accuracy of urinary spot Protein/Creatinine ratio in pre-post treatment in patients with various glomerulonephritis.

**Methods:** The correlation between P/C in random urine specimens and urinary protein excretion in 24-h collections in pre- and post-treatment periods were evaluated in 38 adults (17 male and 21 female). The primary diagnosis were Membranous nephritis (n=10), lupus nephritis (n=7), and FSGS (n=5). Samples was obtained before treatment and remission period or in 6-12 months in those not under remission. Diagnostic accuracy of the P/C ratio was evaluated by receiver-operator curves (ROC) to predict different threshold levels of protein excretion (0.3 and 3 g).

**Results:** Characteristics of patients are in a linear relationship exists between spot P/C and 24 h protein excretion, with a significant correlation in both pre and post treatment values (P<0.0001). he deviation between the methods increased parallel to the amount of proteinuria and was also higher in patients with low creatinine output. [Figure 2] The areas under curve by ROC curve analysis performed to detect pre and post treatment urine protein excretion of 0.3 and 3 g in 24-h collections were >0.95.

**Conclusions:** The P/C in spot urine samples could be used as an alternative to urine protein excretion in 24-h collections. But it is unreliable in patients with high protein excretion. Accuracy of the method needs to be clarified in patient with low creatinine production.

**MP326**

<table>
<thead>
<tr>
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<th>Pre</th>
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<td>3.4±3.2</td>
<td>2.2±3.2</td>
<td>0.005</td>
</tr>
<tr>
<td>SpotP/Cr (mg/mg)</td>
<td>2.8±2.7</td>
<td>1.9±2.5</td>
<td>0.034</td>
</tr>
<tr>
<td>Serum Cr (mg/dl)</td>
<td>0.95±0.43</td>
<td>0.98±0.47</td>
<td>ns</td>
</tr>
<tr>
<td>Serum Albumin (g/dl)</td>
<td>2.8±1.2</td>
<td>3.4±1.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Cr-Clearance (ml/min)</td>
<td>86±35</td>
<td>89±35</td>
<td>ns</td>
</tr>
<tr>
<td>Deviation (g/day)</td>
<td>-0.59±1.6</td>
<td>-0.29±1.5</td>
<td>ns</td>
</tr>
</tbody>
</table>

**MP327**

**AUC for 0.3 gram/day and 3 gram/day were 0.933 and 0.959 for protein at 0.95 and 0.95 at the end of the treatment for post.**
Results: Fifty patients (26.73%) had laboratory evidence of tubular and/or glomerular dysfunction. There were 45 women (90.4%) and 5 men (9.6%), with a mean age of 50, 81±15.95 years (range 25-78 yr). Dry eyes (96%) and dry mouth (80%) were the predominant clinical symptoms. Twenty three patients (46%) tested for ocular signs of pSUS using a Rose Bengal score dye test, Schirmer test or Break up time test, 21 of 23 were consistent with keratoconjunctivitis sicca. In five of our patients, renal disease antedated by an average of 6 years the onset of ocular and oral symptoms. 21 patients (42%) had tubular aculia. Creatinine clearance reduction was found in 36 patients (72%) and hypokalaemia in 3 patients. Pathological proteinuria was found in 23 patients (46%). Hypergammaglobulinaemia was present in 30 patients (60%), six patients had positive serotoxi to SSA and SSB, five patients had positive rheumatoid factor, and three patients cryoglobulinaemia. Salivary gland biopsy was practiced in 47 cases (94%) and showed class 1 in 36 cases (30%) and class 4 in 9 cases (18%). Kidney biopsy (KB) was undergone for 13 patients (26%). In five patients (38.46%), the primary lesion seen on KB was chronic tubulo-interstitial nephritis (TIN). Mild TIN was noted in the context of a primary glomerular lesion in three other patients. Patients (10%) had a primary glomerular lesion on KB, with proliferative glomerulonephritis (two cases), focal segmental nephropathy (one case), and IgA nephropathy (two cases) are the most common pathological findings. Six patients (3.2%) had chronic interstitial nephritis. Two patients were treated by cyclophosphamide (for renal and neurological features). 16 patients were achieved the end stage of renal disease (ESRD) and treated by hemodialysis. Conclusions: Renal involvement in Sjogren’s syndrome may be frequently latent. 32% of our patients had signs of renal involvement at the ESRD stage. The renal involvement in the ESRD is high and more often follows a subclinical course. In some cases it may precede the onset of subjective sicca syndrome.

Introduction and Aims: Microalbuminuria (MA) is a marker of vascular damage that is associated with increased risk of cardiovascular disease and mortality in the general population. Also, MA may be an important early marker of renal damage and cardiovascular risk in persons with HIV infection. Careful screening for MA at first diagnosis of HIV may identify such at risk patients. The aim of the study was to identify these patients by screening newly diagnosed HIV patients for microalbuminuria and determining relevant associations.

Methods: This was a cross sectional study and subjects were recruited from consenting newly diagnosed HIV patients who had attended our health facility. Age and sex matched consenting HIV seronegative members of staff and patients served as controls. Sociodemographic data such as age, occupation, religion, and educational status were obtained from all subjects. Anthropometric data such as weight, height, waist and hip circumference were recorded for all subjects.

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Results: Of the 367 subjects recruited, 380 met the inclusion criteria and had complete data for analysis. Of this number, 86 (28.7%) were males while 281 (71.3%) were females. The median age was 36.0years (range 17-76). Microalbuminuria (Urinary albumin/creatinine ratio, ACR<30mg/g) was detected in 44 (14.7%) of the HIV subjects and in 2 (24%) of control participants (p=0.001). Several factors were associated with the development of microalbuminuria such as low CD4 counts (p=0.037), low HDL-c (0.003), low GFR (p=0.008) and high LDL-c (p=0.035). However, on logistic regression analysis, significant associations were low BMI (p=0.036), low HDL-c and high LDL-c. Electrolyte abnormalities found included hyponatremia in 58 (19.3%), hypokalaemia in 24 (8.0%) and 13 (4.3%) had acidosis but these were not significantly correlated with microalbuminuria.

Conclusions: Microalbuminuria is prevalent among newly diagnosed patients with HIV infection. timely detection and appropriate follow-up would be helpful.

Introduction and Aims: Idiopathic Membranous Nephropathy (iMN) should no longer be considered an idiopathic and anti phospholipase A2 receptor antibody (anti-PLA2 R -Ab) is useful method for its diagnosis. But future studies are needed to confirm its positivity in different population and exploring its mechanisms of action in the pathogenesis of iMN.

Methods: In this study, using an indirect immunofluorescence test we assessed the anti-PLA2 R -Ab in an Iranian cohort of iMN. The serum levels of antibody against the secreted phospholipase A2 (Anti - s PLA2-Ab) were also measured in those with positive results for anti-PLA2 R -Ab.

Results: We studied 23 patients with iMN (M/F 11/12, 34±/9.8 year), two secondary MN and five patients with primary glomerulopathies (GN) other than MN. Anti PLA2 R -Ab was detected in 74% of patients (17/23) with iMN, but not in those with secondary MN or those with other GN. The titers of anti-PLA2 R -Ab was not significantly correlated with the degree of proteinuria ( p=0.05).But there was a significant correlation between the titers of anti PLA2 R -Ab and anti - sPLA2-Ab ( p value< 0.05).

Conclusions: Anti- PL A2 R-Ab is highly specific for iMN. Proteinuria may also reflect glomerular structural damage rather than immunological activity of the disease. Strong correlation between anti -sPLA2 -Ab and anti-PLA2 R -Ab needs future investigation.

Introduction and Aims: Day case renal biopsy represents a valuable, safe, and perhaps cost-effective method of obtaining diagnostic renal tissue. There have been publications which have shown that in a proven driven day case biopsy setting, it is safe and reduces hospital admissions. However, there is no approved national practice guideline on this issue to date. Day case biopsy protocol with nurses-led pre-assessment and discharge has been developed and is viewed as a trend for service innovation, workforce re-structuring, improving patient flow and patient experience. Making such workforce changes generally requires developing effective protocols to ensure best safe practice. The day case renal biopsy protocol is applied to patients who are clinically stable, have no social issues and are able to be discharged on same day. This ensures that day case renal biopsy is used on appropriate patients, who are fully informed of the risks and benefits.

Methods: Between May 2012 to November 2012, data was collected for all patients attending for day case kidney biopsy. All patients were seen by Advanced Nurse Practitioner (ANP) one week prior to biopsy, with the ultimate aim to ensure patient suitability for day case renal biopsy. All blood tests, MRSA swabs taken and kidney ultrasound checked. Information leaflet given and consent obtained. The biopsy was performed by trained renal registrars or renal consultants. All patients stayed at least 6 hours post biopsy as per protocol. All of the patients are seen by ANP or Renal Registrar prior to discharge.

Results: Total of 67 patients’ results reviewed who met the criteria of day case biopsy as per protocol. Among them, 63 (94%), patients discharged on same day. Only one patient stayed overnight due post biopsy Frank haematuria but settled without any intervention and was discharged on following day (Table1). One patient stayed overnight for suboptimal BP control and other 2 for logistical issues. Failure rate of obtaining kidney tissue on biopsy was 3% (n=2).

Conclusions: This audit data has demonstrated the feasibility, effectiveness and safety of a protocol driven day case renal biopsy. Nurse led day case biopsy can help addressing the work force development and re-structuring of services with improved patient outcome and experience.

Introduction and Aims: Management of adults with steroid resistant (SR) minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS) and that of membranous glomerulopathy (MGN) resistant to alternating monthly cycles of steroids and cyclophosphamide for 6 months (modified ponticelli regimen) is a challenging task. Is tacrolimus (Tac) effective in this situation without serious adverse effects? This prospective study was done to answer this question.

Methods: This prospective observational study was done from January 2011 to December 2012. Adult patients of SR MCD, FSGS and MGN were included.
mg/kg/day for at least 16 weeks) and that of MGN resistant to modified ponticelli regimen were enrolled. In patients with SR MCD, FSGS oral Tac was started targeting a trough level of 0.5-1.0 mg/ml and prednisolone tapered to 0.15 mg/kg/day in 4-6 weeks and stopped after 6 months, while Tac was continued for further 6 months. In patients of modified ponticelli regimen resistant MGN Tac monotherapy was given targeting level of 0.5-8 mg/ml after a wash out period of 12 weeks. In both FSGS/MCD and MGN those with complete remission. Tac dose was reduced to target 3-6 mg/ml and hiked again if there was a relapse while in partial responders Tac trough levels were kept at 0.5-10 mg/ml. Tac was discontinued after 6 months if patients were resistant to therapy. Outcome viz complete remission (reduction of proteinuria to <0.3 g/d), partial remission (reduction of proteinuria to 0.3–3.5 g/d) were assessed at the end of 6 months. Relapses defined as increased proteinuria after complete or partial remission were recorded. Adverse effects viz. nephrototoxicity (>25% rise in creatinine), cosmetic effects, impaired fasting glucose and lipid profile were recorded every month and analysed at the end of 12 months.

Results: A total of 31 (FSGS=22, MCD=2, MGN=7) who completed one year of study were analysed. Mean age was 26.7±10.5 and 43.1±8.9yrs in FSGS/MCD and MGN respectively. Serum creatinine pre-treatment was 0.91±0.27 mg/dl and 0.88±0.16 mg/dl in FSGS/MCD and MGN respectively. Of 24 patients of FSGS/MCD remission was seen in 11 (45.8%), complete in 8 (33.3%) and partial in 8(12.5%). Tac resistance was seen in 13 (51.4%) patients. Time taken to achieve remission was 16.3 ± 7.6 weeks. Of 24 patients 6 (25%) had a relapse. Both the patients of MCD had complete remission with Tac but they relapsed when Tac dose was reduced. Of 7 patients of MGN 3 had remission (42.8%), 1 (14.3%) complete and 2 (28.5%) partial. Tac resistance was seen in 4 (57.2%) patients. Time taken to achieve remission was 16 ± 6.9 weeks. In patients who achieved complete or partial remission (114.3%) had relapse. Of 31 patients nephrototoxicity was seen in 6 (19.3%), which was reversible after reduction in Tac dose, impaired glucose tolerance, infections, tremors in 3 (9.7%) each and gum hyperplasia in 2 (6.4%) patients.

Conclusions: Tac is effective in FSGS/MCD. MGN patients resistant to first line therapy. However it needs strict kidney function monitoring due to its potential nephrototoxicity.

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**MP332**

**NON-DIABETIC RENAL DISEASE IN DIABETES MELLITUS: CLINICAL FEATURES AND RENAL BIOPSY FINDINGS**

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1Department of Nephrology Ankara Numune Education and Research Hospital Ankara Turkey

**Introduction and Aims:** Renal diseases in Diabetes Mellitus (DM) include diabetic nephropathies (DN) and non-diabetic renal diseases (NDRD). The clinical differentiation between these two categories is usually not so clear and effective. The aim of this study of renal biopsies in cases with type-2 DM was to know the prevalence and nature of NDRD and to note its correlation with the duration of DM, extent of proteinuria, and presence or absence of retinopathy.

**Methods:** We reviewed clinical data, laboratory data, and renal biopsies from 71 patients who underwent renal biopsy in our center. Patients were divided into two groups according to pathological features (34 in DN group and 37 in NDRD group). Clinical and laboratory data were compared between two groups.

**Results:** There were 42 women and 29 men; ages 55±12 years. Based on biopsy findings patients were categorized as DN and NDRD. In patients with DN (n=34), retinopathy was more common (p=0.01) and they presented a longer duration of diabetes mellitus (p<0.001). Focal segmental glomerulosclerosis was the most frequent diagnosis in patients with NDRD. The significant factors that predict the NDRD included a short duration of diabetes, absence of retinopathy, and level of proteinuria.

**Conclusions:** The prevalence of NDRD is remarkably frequent in type-2 DM patients in whom nephrologists consider renal biopsy an appropriate measure. Our study showed that predictors of NDRD were short duration of DM and absence of retinopathy seen in patients with diabetes.

**Table 1:**

<table>
<thead>
<tr>
<th>DN (n=34)</th>
<th>NDRD (n=37)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54.7±11.1</td>
<td>54.9±14.3</td>
</tr>
<tr>
<td>Male gender (n.%)</td>
<td>14 (41.2)</td>
<td>15 (40.5)</td>
</tr>
<tr>
<td>S Alb</td>
<td>2.8±0.7</td>
<td>2.7±0.9</td>
</tr>
<tr>
<td>Scre</td>
<td>2.1±1.5</td>
<td>2.8±2.5</td>
</tr>
<tr>
<td>HbA1c</td>
<td>7.9±2.1</td>
<td>8.4±2.4</td>
</tr>
<tr>
<td>Ht%</td>
<td>29 (85.3)</td>
<td>23 (62.2)</td>
</tr>
<tr>
<td>Hematuration (%)</td>
<td>13 (38.2)</td>
<td>14 (37.8)</td>
</tr>
<tr>
<td>Presence of retinopathy(%)</td>
<td>16 (47.1)</td>
<td>6 (16.2)</td>
</tr>
<tr>
<td>Duration of DM(months)</td>
<td>108.8±58.8</td>
<td>57.8±55.9</td>
</tr>
<tr>
<td>Proteinuria(gr/day)</td>
<td>641.3</td>
<td>45±4.6</td>
</tr>
</tbody>
</table>

**Figure 1:** Comparison of proteinuria results in the DN and NDRD arms

**Figure 2:** Comparison of proteinuria results in DN and NDRD arms

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**MP333**

**INVESTIGATION OF HISTOLOGICAL IgG4 STAINING AND SERUM ANTI-PLA2R LEVEL IN CLINICALLY PRIMARY AND SECONDARY MEMBRANOUS NEPHROPATHY**

Dóra Bajcs1, György Ábrahám1, Éva Kemény2, Sándor Soroki1, Péter Légrády1, Annamária Letoha1, Kypros Constantinoú1, Zoltán Öndrik1 and Béla Iványi2

11st Department of Internal Medicine University of Szeged Szeged Hungary
2Department of Pathology University of Szeged Szeged Hungary

**Introduction and Aims:** In 70% of cases of adult membranous nephropathy (MNP) M-type phospholipase A2-receptor antibody (anti-PLA2R) can be detected, which belongs to IgG4 subclass. Therefore the histological IgG4 positivity suggests primary cause, yet it is essential to perform basic examinations to exclude secondary disease; on the side the prevalence of antibody-connected MNP has not been investigated so far in Central-Eastern Europe.

**Methods:** We performed the posterior histological IgG4 staining of the stored renal biopsy samples of patients diagnosed with membranous nephropathy from 2007 (43 cases). We evaluated if MNP was clinically primary or secondary and we did the semi quantitative determination of serum anti-PLA2R level.

**Results:** In 6 samples IgG4 staining was positive, in 2 cases there was 1+, in 1 was 2+, in 24 was 3+ and in 10 there was 3+ positivity. Among the 6 IgG4 negative patients, 3 were obviously secondary (in 2 SLE, in 1 NSAID abuse), in 3 cases secondary origin

**Table 1:**

<table>
<thead>
<tr>
<th>DN (n=34)</th>
<th>NDRD (n=37)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of retinopathy(%)</td>
<td>16 (47.1)</td>
<td>6 (16.2)</td>
</tr>
<tr>
<td>Duration of DM(months)</td>
<td>108.8±58.8</td>
<td>57.8±55.9</td>
</tr>
<tr>
<td>Proteinuria(gr/day)</td>
<td>601.4±3</td>
<td>45±4.6</td>
</tr>
</tbody>
</table>

**Figure 1:** Comparison of proteinuria results in the DN and NDRD arms

**Figure 2:** Comparison of proteinuria results in DN and NDRD arms
was only suspected (sclerotising MNP with histological signs of secondary origine; diabetes; C1q positivity despite negative lupus serology). 6 from the 37 IgG4 positive cases were suspected to be secondary (SLE; EBV infection–autoimmune hepatitis; HBAg positivity; mixed connective tissue disease; rheumatic arthritis–NSAID abuse), in 9 patients we could not exclude definitely secondary origine because of diabetes or underetermined quantity of NSAID consummation; in these latter cases it is difficult to differentiate between causality and coincidence. The remaining 22 cases seemed to be primary (as for histological IgG4 positivity and clinical activity, there cases were various). We examined 31 patients with MNP averagely 35 months after the biopsy and determined serum anti-PLA2R level. Anti-PLA2R positivity was only detected in 4 patients: 1 patient was not in remission, 2 was in relapse, 1 was in partial remission (histological IgG4 positivity was also detected in them). In the other 27 patients (1 was transplantated, 3 were in no remission, 11 were in partial, 12 in complete remission) there was no serum anti-PLA2R positivity. In 6 patients we could measure serum anti-PLA2R level in the time of biopsy, but only 2 cases were positive despite clinically 5 seemed to be primary.

Conclusions: In conclusion, histological IgG4 staining can help us to determine if MNP is primary or secondary, but it is still essential to screen for the most common secondary reasons. After 35 months average time of follow-up, the importance of determine the serum anti-PLA2R level can not be proved on the basis of our data. On the time of biopsy, serum anti-PLA2R positivity was only detected in 1/3 of cases, which can refer as maller importance of this antibody in this reason of Europe.

**MP334**

**THE PRESENCE OF FOCAL SEGMENTAL GLOMERULOSCLEROSIS IS ASSOCIATED WITH A POOR RESPONSE TO RITUXIMAB IN ADULTS WITH IDIOPATHIC MEMBRANOUS NEPHROPATHY**

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**Introduction and Aims:** Idiopathic membranous nephropathy (IMN) is the leading cause of nephrotic syndrome in western countries. Rituximab (RTX), a B-cell depleting monoclonal antibody, has been proven to be effective for treatment-resistant IMN. However, whether any histological prognostic factor may help in predicting responsiveness to RTX, is, as yet, unknown. In our single-center study, we have evaluated this possibility.

**Methods:** We report data from eight (3 women) patients with nephrotic syndrome secondary to IMN unresponsive to traditional immunosuppressive therapy and treated with RTX during a follow-up of at least 12 months. Kidney biopsies were independently reviewed by two nephropathologists and scored with a modified Ranft 1997 scoring system taking into account the extent of mononuclear cell interstitial inflammation, arterosclerotic hyaline thickening, interstitial fibrosis, tubular atrophy, fibrous intimal thickening, mesangial matrix increase, segmental glomerulosclerosis, and global glomerulosclerosis. Outcome endpoints were complete and partial remission, defined as 24-hours urinary protein excretion <0.5 g and <3.0 g (with at least 50% reduction versus baseline), respectively. RTX was administered in four weekly infusions of 375 mg/m² in 5 patients, and in a single 1000 mg infusion in 3 patients. All received RTX as third-line immunosuppressant therapy and RAS-blockers throughout the study.

**Results:** Mean age at RTX administration was 67 ± 10 years. Proteinuria significantly decreased during the follow-up (Table in Figure), with significantly lower values after 9 and 12 months from RTX infusion as compared with baseline. Over the 12 months follow-up, 6 patients achieved partial remission and one complete remission. The components of the scoring system were found to be not associated with the in-study outcome endpoints except for segmental glomerulosclerosis (≥35% of glomeruli affected), which presence was associated with the absence of partial remission after 6 and 9 months from RTX administration (p=0.036). eGFR did not change throughout the study period. No difference between the two different RTX regimens (four 375 mg/ m² infusions or one 1000 mg infusion) and the outcome measures was observed.

**Conclusions:** In our cohort, RTX was associated with a significant decrease of proteinuria values during the follow-up. The presence of focal segmental glomerular lesions in kidney biopsies appears to be inversely correlated with the responsiveness to the drug.

**MP335**

**THE ROLE OF NGAL AND CYSTATIN-C ESTIMATION IN PATIENTS WITH PRIMARY GLOMERULOPATHIES**

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1Saint-Petersburg Pavlov State Medical University Saint-Petersburg Russian Federation

**Introduction and Aims:** NGAL and cystatin C are well known as biomarkers of acute kidney injury. Some studies during last years showed that using of this markers can reflect the course of chronic kidney disease. The aim of our investigation was assessment of relationship between level of biomarkers and clinical and pathomorphological signs of glomerular diseases.

**Methods:** In cross-section study 71 patients with biopsy proven primary glomerulonephritis were included. Patients with acute kidney injury, infectious diseases, heart failure, respiratory insufficiency and cancer pathology were excluded. According the results of light and electron microscopy 23 (32,4%) patients had IgA-nephropathy (mesangial proliferative glomerulonephritis), 14 (19,7%) – focal segmental glomerulosclerosis, 22 (31,0%) – membranous nephropathy, 12 (16,9%) – minimal change disease. Besides standard laboratory and instrumental investigations samples of serum and daily urine were obtained in the day of biopsy. NGAL level was studied using ELISA-method, cystatin C using turbidometry. GFR was estimated using creatinine clearance rate. CKD-EPI equation and cystatin C formula by Hoek (r=4,32 + 80.35 × 1/CysC in mg/L). Glomerulosclerosis, tubulointerstitial sclerosis and tubular atrophy were estimated quantitatively and semi quantitatively.

**Results:** GFR estimated using cystatin-C most accurately reflects the degree of glomerular sclerosis than GFR CKD-EPI and creatinine clearance rate (r=0,63, r=0,49, r=0,036 respectively p<0,05). Serum NGAL correlated with GFR estimated using cystatin-C (r=0,37, p<0,05) while there was no correlation with CCr and GFR CKD-EPI. Urine cystatin C did not correlate with such morphological signs of chronic kidney injury as glomerulosclerosis, tubulointerstitial sclerosis and tubular atrophy while urine NGAL correlated with tubular atrophy as well. The rates of urine NGAL and cystatin-C excretion were the highest in patients with high range proteinuria (figure 1).

**Conclusions:** The applying of GFR estimated using cystatin-C is preferable in assessment of glomerulosclerosis degree. Urine NGAL excretion most accurately shows the severity of tubular atrophy while serum NGAL reflects the earliest stages of glomerular cell injury. Low correlation between urine excretion of NGAL and cystatin C and sclerotic changes can be explained by depending of urinary excretion of this biomarkers on proteinuria and this fact should limit their exploitation in acute kidney injury diagnostics in patients with primary glomerulopathies and high range of proteinuria.
Introduction and Aims: Lipoprotein glomerulopathy (LPG) is a rare disorder characterized by lipoprotein thrombi distending and occluding glomerular capillary lumina and variable degree of mesangial proliferation. It frequently progresses to renal failure. Rare mutations in apolipoprotein E (apoE) may contribute to its pathogenesis. From then, more than 70 cases have been reported worldwide, essentially in China and Japan. We described a case of LPG in a French man, the twelfth ever reported from Europe, with a mutation in the apoE gene. To enlighten the pathogenesis, we reviewed the literature for every mutation described.

Methods: A 40-year-old white man, treated for hypertension, consulted with nephrotic syndrome, with normal renal function. Lipid disorder resembling type II hyperlipoproteinemia and elevated levels of serum apoE were noticed. Histopathology showed LPG with amorphous thrombi in glomerular capillaries, staining positive for lipids. DNA sequencing of ApoE found a heterozygous single nucleotide change at position 147, substituting proline for arginine. This Arg147Pro mutation had been described as ApoE Chicago in 2006 by Sam et al. Nor lipid-lowering therapy nor weekly LDL apheresis by cascade filtration decreased proteinuria.

Results: The pathogenesis of LPG is uncertain but the contribution of apoE mutants is clear. Fourteen apoE mutations are described in the literature. Nine mutations (among the most frequent) implicate the LDL-receptor binding domain (from residue 136 to 160). The mutations alter LDL-receptor binding activity or the three-dimensional structure of ApoE, leading to low clearance of lipoproteins, that may aggregate and deposit in the glomeruli. After oxidation, these lipids participate in the local injury, with impact on endothelial cells and mesangial proliferation. ApoE produced by mesangial cells plays a crucial role in the regulation of proliferation and survival of mesangial cells and matrix overproduction.

Conclusions: We reported the second case of LPG with a variant gene, ApoE Chicago (Arg147Pro) in a French man. Like in most case, LDL-receptor binding domain is altered.

Introduction and Aims: The spectrum of glomerulopathies related with MG is increasing. Particularly MG seems to interfere with complement regulation for associated MPGN cases. TMA generally recognizes a similar pathogenetic mechanism.

Methods: We present 3 MG-glomerulopathies with both chronically reduced serum C3 and TMA.

Results: Case 1 A 59-year-old woman was admitted for the appearance of proteinuria and renal failure. She had serum IgG monoclonal immunoglobulin. Kidney biopsy showed a dense deposit disease (DDD). Five years later the patient had renal failure, nephrotic proteinuria with signs of systemic hemolysis (anemia, suppressed haptoglobin and schistocytes) and serum C3 reduction. Coombs test was negative. A novel kidney biopsy was performed that documented DDD and TMA. Steroids, cyclophosphamide and rituximab were all ineffective. At 18 month follow up the patient developed advanced renal insufficiency, chronic hemolysis and serum C3 reduction persisted. Case 2 A 73 years old man was admitted for acute renal failure and nephrotic proteinuria. IgG lambda monoclonal immunoglobulin and complement C3 consumption were documented. Kidney biopsy showed C3 glomerulopathy/DDD. Oral steroids were started with partial recovery of kidney function and reduction of proteinuria. One month later the patient presented acute hemolysis (thrombocytopenia, anemia and renal failure) that remitted with steroid boluses. At 6 months follow up the patient is stable but serum C3 is still reduced. Case 3 A 62 years old woman with history of pre-eclampsia, hypertension and carrier of kidney transplant from 2005 was admitted to our department for acute renal failure. She was found to have IgA lambda monoclonal immunoglobulin, bone marrow biopsy showed smouldering multiple myeloma. Hemolysis, chronic reduction of serum C3 and nephrotic proteinuria were observed. Kidney biopsy showed signs of chronic rejection and severe TMA. IF showed intense C3 deposition. The patient was treated with steroid boluses associated with PE. Renal function worsened quickly and she started hemodialysis.

Conclusions: Complement AP overactivation is implicated in some glomerulopathies but also in TMA. Recently the role of MG is a discussed as a possible cause of complement dysregulation. MG would act as an antibody disturbing complement alternative pathway regulators. Our 3 cases of MG-glomerulopathies associated with TMA and chronic AP dysregulation proposes a possible growing spectrum of MG associated nephropathies. The identification of this condition would suggest a precocious therapeutic approach of MG that could control AP hyperactivation and associated glomerulopathies/TMA.

Introduction and Aims: The prevalence of kidney disease, particularly diabetic and hypertensive kidney disease is increasing rapidly throughout the world. This study was designed to detect the prevalence of diabetes, hypertension, and proteinuria in a rural area of Bangladesh as these are the most common causes of CKD. Result of this study may give some idea about the prevalence of these three conditions as a whole among the rural population of Bangladesh.
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Methods: In this prospective cross sectional study, 1240 adult subjects were screened for proteinuria (dipstick protein≥1+), high blood pressure (BP≥140/90 or antihypertensive treatment), and diabetes (WHO criteria). Results: The mean age of 37.1 ± 10.9 years, 48% were female, and 88.7% were married. Prevalence of diabetes was about 4.9%, of them 49% self reported and 51% detected during the survey. Among self reported cases only 48% were on regular treatment. Prevalence of hypertension was 19.3%, of them 35% were self-reported, 65% detected during the survey. Participants were complicated with acute kidney injury (AKI) whereas only one AKI occurred in 4 patients without mortality. In ACEI/ARB-treated group, 70/79 cases occurred rhabdomyolysis which might be induced by fenoverine, with excluding other well known risk factors. Rhabdomyolysis occurred in 16 patients of them (1.8%) whether other 2 cases occurred in patients without antihypertensive therapy, and their response to therapy. Finally out of 581 patients of primary hypothyroidism, estimated GFR was found to be high incidence of rhabdomyolysis. Hyperkalemia; it is reversible with appropriate management. Introduction and Aims: Hypothyroidism is a cause of renal impairment has not been well discussed and there is no much information available in this subject. The incidence of hypothyroidism and renal impairment found to be directly related to age, more the age more the risk. Ultrasonography of kidneys was normal in all patients. Conclusion: Renal impairment is found to be a common association with primary hypothyroidism; it is reversible with appropriate management.

Methods: In this single-arm, open, multi-center clinical study showed that calcium polystyrene sulfonate is effective and safe in treating hyperkalemia due to chronic kidney disease (CKD).

Results: Of the 168 cases of primary FSGS, 108 were males (64.3%) and 60 females (35.7%). The median age of onset was 38 yrs (ranging 12-78 yrs). The median history was 10 months (range 4 days to 30 months). The proteinuria level was 1.90±0.52 g/day, 18 months. The prognosis is correlated with the amount of proteinuria, level of hypertension, and their response to therapy.

Introduction and Aims: To analyzed the treatment, clinical outcomes, and risk factors for prognosis and intend to provide theoretical evidences for the options of treatment in primary FSGS patients.

Methods: The clinical characteristics, laboratory and pathologic data from 168 patients with primary FSGS in Rui Jin Hospital from January 2002 to October 2011 were collected and reviewed.

Results: TREATMENT AND PROGNOSIS OF PRIMARY FOCAL SEGMENTAL GLOMERULOSCLEROSIS

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Introduction and Aims: To evaluate the efficacy and safety of calcium polystyrene sulfonate in treating hyperkalemia patients with chronic kidney disease (CKD).

Methods: A single-arm, open, multi-center, phase IV clinical trial was carried out. Ninety-eight CKD patients with hyperkalemia dependent, whose age were 18 yrs and serum potassium levels were 5.5 ± 0.6 mmol/L were enrolled in 11 centers from September 5, 2011 to June 21, 2012. The patients took calcium polystyrene sulfonate (Kalimate provided by Kowa (Shanghai) Pharma Consulting Co. Ltd.) 15g / day for one week. Total 5 visits were on 0, 1, 3, 7, and 14 days respectively.

Results: One day after treatment, serum potassium levels decreased significantly from (5.85 ± 0.257) mmol/L to (5.16 ± 0.511) mmol/L (P=0.01) and average value dropped to normal range. Three days after treatment, serum potassium levels decreased to (4.88 ± 0.583) mmol/L. After week of treatment, serum potassium levels decreased to (4.67 ± 0.574) mmol/L (P<0.01). A week after the withdrawal, potassium levels were (4.96±0.655) mmol/L (P<0.01). Serum potassium levels in all visits during the treatment and after discontinuation of calcium polystyrene sulfonate were all significantly decreased comparing to the baseline level. PPS results were similar to FAS. At the same time, serum levels of sodium, phosphorus, calcium showed no significant changes during the treatment (P>0.1). Major side effects were mild gastrointestinal reactions, such as constipation (9/98 cases) and abdominal discomfort (1/98 cases).

Conclusions: This single-arm, open, multi-center clinical study showed that calcium polystyrene sulfonate is effective and safe in treating hyperkalemia due to chronic kidney disease.

Conclusions: The incidence of hypothyroidism and renal impairment found to be directly related to age, more the age more the risk. Ultrasonography of kidneys was normal in all patients. Conclusion: Renal impairment is found to be a common association with primary hypothyroidism; it is reversible with appropriate management.
**IMMUNE AND INFLAMMATORY MECHANISMS**

**ROLE OF DENDRITIC CELL DERIVED INTERFERON-ALPHA IN THE ACTIVATION OF TUBULAR EPITHELIAL CELL IN LUPUS NEPHRITIS (LN)**

Giuseppe Castellano, Cesira Cafiero, Chiara Divella, Fabio Sallustio, Margherita Gigante and Loreto Gesualdo

**Introduction and Aims:** Plasmacytoid dendritic cells (pDCs) play a key role in the activation of the autoimmune response in LN. Recently we demonstrated that these cells infiltrate the kidney of patients with LN at tubulointerstitial level. The pDCs are the main producers of IFN-alpha, whose effects on the renal tubule are poorly understood. The aim of the study was to investigate the pathogenic role of INF-alpha on renal epithelial cells (RPTEC).

**Methods:** Through microarray studies (Illumina), we compared the gene expression profile of RPTEC cells, stimulated with INF-alpha 100IU/ml for 48h, to control cells. We validated microarray results through real-time RT-PCR and cytometry experiments on RPTEC, stimulated with INF-alpha and through immunohistochemical analysis and confocal microscopy on human renal biopsies.

**Results:** Genomic analysis showed that after stimulation, 108 genes were up-regulated and 7 were down-regulated, with a fold-change >2. The Gene Set Enrichment analysis confirmed that between 123 processes regulated, INF-alpha induced the pathway of antigen presentation and the inflammatory signalling in RPTEC. Among the genes up-regulated and involved in these pathways, there were HLA-I, the ubiquitin (FBXO6 and DTX3L) and the immunoproteasome subunits LMP7. After validation of the microarray data by RT-PCR, FACS experiments on INF-alpha activated RPTEC confirmed a significant increase of the antigen presentation pathway (HLA-I 75%±2 basal vs 90%±2 INF-alpha) and of the inflammatory signalling (LMP7 49%±2 basal vs 72%±2 INF-alpha). When we analyzed patients with LN class IV by immunohistochemistry, we found a significant increase of LMP7 expression at tubular interstitial level compared with class II LN. (LMP7 expression 5%±2 LN class II vs 16%±5 class IV, p <0.0001); in addition, LMP7 correlated with MXA protein expression, a specific marker of INF-alpha (MxA 0%±1 class II vs 4.5%±1 class IV, p <0.0001).

**Conclusions:** Our data demonstrate that local production of INF-alpha by pDC might represent a novel pathogenic process mediating renal tubular damage in patients with LN.

**MP345**

**PARICALCITOL EXERTS POTENT IMMUNOMODULATORY EFFECTS ON TREGS AND TH17 CELLS IN PATIENTS WITH SEVERE KIDNEY DISEASE**

Pascal Meier

**Introduction and Aims:** With chronic kidney disease (CKD) progression, the tendency to vitamin D substrate insufficiency leads to progressive calcitriol deficiency. Importantly, calcitriol has significant immunomodulatory effects in addition to its role in calcium homeostasis. A variety of immune cells, including activated T cells express the intracellular vitamin D receptor and are responsive to calcitriol. While the exact mechanisms still require clarification, there is now compelling evidence that the hormonally active calcitriol can activate regulatory T cells (Tregs) and reduce the activity of the proinflammatory TH17 cells. Paricalcitol is a synthetic analogue of vitamin D approved for treatment of secondary hyperparathyroidism. There have been a limited number of studies addressing the immunomodulatory effects of paricalcitol.

In this study we aimed to evaluate the effects of oral calcitriol and paricalcitol supplementation in various inflammation markers (Tregs, TH1, IL-17, IL-21, IL-22, IL-6, IFN-γ, TNF-α, suPAR). Corollarily, T cell immune response to hepatitis B (HBV) vaccination (blood antibody titers) was also determined in patients with stage 5D CKD.

**Methods:** Stained cells are assessed by flow cytometer. The frequency of Tregs (CD4+CD25+Foxp3+) and TH17 (CD4+IL17+) cells is expressed as a percentage of CD4+ T cells by sequential gating on lymphocytes and CD4+ T cells. The levels of serum cytokines and other markers were examined by ELISA. All patients underwent dialysis with high-flux membranes and ultrapure water. All patients included were HBV vaccination non-responders (Titters < 10 U/L). After 6 months of treatment, a full course of 40 μg anti-HBV vaccination (1, 2, 3, 5, 6 mo) was scheduled.

**Results:** Ten patients were included in each treatment arm with mean age of 63.6 ± 12.4 years. Mean hemodialysis vintage was 41.1 ± 16.2 months. Five (25%) patients had diabetes, and seven (35%) had hypertension. We observed a significant increase in Tregs and a decrease in TH17 cells numbers in both treated patients with a significantly higher increase in Tregs of 43% and decrease in TH17 cells of 32% in paricalcitol-treated patients compared with those treated with calcitriol. This was in association with increased IFN-γ and decreased IL-17, IL-21, IL-22, IL-6, TNF-α and suPAR levels. CD4+/CD25+ T cells from the paricalcitol group showed reduced proliferative activity in co-culture with Tregs compared with calcitriol-treated patients (p = 0.002), suggesting an improved suppressive activity of Tregs with paricalcitol. Six months after HBV vaccination, all paricalcitol-treated stage 5D CKD patients significantly improved their anti-HBs Ab titers (> 100 U/L) compared with those on calcitriol treatment.

**Conclusions:** A better neutralization of TH17 in vivo with paricalcitol reveals that paricalcitol inhibits micro inflammatory process mainly in a Tregs-dependent manner but also partly because of a decrease in TH17 number and function. These findings suggest that systemic immune modulation by paricalcitol may be a potentially valuable therapeutic approach against micro inflammation and to improve immune response in stage 5D CKD patients.

**MP344**

**REGULATORY T-CELLS MODULATE Nephrocalcinosis in Mice**


**Introduction and Aims:** Nephrocalcinosis describes the ectopic deposition of calcium crystals in the kidney and is seen in a multitude of clinical settings such as acute phosphate nephropathy, inherited tubulopathies, and renal allograft rejection. Nephrocalcinosis is associated with intrarenal inflammation. To further evaluate the specific pathophysiological role of T cells in acute phosphate nephropathy, we used DBA/2 mice that have a natural splice variant in the ABCC6 gene and are prone to develop ectopic soft tissue calcifications under phosphate-rich diet.

**Methods:** Female DBA/2 mice were depleted of T cells (n=10) or regulatory T cells (Treg) (n=15) using either an anti-CD3e or an anti-CD25 monoclonal antibody, and were compared to isotype-treated controls (n=10; n=15). After this immunomodulation, the DBA/2 mice were set on a phosphate-rich diet for 9 days and sacrificed for radiological and histopathological analyses. Successful depletion was confirmed by flow cytometry of spleenic single cell suspensions.

**Results:** Feeding a phosphate-rich diet to DBA/2 mice induced a clear phenotype of nephrocalcinosis. T-cell depletion significantly increased renal calcification as shown by higher calcium score in micro-computed tomography (p<0.002). Concordantly, Treg depletion significantly deteriorated acute phosphate nephropathy (p<0.039) and was associated with significantly increased serum FGF23 levels (p<0.005) without affecting serum phosphate levels. Moreover, semi-quantitative histopathological evaluations with Alizarin red stainings independently confirmed the respective radiological measurements.

**Conclusions:** In summary, our data suggest a pivotal role of T cells, most likely regulatory T cells, in the progression of nephrocalcinosis, and emphasize the fact that intrarenal inflammation deteriorates the outcome in acute phosphate nephropathy.

**MP346**

**ACUTE PARICALCITOL ADMINISTRATION REDUCE INFLAMMATION IN CKD PATIENTS IN VIVO AND IN VITRO**

Silvia Lucisano, Adriana Arena, Valentina Donato, Maria Rossaria Fazio, Domenico Santoro and Michele Buemi

**Introduction and Aims:** Microinflammation state is a pathologic feature of chronic kidney diseases(CKD). Recent evidence suggests that vitamin D deficiency, common in CKD patients, has a role in the modulation of immune response and inflammation. Evidence is also mounting that Paricalcitol (Pr), a synthetic vitamin D analogue, is renoprotective in different inflammatory nephropathies. Neutrophil
At univariate analysis, NGAL was found to be directly correlated with ESR, hsPCR, IL-17, IL-1β, proteinuria, PTH, Ca or P. In a multivariate model using NGAL as a dependent variable, it was also found with 25(OH)D. No significant correlation was found for albuminuria, MMP2 and tissue inhibitors of metalloproteinase (TIMP) 1 and TIMP2. Procoagulatory factors plasmaglobulin activator inhibitor 1 (PAI-1) and tissue factor were increased by poly (dA:dT) treatment without affecting basal expression of fibrinolytic factor t-PA. When knockedown experiments with siRNAs specific for viral receptors were performed only expression of IFNα was blocked by the siRNAs for the RNA receptors TLR3, RIG-1 and MDA5. None of the siRNAs for TLR3, RIG-1, MDA5, NALP3, AIM2 and DA1 had an effect on the poly (dA:dT) induced expression of the other factors tested. Poly (dA:dT) increased protein expression of p38α and pERK1 as demonstrated by Western blot. Expression of TRAF6 was not influenced and expression of TRAF6 was downregulated by poly (dA:dT) stimulation.

Immunohistochemistry showed nuclear translocation of IFR3 and NF-κB after poly (dA:dT) treatment.

Conclusions: Our results demonstrate that viral DNA could play a role in virus associated GN by synthesis of cytokines, chemokines, type 1 interferons, adhesion molecules and effects on modification of mesangial matrix and glomerular fibrin deposition. These effects are only in part mediated by known receptors of the innate immune system. Knockdown experiments with siRNAs specific for viral RNA and DNA receptors suggest that unknown TLR independent mechanisms are involved in DNA associated viral GN.

**MP348**

**CATHEPSIN S INHIBITION ABROGATES IMMUNE COMPLEX GLOMERULONEPHRITIS**

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**Introduction and Aims:** Systemic lupus erythematosus (SLE) is a chronic autoimmune disease and is characterized by loss of self-tolerance. Genetic studies consistently suggest the most common forms of immune complex glomerulonephritis (IC-GN) to develop from polymorphisms in HLA genes, i.e. MHC class II mediated priming of (auto-)antibody production. Cathepsin S is a lysosomal protease and is responsible for the final proteolysis of MHCII associated chaperone invariant chain (Ii) in antigen-presenting cells, thus plays an important role in antigen presentation. We hypothesized that cathepsin S inhibition would suppress SLE and lupus nephritis.

**Methods:** In this study we used medicated diet formulated by mixing cathepsin S inhibitor (RO546111 - 262.5mg/kg chow) with the chow. Autoimmune female MRL-Fas (lpr) mice were given cathepsin S inhibitor diet starting from week 12

**Results:** RO546111 significantly reduced the activation of spleen dendritic cells and the subsequent expansion and activation of CD4+ T cells and CD4/CD8 double negative 'auto reactive' T cells. Cathepsin S inhibition impaired germinal center formation, suppressed B cell maturation to plasma cells, and Ig class switch. This reversed hy ergammaglobulinemia and significantly suppressed the plasma levels of numerous IgG autoantibodies below baseline, including most IgG isotypes of anti-dsDNA. Cathepsin S inhibition significantly reduced rheumatoid factor, nucleosome and RNP Sm autoantibodies in the plasma. This effect was associated with less glomerular IgG and complement C3c deposits, less infiltration of glomerular macrophages, which protected kidneys from IC-GN and also lungs from autoimmune peribronchitis.

**Conclusions:** Together, cathepsin S promotes IC-GN by driving MHC II-mediated T and B cell priming, germinal center formation, and B cell maturation towards plasma cells. This data demonstrate that cathepsin S inhibition has a profound effect on pathogenic autoantibodies. These afferent immune pathways can be specifically reversed with the orally available cathepsin S antagonist RO546111, even when given after disease onset, and prevents IC-GN progression. This novel therapeutic strategy could correct the common pathomechanism of various IC-GNs.

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**MP347**

**ROLE OF DNA RECOGNIZING RECEPTORS OF THE INNATE IMMUNE SYSTEM IN VIRUS ASSOCIATED GLOMERULONEPHRITIS**

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**Introduction and Aims:** Glomerulonephritis (GN) may result from several viral infections, most commonly from infections with hepatitis B or hepatitis C virus and HIV. Viral infections can also trigger exacerbation of other forms of glomerular injury, e.g. IgA nephritis or systemic lupus erythematosus. Disease mechanisms include deposition of immune complexes as well as the release of cytokines, chemokines, adhesion molecules and growth factors. We have previously demonstrated a predominant role of viral RNA receptor Toll-like receptor 3 (TLR3) in Hepatitis C associated GN. Here we investigated the role of viral receptors of the innate immune systems in DNA associated viral GN.

**Methods:** Experiments were performed on human mesangial cells (MC) in cell culture. Stimulation experiments were performed with poly (dA:dT), a synthetic analogue of viral DNA. To show specific effects of viral receptors transfection with siRNAs for RNA and DNA receptors TLR3, RIG-1, MDA5, NALP3, AIM2 and DA1 was performed. Analysis of signal transduction pathways was performed by Western blot and immunohistochemistry.

**Results:** Stimulation with poly (dA:dT) increased expression of selected cytokines and chemokines IL-6, IL-8, RANTES, MCP-1, IP-10, type I interferon IFNo and IFNβ as well as adhesion molecules ICAM-1 and VCAM-1. Furthermore expression of matrix metalloproteinase (MMP) 9 was increased without affecting basal expression of MMP1 and MMP2 and tissue inhibitors of metalloproteinase (TIMP) 1 and TIMP2. Procoagulatory factors plasmaglobulin activator inhibitor 1 (PAI-1) and tissue factor were increased by poly (dA:dT) treatment without affecting basal expression of fibrinolytic factor t-PA. When knockedown experiments with siRNAs specific for viral receptors were performed only expression of IFNα was blocked by the siRNAs for the RNA receptors TLR3, RIG-1 and MDA5. None of the siRNAs for TLR3, RIG-1, MDA5, NALP3, AIM2 and DA1 had an effect on the poly (dA:dT) induced expression of the other factors tested. Poly (dA:dT) increased protein expression of p38α and pERK1 as demonstrated by Western blot. Expression of TRAF6 was not influenced and expression of TRAF6 was downregulated by poly (dA:dT) stimulation.

Immunohistochemistry showed nuclear translocation of IFR3 and NF-κB after poly (dA:dT) treatment.

Conclusions: Our results demonstrate that viral DNA could play a role in virus associated GN by synthesis of cytokines, chemokines, type 1 interferons, adhesion molecules and effects on modification of mesangial matrix and glomerular fibrin deposition. These effects are only in part mediated by known receptors of the innate immune system. Knockdown experiments with siRNAs specific for viral RNA and DNA receptors suggest that unknown TLR independent mechanisms are involved in DNA associated viral GN.

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**MP349**

**THE URAEMIC TOXIN INDOXYLSULFATE INDUCES LEUKOCYTE-ENDOTHELIAL ADHESION AND INDUCES IMPAIRED BLOOD FLOW IN THE RAT PERITONEAL MICROCIRCULATION**

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**Abstracts**

Nephrology Dialysis Transplantation
Introduction and Aims: Cardiovascular disease, a major cause of death among CKD patients, is associated with leukocyte-endothelial interactions and endothelial dysfunction. In vitro and in vivo data link several protein-bound uraemic retention solutes to cardiovascular damage and progression of kidney failure. However, these models never took into account the complicated cross-talk between endothelium and leukocytes, as present in vivo. This study evaluated the effects of local and systemic exposure to indoxylsulfate (IS), on the recruitment of circulating leukocytes in the rat peritoneal vascular bed, using intravital microscopy.

Methods: Two series of experiments were performed: (1) The visceral peritoneum (VP) was superfused by a control solution (n=12) or by an IS containing solution at stable continuous levels in the high uraemic range (23.3 ±0.9 mg/dl) induced also significantly more adherence (2.28±0.97 vs 0.22±0.11 p<0.05) and extravasation (3.57±1.73 vs 189.8±12.7 ±0.01) compared to the control. Also, here, 5/6 rats showed a disturbed blood flow pattern with a significant reduced red cell velocity (0.72±0.38 vs 1.85±0.33 ±p<0.05), although no complete flow-stop occurred.

Conclusions: These results provide strong in vivo evidence that IS exerts proinflammatory effects by stimulating the cross-talk between leukocytes and endothelial cells that could contribute to vascular damage. In addition, IS induced impaired blood flow patterns, which may adversely affect overall organ perfusion. Potential damage to the endothelial glycocalyx, which normally helps to maintain vascular homeostasis, will be further investigated by performing immunofluorescence stainings of the VP or by measuring glycocalyx constituents in rat blood.

In vitro

Experiments were performed on human mesangial cells (MC) in cell culture. Methods: For 3 hours at stable continuous levels in the high uraemic range (23.3 ±0.9 mg/dl) induced also significantly more adherence (2.28±0.97 vs 0.22±0.11 p<0.05) and extravasation (3.57±1.73 vs 189.8±12.7 ±0.01) compared to the control. Also, here, 5/6 rats showed a disturbed blood flow pattern with a significant reduced red cell velocity (0.72±0.38 vs 1.85±0.33 ±p<0.05), although no complete flow-stop occurred.

Conclusions: These results provide strong in vivo evidence that IS exerts proinflammatory effects by stimulating the cross-talk between leukocytes and endothelial cells that could contribute to vascular damage. In addition, IS induced impaired blood flow patterns, which may adversely affect overall organ perfusion. Potential damage to the endothelial glycocalyx, which normally helps to maintain vascular homeostasis, will be further investigated by performing immunofluorescence stainings of the VP or by measuring glycocalyx constituents in rat blood.

THE ROLE OF OBESITY AND ADAPTER MOLECULE MyD88 IN THE SEVERITY OF ACUTE KIDNEY INJURY INDUCED BY EXPERIMENTAL SEPSIS

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Introduction and Aims: Obesity is a complex disorder, affecting individuals of all ages and is characterized by a moderate state of chronic inflammation, with increased levels of pro-inflammatory cytokines and acute phase proteins that maintain the inflammatory state. Obesity has also been shown to be a risk factor of several pro-inflammatory cytokines and acute phase proteins that maintain this inflammatory state. Obesity has also been shown to be a risk factor of several pro-inflammatory cytokines and acute phase proteins that maintain this inflammatory state. Here, we concluded that the innate immunity mainly through MyD88 and Niels Câmara1,2

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Nephrology Dialysis Transplantation

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Methods: We assessed the regulation of MIF secretion and its effects on glomerular cells in vitro. In particular we studied primary murine podocytes and parietal epithelial cells (PEC), since these cells are involved in the development of crescentic glomerulonephritis. Next, we studied the effects of genetic deletion of the MIF gene in mice with NTN (day 14).

Conclusions: In conclusion, genetic deletion of MIF ameliorated the development of glomerulonephritis and reduced the number of crescents in mice. Our in vitro data suggest a novel, intrinsic glomerular mechanism in which MIF is locally upregulated in glomerular cells and directly increases PEC proliferation.

IMMUNOMODULATORY ROLE OF THE TNF / TNF RECEPTOR SYSTEM IN HEPATITIS C ASSOCIATED GLOMERULONEPHRITIS

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Introduction and Aims: In viral infections, disease manifestations often result primarily from immune cells infiltrating target organs on the basis of an ineffectual viral clearance with persistent antigenemia or an inappropriate immune response. The type of tissue injury depends not only on the extent of initial inflammation but also on its persistence or resolution or reactivation, which leads to the pathogenesis of both damage and scarring. Glomerulonephritis (GN) may result from several viral infections, most commonly from infections with hepatitis B or hepatitis C virus (HCV) and HIV. Disease mechanisms include deposition of immune complexes as well as the release of cytokines, chemokines, adhesion molecules and growth factors. TNFα is known to exert multiple effects on the immune system, including the release of cytokines, chemokines, adhesion molecules and coordination of the migration of leukocytes to targeted organs. The biological activity of TNFα requires binding to one of the TNFα receptors, TNFR1 or TNFR2. We have previously demonstrated an irreversible dominant role of viral receptor Toll-like receptor 3 (TLR3) in Hepatitis C associated GN.

Methods: Experiments were performed on human mesangial cells (MC) in cell culture. Stimulation experiments were performed with poly (I:C) and Hepatitis C RNA from
patients with Hepatitis C infection. To show specific effects of viral receptors transfection with siRNA for TR2 and retinoic acid-inducible gene-1 (RIG-I) was used. Results: In HCV associated GN, selected cytokines and chemokines IL-6, IL-8, RANTES and MCP-1 were increased. After transfection of the proinflammatory cytokines a significant upregulation which is mediated specifically by the viral receptor TR2 was expressed on mesangial cells. Induction of these factors is further potentiated by TNFα with its signaling occurring preferentially via the TNFα receptor subtype 2 that is selectively increased upon stimulation of viral receptors in the proinflammatory milieu. Conclusions: We show a specificity of TR3 mediated expression of cytokines, chemokines and adhesion molecules in human MC infected with HCV. We provide evidence for the expression of functional TNFα receptors of both subtypes on MC and a primary role of TNFα mediated induction of factors important for inflammation and attraction of leukocytes in the setting of viral infection. These findings are of particular interest from a therapeutic point of view in chronic HCV infection and disease manifestations as vasculitis and GN. The observation of a predominant role of TR2 and TNFα receptor subtype 2 in Hepatitis C associated GN might be of further interest for therapeutic interventions.

**Abstracts**

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**Introduction and Aims:** Indoxyl sulfate, a uremic toxin, is associated with cardiovascular disease and mortality in chronic kidney disease patients. The aryl hydrocarbon receptor (AhR) is a ligand-inducible transcription factor known to mediate the toxic effects of numerous environmental contaminants such as dioxin. We examined the role of AhR in indoxyl sulfate-induced leukocyte-endothelial interaction. Methods: Human umbilical vein endothelial cells (HUVEC) were transfected with siRNA of AhR (siAhR) and then treated with indoxyl sulfate for 20 h, followed by stimulation with TNFα or for 4 h. Leukocyte-endothelial interaction was assessed under flow condition that mimic vascular flow conditions in vivo. mRNA and protein expression were determined by real-time RT-PCR and Western blotting, respectively. Transcriptional activity was by luciferase assay. Results: Indoxyl sulfate induced mRNA expression of Cyp1a1 and Cyp1b1 which are downstream targets of AhR. Luciferase assay using dioxin response element revealed that indoxyl sulfate induced AhR transcriptional activity, as well as AhR agonist, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). AhR silencing significantly decreased indoxyl sulfate-enhanced leukocyte adhesion. Indoxyl sulfate enhanced mRNA and protein expression of E-selectin, which were significantly compromised after AhR silencing. To assess the functional role of AhR in the indoxyl sulfate stimulated E-selectin gene induction, we conducted luciferase promoter assay using serial deletion constructs of E-selectin promoter. We found that the promoter region of E-selectin, corresponding to -166 to +107 bp, was essential for the effect of indoxyl sulfate mediated by AhR. Conclusions: Our data suggest an important role for AhR in Indoxyl sulfate-enhanced leukocyte-endothelial interaction through transcriptional regulation of E-selectin and provides a novel mechanistic insight into the CKD-related vascular inflammation.

**RESULTS OF TOLL-LIKE RECEPTORS, CATHELICIDIN AND MCP-1 IN HEMODIALYSIS PATIENTS WITH VITAMIN D DEFICIENCY**

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**Introduction and Aims:** Toll like receptors (TLR) and antimicrobial peptides are involved in mechanisms of immune response. Recently, it has been reported that vitamin D may regulates these response. However, data on expression of TLR, MCP-1 and cathelicidin in HD patients with deficiency of vitamin D are limited. The aim of this study was to evaluate the expression of TLR-2 and TLR-4 on PMN and MN by flow cytometry. We measured serum levels of cathelicidin, CRP, monocyte chemotactic protein (MCP-1) by ELISA and vitamin D (Vit D) by Chemiluminescence. Results: HD patients had low Vit D (19±7 vs. 26±7; p = 0.008), high CRP (0.51±0.65 vs. 0.29±0.33; p = 0.04), cathelicidin (168±351 to 468±3418; p = 0.01), MCP-1 (208±71 vs. 84±59) serum levels. Neutrophils and monocytes from HD patients exhibited significant upregulation of TLR2 (313±168 vs. 249±56; p = 0.04), TLR4 (212±157 vs. 121±35; p = 0.02) and TLR2 (369±210 vs. 269±144; p = 0.03) expression, respectively. Vit D correlated negatively with TLR2 (r = 0.31; p = 0.01) and TLR4 (r = 0.30; p = 0.03) expression. We did not observe any correlations between Vit D and TLR2, TLR4 and cathelicidin expression. Conclusions: TLR2, TLR4, cathelicidin and MCP-1 are increased in hemodialysis patients, probably reflecting the priming inflammatory state in this population. It was possible that average of 20 mg/ml of Vit D levels observed in HD patients were not enough to downregulate TLR2, TLR4 and cathelicidin expression in a sufficient population. So, these results suggest that these mechanisms may contribute to higher inflammation and possibly to cardiovascular and infections in these patients. However, future study is necessary to observe if supplementation with vitamin D in HD patients will have effect in to diminish these markers expressions and inflammation.

**MP555 ROLE OF RECEPTORS OF THE INNATE IMMUNE SYSTEM IN GLOMERULAR FIBRIN DEPOSITION, FIBROSIS AND MATRIX METABOLISATION**

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**Introduction and Aims:** Viral infections are a major problem worldwide and many of them are complicated by virally induced glomerulonephritis. Progression of kidney disease to renal failure is mainly attributed to the development of renal fibrosis characterized by the accumulation of extracellular matrix components in the mesangial cell compartment and the glomerular basement membrane. Tissue factor (TF), tissue plasminogen activator inhibitor type 1 (PAI-1) and tissue plasminogen activator (t-PA) are major regulators of plasmin turnover and play an important role in generation and degradation of glomerular fibronectin deposits and extracellular matrix components. Extracellular matrix is metabolized by matrix metalloproteinases (MMP) and its tissue inhibitors (TIMP). Viral receptors expressed by mesangial cells are known to be key mediators in immune mediated glomerulonephritis. We have previously shown an expression of the viral receptors TLR2 and TLR4 in human mesangial cells. So, these results suggest that these mechanisms may contribute to higher inflammation and possibly to cardiovascular and infections in these patients. However, future study is necessary to observe if supplementation with vitamin D in HD patients will have effect in to diminish these markers expressions and inflammation.

**MP556 UREMIC TOXIN TRANSCRIPTIONALLY UP-REGULATES ENDOTHELIAL E-SELECTIN VIA ARYL HYDROCARBON RECEPTOR**

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**Introduction and Aims:** Indoxyl sulfate, a uremic toxin, is associated with high IgG4 levels were found in 3 healthy (5.8%), 2 neoplastic (5.5%), and 2 (9%) aortitis patients. High IgG4 levels were found in 3 healthy (5.8%), 2 neoplastic (5.5%), and 2 (9%) aortitis patients. The median (IQR) IgG4 levels was 46 mg/dL (26-122.8) in CP vs 35(14.4-69.5) in healthy controls (p=0.048), 40 mg/dL in neoplastic controls (17.5-68.8) (p=0.14) and 30.5 mg/dL (12.3-63) in aortitis patients (p=0.14). The area under the ROC curve (IgG4 in CP vs in all control subjects) was 0.597 (95% CI 0.509-0.685).

Conclusions: Only 26% of CP patients have high IgG4 levels. IgG4 do not seem to discriminate different CP subsets and its diagnostic reliability for CP is low.
affecting PAI-1 synthesis. MMP9 expression was also increased by viral RNA from patients with HCV infection.

Conclusions: Our findings demonstrate a link between the activation of viral receptors on mesangial cells and potentially causative agents in the development of glomerulosclerosis by effects on glomerular fibrin deposition and changes in extracellular matrix. Therefore progression of inflammatory processes to glomerulosclerosis can be postulated to be directly enhanced by viral infection under specific conditions.

MP357  IS THERE ANY RELATIONSHIP BETWEEN SEROLOGICAL RESPONSIVENESS TO THE EBSTEIN-BARR VIRUS ANTIGENS AND SERUM LEVELS OF MANNOSE BINDING LECTIN IN PATIENTS WITH LUPUS NEPHRITIS AND PRIMARY GLOMERULONEPHRITIDES?

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Introduction and Aims: A link between the Epstein-Barr virus (EBV) infection and the development of systemic lupus erythematosus (SLE) and some forms of primary glomerulonephritis (PGN) has been suggested. On the other hand, it has been shown that insufficiency of mannose binding lectin (MBL) retards the EBV infection. MBL appears to have a dual mode of action. Increased MBL leads to enhanced complement activation and tissue damage, while its deficiency results in aggravation of autoimmunity and increased susceptibility to secondary infections. Hence, we decided to compare the levels of serum MBL and antibodies to EBV antigens in patients with PGN, lupus nephritis (LN) and healthy controls (C).

Methods: The study involved 145 subjects: 78 with PGN (among them 26 with IgA-MesPGN, 20 with non-IgA-MesPGN, 2 with membranoproliferative GN, 14 with idiopathic membranous GN, and 16 with focal-segmental glomerulosclerosis), 32 patients with LN (among them 26 with active lupus flare), and 35 C. The serum levels of MBL and antibodies to EBV early antigen (EA), EBV viral capsid antigen (VCA) and EBV nuclear antigen-1 (EBNA-1) were determined in immunoglobulin (Ig) G, A and M classes using the specified enzyme-linked immunosorbent assays.

Results: The median levels of MBL were 1.11 (range 0.009 to 8.00) in PGN, 0.66 (range 0.015 to 4.61) in LN and 1.22 (range 0.01 to 6.64) mg/ml in C with no significant differences between these groups and also subgroups of PGN. The majority of LN (90.6%) and PGN (82%) patients, and also subjects from the C group (77.1%) were shown to be seropositive for EBNA-1 IgG revealing previous EBV infection. These was also confirmed by seropositivity for VCA IgG in 96% of patients with PGN, 96% of those with LN and 94% of C. Interestingly, the median levels of anti-EA IgG and anti-EA-IgA in LN differed significantly compared to C (p<0.001 and p<0.001, respectively). In addition, the prevalence of these Abs in LN was highly significant compared to C (p<0.005 for both Abs). However, no significant correlation between the levels of these Abs and serum concentrations of MBL could be found in LN. In contrast, significant correlations between serum levels of MBL and anti-EA-IgA and anti-EBV-VCA-IgA Abs could be found in MesPGN (r=0.23; p=0.05 and r=0.26; p=0.05, respectively). This was particularly apparent in IgA-MesPGN, where the above correlations were significantly higher (r=0.56; p<0.001 and r=0.66; p=0.02, respectively).

Conclusions: MBL, being a component of innate immunity system, seems to control the EBV infection and thus can modulate the acute phase of experimental AAN. These immune regulatory functions are also confirmed by seropositivity for VCA IgG in 96% of patients with PGN, 96% of those with LN and 94% of C. Interestingly, the median levels of anti-EA IgG and anti-EA-IgA in LN differed significantly compared to C (p<0.001 and p<0.001, respectively). In addition, the prevalence of these Abs in LN was highly significant compared to C (p<0.005 for both Abs). However, no significant correlation between the levels of these Abs and serum concentrations of MBL could be found in LN. In contrast, significant correlations between serum levels of MBL and anti-EA-IgA and anti-EBV-VCA-IgA Abs could be found in MesPGN (r=0.23; p=0.05 and r=0.26; p=0.05, respectively). This was particularly apparent in IgA-MesPGN, where the above correlations were significantly higher (r=0.56; p<0.001 and r=0.66; p=0.02, respectively). These findings indicate a link between the EBV infection and glomerulosclerosis by effects on glomerular fibrin deposition and changes in extracellular matrix. Therefore progression of inflammatory processes to glomerulosclerosis can be postulated to be directly enhanced by viral infection under specific conditions.

MP358  CD4+ AND CD8+ T CELLS EXERT REGULATORY PROPERTIES DURING EXPERIMENTAL ARISTOLOCHIC ACID NEPHROPATHY

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Introduction and Aims: Experimental aristolochic acid nephropathy (AAN) is characterized by acute tubulo-interstitial (TI) injuries (necrosis of proximal tubules and inflammatory infiltrate) followed by chronic kidney disease (tubular atrophy and interstitial fibrosis). Inflammatory cells are considered as a physiopathological link between both phases. We investigated the role of T cell subpopulations in AAN by using selective depleting antibodies (Ab).

Methods: In a 1st step, we injected daily for 3 weeks C57BL/6 mice with AA and depleting CD4+ T cells Ab (AA+oCD4 group) or control Ab (AA group). Controls were injected with AA vehicle (polyethylene glycol (PEG)) and depleting Ab (PEG +oCD4). In a 2nd step, we only focused on day 5 and 2 additional groups were investigated: AA+ + depleting CD8+ T cells Ab (AA+oCD8 group) and AA+oCD4tCD8 group. We examined plasma creatinine (pCr), blood urea nitrogen (BUN), histological lesions and mRNA expression for inflammatory cytokines.

Results: During the 1st protocol, a significant mortality rate was observed in AA+oCD4 group as soon as day 7 as compared to controls. In the 2nd protocol, no death was observed at day 5. As compared to AA mice, a significant increase in pCr, BUN and tubular necrosis score was observed in AA+oCD4 and AA+oCD8 groups. Pcr on renal tissue samples revealed a significant increase in TNF-α expression in AA+oCD4tCD8 and AA+oCD8 groups and a significant increase in MCP-1 expression in AA+oCD4 group. T-cells deletions had no impact on the % of particular macrophages CD1H143F4/80- in controls. By contrast, a significant increase was observed in AA+oCD4 and AA+oCD8.

Legend: Values are expressed as median (min-max). AA+ selective Ab groups are compared to AA group. P values are * p<0.05; **p<0.01; *** p<0.001 (Kruskal-Wallis followed by Dunn post test).

Conclusions: Our results suggest that both CD4+ and CD8+ T cells are able to modulate the acute phase of experimental AAN. These immune regulatory functions need to be further investigated.

MP359  THE NEW IMMUNOSUPPRESSIVE DRUG FTY720 ATTENUATES TUBULOINTERSTITIAL INFLAMMATION AND FIBROSIS IN 5/6 NPREHRECTOMIZED RATS

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Introduction and Aims: Tubulointerstitial fibrosis is the common pathway that lead to kidney failure, while persistent tubulointerstitial inflammation is a key event in the development of tubulointerstitial fibrosis. The new immunosuppressive drug FTY720 modifies lymphocyte migration into injured tissues by lymphocyte sequestration to secondary lymphoid organs. This study was designed to explore the effect of FTY720 on tubulointerstitial inflammation and fibrosis in 5/6 nephrectomized rats.

Methods: Seven days after surgery, Sprague-Dawley rats were allocated to the following groups: sham surgery, 5/6 subtotal nephrectomy(SNX) + vehicle, and SNX+FTY720 (0.3 mg/kg body wt). Rats were killed on week 12 after surgery and blood, urine and kidneys were collected for analyses. Weight and blood pressure were detected before killed. Pathological changes of the renal tissues were observed by PAS staining and Masson staining. Tubulointerstitial infiltrating inflammation cells such as T cells (CD3,CD4, CD8), B cells (CD20) and macrophages (CD68, CD163, CCR7) were detected by immunohistochemical staining. Protein expression of pro-inflammatory molecules(IL-6, TNF-α, MCP-1) and pro-fibrotic molecule(TGF-B1) were analyzed by immunohistochemical staining and western blot. Protein expression of SMA and E-cadherin were detected by immunofluorescence analysis and western blot.

Results: FTY720 significantly attenuated the rise in blood pressure, proteinuria, serum creatinine, urine nitrogen and NAG in SNX(P<0.01). Treatment with FTY720 was found to reduce the numbers of perihilar whole white blood cell and Lympocyte (P<0.01). PAS and masson staining of the renal tissues revealed that there appeared severe tubulointerstitial inflammation and fibrosis in SNX, but the lesions were attenuated mostly in FTY720-treated group (P<0.01). Tubulointerstitial infiltrating inflammation cells expressing CD3, CD4, CD8, CD20, CD68, CD163 and CCR7 in SNX were attenuated mostly in FTY720-treated group (P<0.01). FTY720 decreased the expression of pro-inflammatory molecules(IL-6, TNF-α, MCP-1) and pro-fibrotic molecule (TGF-B1, P<0.01). The protein expression of E-cadherin was down-regulated, while the expression of α-SMA was up-regulated in kidneys of SNX rats where compared with those of sham surgery rats(P<0.01). FTY720 administration attenuated these abnormalities(P<0.01).

Conclusions: FTY720 ameliorates progression of tubulointerstitial inflammation in 5/6 Nprehrectomized rats by inhibiting tubulointerstitial inflammatory response and tubular epithelial-to-mesenchymal transition.
**Abstracts**

**MPS60**

**EFFECTS OF CYCLOSPORINE A AND RAPAMYCIN ON PRO-INFLAMMATORY CYTOKINE PRODUCTION BY DENDRITIC CELLS IN VITRO**

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**Introduction and Aims:** The most important antigen-presenting cells (APCs) are dendritic cells (DCs), which present antigen to T cells. The state of maturation of DCs is crucial for induction of a T-cell lymphocyte response. It was noted that immature DCs play an important role in peripheral tolerance, whereas mature DCs induce a complete immune response. Depending on the state of maturation DCs produce a variety of pro- and anti-inflammatory cytokines. We have studied the effect of immunosuppressive agents: rapamycin and cyclosporine A on immature DC: pro-inflammatory cytokine production and after LPS stimulation.

**Methods:** Human peripheral blood monocytes were induced by using cytokines: IL-4 and GM-CSF, in the direction of DCs in the presence of rapamycin (Rapa-DCs) and cyclosporine A (CsA-DCs) or without drugs (control). Then these immature DCs were stimulated with LPS to create mature DCs. The supernatants have been collected and measured for the cytokine levels.

**Results:** We have observed a diminished production of IL-6 by Rapa-DCs and CsA-DCs, compared to control. The lowest production of IL-6 was noted in an environment of rapamycin. LPS-activated DCs also produced less IL-6, when these cells were differentiated in the presence of immunosuppressive agents. Production of IL-12 by immature DCs and LPS-activated DCs was notably undetectable in all culture conditions.

**Conclusions:** We have shown that the immunosuppressive agents: rapamycin and cyclosporine A change the dendritic cells pro-inflammatory cytokine production.

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**MP362**

**EXPRESSION AND ROLE OF CEBP SUBTYPES IN CHRONIC KIDNEY DISEASE**

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**Introduction and Aims:** The effect of nuclear factors in renal diseases is clearly unknown. In this research we studied the expression and role of CEBP subtypes in chronic kidney disease and tried to find a new target to inhibit or slow the progression of chronic renal injury.

**Methods:** Animal models of adriamycin nephropathy (ADR) and the unilateral ureteral obstruction (UUO) nephropathy were established. Tumor necrosis factor (TNF-α) and interleukin-1β (IL-1β) was used to stimulate the NRK-49F cells with different concentrations. Western blot assay and immunohistochemistry were used to detect CEBPs subtypes (CEBP-β, CEBP-δ, CEBP-γ, CHOP). In this model, we analyzed the immune cell infiltrate and the expression of CEBPs in the kidney tissue.

**Results:** Phosphorylation of CEBP-β was increased in the renal glomerular and interstitial cell nuclei in ADR nephropathy model. Comparing with the control, the level of CEBP-β is the same in 4 weeks and 8 weeks after ADR and the level of p-CEBP-β was increased (p<0.05). Comparing with the control, the level of CEBP-δ is the same on day 2, 5, 9 and 14 after UUO, on day 9 and 14 after UUO, the phosphorylation and expression of CEBP-δ was increased by 3.3 fold and 2.4 fold respectively. The level of CEBP-γ & CHOP in 4 weeks and 8 weeks after ADR was more than in the normal control group (p<0.05). Comparing with the control, on day 2 after UUO, the level of CEBP-δ immediately increased by 2.1-fold; on day 14 after UUO, the expression of CHOP was increased by 2.3 fold and researched to the peak. We also found the level of CEBP-β in NRK cells stimulated by TNF-α & IL-1β with different concentrations showed no significant difference comparing with the control; however, after treatment with 10ng/ml and 20ng/ml IL-1β for 24 hours, the phosphorylation of CEBP-β was increased by 1.9-fold and 6.1 fold, in TNF-α group, it was increased by 2.6 fold and 5.2 fold. The level of CEBP-δ showed no significant difference with different concentrations of IL-1β in TNF-α group, after treatment with 10ng/ml & 20ng/ml TNF-α for 24 hours, comparing with the control, it was increased by 1.3 fold and 1.5 fold. After treatment with 10ng/ml IL-1β and TNF-α respectively, the level of CHOP in NRK cells was increased by 2.3 fold and 9.9-fold.

**Conclusions:** (1) In the ADR and UUO nephropathy model, the expression of CEBP-β did not change. With the aggravating kidney injury, the expression of phosphorylation of CEBP-β & CEBP-δ & CHOP were increased. (2) Inflammatory factors could regulate the expression of CEBP-β, CEBP-δ & CHOP. Guess that inflammatory factors may damage the kidney through activating these nuclear factors. (3) The blockade of CEBP-β/CEBP-δ/CHOP transcription factor activation may relieve renal inflammation.

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**MP363**

**APOLIPOPROTEIN A-II AMYLOIDOSIS (ApоСаЬII) IS ASSOCIATED WITH KIDNEY AGING AND INCREASED EXPRESSION OF INFLAMMASOME RELATED MOLECULES IN CD-1 MICE**

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**Introduction and Aims:** Human APOaII is an autosomal dominant inherited form of systemic amyloidosis caused by mutation of the ApоСаЬII gene and characterized by amyloid deposits in the kidney and heart. The occurrence of amyloid deposits in the kidney is also a well-known age-related phenomenon. However the mechanisms involved in kidney damage in ApоСаЬII and senile amyloidosis have not been yet elucidated. It is known that amyloid-β can activate inflammasome, signaling platform which integrates various danger signals and regulates the secretion of pro-inflammatory cytokines. The role of inflammasome is also emerging in kidney disease. We have characterized a mouse model of spontaneous senile systemic amyloidosis that exhibits ApоСаЬII amyloid deposits. Aims: to evaluate the association between ApоСаЬII amyloidosis, age-related alterations in the kidney and the possible mechanisms involved in the kidney damage.

**Methods:** 50 CD-1 mice, which develop spontaneous senile systemic amyloidosis with kidney involvement, were followed up to 17 months of age. The presence of proteinuria was assessed during the follow up by urinary Albumin to Creatinine Ratio (ACR) ELISA assay. Kidneys were collected at different ages to evaluate morphology and histology, to identify the amyloid deposits and for molecular studies.

**Results:** Red Congo staining revealed significant and progressive kidney amyloid deposition in both interstitium and glomeruli starting from 14 months of age. Amyloid

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**MP361**

**THE ROLE OF ADIPONECIN IN ACUTE KIDNEY INJURY**

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**Introduction and Aims:** Acute kidney injury (AKI) can be generated by several causes and it is associated to an inflammatory response that progress to renal failure and may lead to chronic kidney disease. Adiponectin is a protein expressed by adipocytes, which is involved in insulin sensitizing and preventing atherosclerosis. Recently, it was described an anti-inflammatory role for this protein, by decreasing cytokines such as TNF and IL-6. Proximal tubular cells were shown to express functional adiponectin receptors and adiponectin is detectable in urine. These data suggest that adiponectin plays a role in the maintenance of homeostasis in several injuries. Our objective was to investigate whether adiponectin is involved in acute kidney injury.

**Methods:** We used adiponectin knockout ADIPO-KO mice and C57Bl6 as control and we induced AKI by two protocols: bilateral ischemia-reperfusion (IR) by inducing ischemia for 45 min and 24h of reperfusion and sepsis by cecal ligation and puncture. We also analyzed the creatinine and urea levels in the serum in both model. We also analyzed the profile of pro-inflammatory cytokines by quantitative PCR and CBA. These cytokines were increased in ADIPO-KO group. In order to further understand the involvement of adiponectin in renal injury, we evaluated the activation of mTOR pathway, as it is a cell signaling associated to metabolism and also immune responses. We noticed different patterns of activation when comparing ADIPO-KO and C57Bl6, indicating that this pathway may be involved in adiponectin protection during AKI.

**Conclusions:** These results suggest that adiponectin is involved in AKI by regulating inflammatory response through mTOR pathway.
deposition was accompanied by increased values of ACR (p<0.05 14 vs 10 months old mice). Furthermore, AFOG staining revealed significant tubulointerstitial renal fibrosis and glomerular sclerosis. While the morphological and functional renal alterations were not present or they were mild in mice younger than 14 months, they were mainly represented at 17 months of age. At 17 months of age kidney PAS staining showed also significant interstitial inflammatory infiltrate. qRT-PCR showed that expression of caspase-1 mRNA, a key component of inflammasomes activation, and IL-1β mRNA, the inflammatory cytokine cleaved in the active form by the inflammasome complex, were significantly increased in the kidneys of mice of 14-17 months of age compared to mice of 10-11 months of age (p<0.001).

Conclusions: Our study shows that kidney amyloid deposition is associated with renal functional and morphological alterations and it is likely associated with inflammasome activation in aging CD1 mice with ApoAI systemic amyloidosis.

DISTINCT IMMUNOLOGIC EFFECTS OF INDIVIDUAL I.V. IRON FORMULATIONS ON MONOCYTES

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Introduction and Aims: Iron deficiency is a common contributor to anemia in patients with chronic kidney disease (CKD). While treatment of iron-deficiency anemia with intravenous iron can improve quality of life, long-term i.v. iron therapy may induce oxidative stress and inflammation. Different i.v. iron formulations exist, which may exert distinct immunomodulatory effects. Monocytes are pivotal players in immune response, inflammation and activation of apoptotic pathways. We conducted a pilot study to examine the possible role of the immune-mediated and inflammatory mechanisms in the pathogenesis of CRS1. The main objective was to analyze in vitro that plasma from patients with CRS1 was able to trigger a response in renal tubular cells (RTCs).

Methods: We enrolled 29 patients with Heart Failure (HF) (age 73.6±9.5yrs), 11 patients with CRS1 (74.0±13.1yrs) and 15 healthy controls (CTR 62±6yrs). Plasma from different groups were incubated with RTCs for 24h and the inflammatory cytokines (sICAM, RANTES (Regulated on Activation Normal T cell Expressed and Secreted) in supernatants were performed by ELISA.

Results: RTGs treated with CRS1 plasma showed higher DNA ladder formations, suggesting presence of apoptotic events. Indeed, a quantitative analysis of apoptosis using AnnexinV/Propidium Iodide (PI) showed significantly higher apoptosis rates in CRS1 compare with CTR (both p<.005). However, no significant difference was found between supernatant TNF-α and sICAM levels among these 2 groups. Furthermore, in CRS1 patients IL-6, IL-18, NGAL, RANTES levels in supernatant were significantly higher correlated with serum albumin and pressure changes (Rs<.005) and negatively correlated with GFR (Rs-.49, p=.005).

Conclusions: Thus, the anti-HSP-70 levels (as protective factors) were increased in active CGN, especially in pts with NS, in response to inflammatory kidney damage. Conversely, decreased levels of anti-HSP-70 can indicate on kidney self-defence system insufficiency in progressive CGN.

CARDIORENAL SYNDROME TYPE 1: INFLAMMATORY EFFECTS ON RENAL TUBULAR CELLS

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Introduction and Aims: Heat performance and kidney function are closely interconnected and communication between these organs occurs through a variety of pathways. This special connection is of particular importance for patient wellbeing. Up to now, the toxicity of different iron formulations on monocytes subhats has not been assessed. Therefore, we investigated the impact of iron isomaltoside, ferric saccharate, and iron sucrose on monocyte subsets, i.e. CD14+CD16-, CD14+CD16+ and CD14-CD16- of monocytes. The production of proatherogenic markers (C5R5, CX3R1) via flow cytometry. Next we analyzed monocyte ability to induce proliferation of CD4+ T cells and subset-specific capacity to phagocytze and to produce reactive oxygen species (ROS). Finally we quantified the production of the proinflammatory cytokines (IL-1β, IL-6, TNF-α), and expression of proatherogenic markers (C5R5, CX3R1) via flow cytometry. Our findings demonstrate immunologic differences between individual i.v. iron formulations, monocytes subsets, and different iron formulations on monocytes subsets has not been assessed. Additionally, differentiation of monocytes from hematopoietic stem cells of different groups were incubated with RTCs for 24h and, subsequently, cell death was assessed using AnnexinV/Propidium Iodide (PI) showed significantly higher apoptosis rates in CRS1 compare with HF and CTR (both p<.005). However, no significant difference was found between supernatant TNF-α and sICAM levels among these 2 groups. Furthermore, in CRS1 patients IL-6, IL-18, NGAL, RANTES levels in supernatant were significantly higher correlated with serum albumin and pressure changes (Rs<.005) and negatively correlated with GFR (Rs-.49, p=.005).

Conclusions: In conclusion, the inflammatory pathway could be proved an important contribution of the development of CRS1 and we can speculate that cytokines or other mediators may play a role in the mechanism of CRS1 and may be essential for the damage of distant organs.
Introduction and Aims: Profibrotic and inflammatory changes within the kidney are well known in renal disease; much less data are available for normal aging processes. Using a well-defined rat model we were interested to analyze not only functional and histomorphological changes in aging kidneys, but also age-dependent regulation of the TGF system (as key player of fibrosis), of Toll-like receptors (TLR, as part of the innate immune system) and of chemokines (as prototypic signaling molecules).

Methods: 3 and 24 months old male Sprague Dawley rats were investigated (n=8 per group). At the time of sacrifice blood pressure was measured and overnight urine and serum was collected. To analyze age-specific histological changes Sirius red, PAS, Ki67, αSMA, CD68, CD3 and Desmin staining were performed. Using quantitative PCR the gene expression of TGFβetas, Smads, CCL2, CCL5, TLRs, Desmin, Nephrin and Podocin was evaluated. Complementary electronmicroscopy from kidney specimens, NMR spectroscopy from urine and magnetic resonance imaging from quadriceps muscles a higher lipid to muscle ratio could be detected in older rats. By magnetic resonance imaging from quadriceps muscles a higher lipid to muscle ratio could be detected in older rats.

Results: Comparing rats 3 months of age with 24 months old rats no changes in blood pressure and heart rate could be detected. Old rats showed significantly increased proteinuria. NMR spectroscopy from urine showed significant differences in betaine, taurine and hippuric acid, e.g.. Computer-aided morphometry of glomeruli demonstrated significantly increased accumulation of matrix, collagen and desmin, a marker for podocyte damage in old rat kidneys. Ki 67 staining revealed that cell proliferation was significantly reduced in older rat kidneys. Electron microscopy confirmed structural changes of glomerular cells, membranes and matrix. TGFβetas1, TGFβetas2, Smad2, CCL5 and several TLRs showed a significant higher mRNA expression in 24 months old rat kidneys. By immunohistochemistry CCL5 expression could be localized mainly in tubular cells. Corresponded there was an influx of T cells but not CD68 positive macrophages into the aging rat kidneys. By magnetic resonance imaging from quadriceps muscles a higher lipid to muscle ratio could be detected in older rats.

Conclusions: Healthy 24 months old rat kidneys show significant structural changes compared to younger kidneys. Locally expressed markers of fibrosis and immune activation were associated with kidney aging.

Introduction and Aims: Monocyte dysfunction, characterized by higher production of proinflammatory cytokines and increased cell counts of proinflammatory CD14++CD16+ and CD14+CD16++ monocytes, substantially contributes to morbidity and mortality in patients with chronic kidney disease. The underlying pathophysiological pathways that induce monocyte dysfunction are not understood so far. Recently, the phosphaturic hormone FGF23 was characterized as a potent immune modulator. Therefore we now aimed to elucidate the impact of FGF23 on monocyte subset biology.

Methods: Human monocytes were stimulated with increasing FGF23 concentrations (0; 0,25; 0,5; 1; 10; 50 ng/ml) for 5 hours and the expression of pro-atherogenic (CCR5, CX3CR1) and proinflammatory markers (ROS, CD86) was determined flow-cytometrically. Furthermore, monocytic capacity to phagocyte and to induce T-cell proliferation was measured after FGF23 stimulation was analyzed flow-cytometrically.

Results: FGF23 stimulation neither increased expression of activation markers (CD86) nor of chemokine receptors (CCR5, CX3CR1). FGF23 stimulated monocytes showed no functional impairment (phagocytosis, induction of T cell proliferation and ROS production) compared to control stimulated monocytes. Differentiation of proinflammatory CD14++CD16+ monocytes from CD34+ hematopoetic stem cells after FGF23 stimulation was analyzed flow-cytometrically.

Conclusions: In our study, human monocytes are not activated after FGF23 stimulation. As these findings are in contrast to recent reports from other groups, further experimental and clinical studies are needed which should analyze the impact of long term FGF23 stimulation on differentiation of distinct monocyte subsets.

Introduction and Aims: Erdheim-Chester disease is a rare form of histiocytosis characterized by xanthomatosis multiorgan tissue infiltration by histiocytes CD68+ / CD1. Bone involvement is the most common symptom. Half of the patients also have exophtalmos, pulmonary and retroperitoneal fibrosis, diabetes insipidus and involvement of the central nervous cardiovascular and renal system.

Methods: A 77 years man came to our observation for 'increase of renal function index (creatinine 2.8mg/dl), marked anemia and hypertension. MRI of the upper abdomen documented the presence of pathological tissue infiltrating the renal sinus fat up to the region of the joint pielo ureter, surrounding the renal parenchyma bilaterally and pelvis sleeve. The x-ray of the long bones showed the presence of medullary osteosclerosis. The ecochardiographic examination documented the presence of abundant pericardial effusion (570cc), a cloth epicardial and masses atrial on the interatrial septum. After performing brain MRI was diagnosed with Erdheim-Chester syndrome with renal, cardiac, bone long involvement, without pulmonary and cerebral localization. Was initiated therapy with interferon-α before, with clinical worsening general and with interleukin-1 receptor antagonist after.

Results: From January 2010 to December 2010, the patient was treated with interferon-α (1 vial per week), with worsening renal function (creatinine 3.8mg/ dl), of framework failure (increased pericardial flap, thickening of the epicardial cloth, increase atrial masses ) [Figure 1] and with the onset of muscle aches, lack of appetite and mood disorders. Was discontinued therapy with interferon-α and started therapy with interleukin-1 receptor antagonist (one ampoule every other day) with improvement in renal function (creatinine 2.7mg/ml), the picture heart (pericardial effusion 150cc) and conditions mental and general physical fitness.

Conclusions: At present there is no specific therapy for Erdheim-Chester syndrome, many authors suggest as first line treatment interferon-α, which in our case has yielded poor results. Among the future perspectives may play an important role in receptor antagonist interleukin-1.
study aimed to investigate possible mechanisms that underlie renal damage following heart dysfunction using a rat myocardial infarction model, focusing on inflammatory pathway.

Methods: Rats were randomized into four groups: normal, volume depletion, sham operation, and myocardial infarction (MI). MI was induced by left coronary artery ligation and volume depletion model was produced by low salt diet and furosemide injection. Biochemical, histological and flow cytometric analyses were performed at 3 days, 2, 4 and 8 weeks after MI.

Results: On day 3 of MI, the development of subclinical acute kidney injury was identified through significantly increased serum and urine NGAL level. We also detected the increase of activated monocytes (CCR2+ ED-1+) in peripheral blood, along with the infiltration of ED-1+ macrophages and the increment of nuclear p65 in the kidney of MI rats, suggesting the activation of NF-κB mediated inflammation in the development of type 1 cardiorenal syndrome. Inflammatory cytokines, IL-6 and TNF-α mRNA expression as well as microvascular endothelial permeability significantly increased in the kidneys of MI rats. At 4, 8 wks after MI, tubular cell apoptosis, ED-1+ macrophage infiltration and interstitial fibrosis were observed in MI rats and these chronic changes were significantly mitigated by systemic monocyte/macrophage depletion using liposome clodronate.

Conclusions: This study identified possible important role of inflammatory response as a mediator of heart-kidney crosstalk in cardiorenal syndrome. Further studies elucidating underlying pathophysiology are warranted to develop strategies to interrupt the harmful interaction between these organs and ultimately to improve patient’s outcome.
HEMODIALYSIS TO ONLINE-HEMODIAFILTRATION CHANGE IS ASSOCIATED TO A DECREASE IN CIRCULATING CELL-FREE DNA LEVELS

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Introduction and Aims: Hemodialysis (HD) patients are characterized by the presence of chronic inflammation, which contributes to the high morbidity and mortality of these patients. Recently, it was demonstrated that HD patients present increased levels of cell-free circulating DNA, probably due to the release of DNA from cellular necrosis and apoptosis. As cell-free DNA could lead to inflammation, and online-hemodiafiltration (OL-HDF) technique was proposed to associate a reduction in inflammation, we aimed to evaluate the effect of HD to OL-HDF change in cell-free circulating DNA serum levels.

Methods: In this longitudinal study, 59 patients changed from HD to OL-HDF were evaluated before, and ten months after they changed to OL-HDF. The levels of circulating free-cell DNA were evaluated directly in serum samples, as recently described by Goldstein et al. (Ann Clin Biochem 2009; 46:488-94). Moreover, hematological and dialysis adequacy data, iron metabolism and inflammatory markers were also evaluated.

Results: HD to OL-HDF change was associated to an improvement in dialysis adequacy, as showed by the significant increase in Kt/Ve and URR. Concerning to hematological data, no differences were found in hemoglobin levels; however, a significant decrease in MCV, RPI, reticulocyte and platelet counts, and a significant increase in MCHC were found. Significant changes in iron metabolism were also observed, namely, an increase in iron, sTfR, and transferrin saturation, and a decrease in transferrin levels. After change from HD to OL-HDF our patients presented a significant decrease in circulating cell-free DNA levels [mean (SD), 8459.6 (1502.6)mg/mL; mean (SD), 7983.4 (1863.3)mg/mL, p=0.006]. In OL-HDF patients, significant correlations were found between cell-free DNA serum levels and CRP (r=0.361, p=0.002), iron (r=−0.243, p=0.04), sTfR (r=0.260; p=0.027) and rhEPO doses (r=0.280; p=0.017).

Conclusions: Our data showed that HD to OL-HDF change is associated to a decreased in cell-free DNA levels, to an improvement in erythropoiesis, resulting from increased iron availability, and in dialysis adequacy, when compared with HD procedure. Moreover, OL-HDF patients present correlations between circulating cell-free DNA levels with inflammation and iron metabolic disturbances, as well as with rhEPO doses, suggesting that a decreased in cell-free DNA could be related to a decreased in cellular necrosis and apoptosis, and in inflammation in OL-HDF patients.

SENSITIVITY OF BLOOD VOLUME MONITORING FOR FLUID STATUS ASSESSMENT

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Introduction and Aims: Blood volume monitoring (BVM) is traditionally used to assess the degree of intradialytic vascular refilling. In recent years however, BVM has also come into focus for assessing the fluid status of dialysis patients. It has been shown previously that mortality increases significantly beyond a pre-dialysis fluid overload level >2.5L. It was the aim of this study to evaluate how useful BVM is for the assessment of fluid overload.

Methods: Relative blood volume (RBV) and pre-dialysis fluid overload (PO) were collected in 55 chronic HD patients in more than 300 treatments, using the Fresenius Blood Volume Monitor and the Fresenius Body Composition Monitor (BCM), respectively. Receiver-Operator Characteristic (ROC) analysis was performed for different fluid overload cutoff levels, using the slope of the RBV drop normalized by ultrafiltration volume as continuous variable. The area under the curve (AUC) of the ROC curves was used to assess sensitivity of blood volume monitoring for fluid overload classification. High AUC values up to 1.0 indicate good sensitivity; values close to 0.5 indicate random classification or no sensitivity.

Results: The degree of RBV drop was related with the pre-dialysis fluid overload level: Patients with high fluid overload >5L had almost no RBV drop during the treatment, while patients who became dehydrated in the course of the 4h treatment presented a strong RBV drop [Figure 1] ROC curves for three different FO cut-off levels (2, 3 and 4L) demonstrate best performance for high fluid overload [Figure 2]. The highest AUC values were achieved at FO levels greater than 4L, indicating better performance of the Slope4h marker in detecting high fluid overload; lowest performance was found in medium FO ranges.

Conclusions: Blood or plasma volume monitoring is well suited to detect high pre-dialysis fluid overload, less sensitive in low hydration status, and rather insensitive in a range between 1 and 3 litres.
FLUID BALANCE EVALUATION IN A LARGE POPULATION OF HEMODIALYZED PATIENTS

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Introduction and Aims: Despite continuous improvement in quality of dialysis therapy, cardiovascular diseases remain the first cause of death in dialysis patients. Avoiding chronic fluid overload may reduce secondary hypertension and left ventricular hypertrophy. Clinical fluid management is facilitated by a device that allows the objective measurement of patients’ hydration state via multi-frequency bioimpedance spectroscopy (Body Composition Monitor, BCM) in a rapid and non-invasive way. Implementation of a Fluid Management Program in all dialysis units of NephroCare Italy, reaching a target of 60% of patients with a controlled hydration status (relative overhydration as percentage of extracellular water (ROH) <15%). Train physician and nurse trainers on BCM use and data evaluation.

Methods: In order to properly implement a Fluid Management Program in all the dialysis units of NephroCare Italy, a training program on BCM use for all physician and nurse trainers was performed. This addressed how to use the BCM correctly which requires patient’s height and weight control, patient in supine position for 2 minutes with limbs at 45 degrees from the trunk in absence of contact with metal objects and correct position of the electrodes, the correct way to evaluate results and how to organize a fluid management program. In a period of one year, all patients underwent BCM analysis every month, monitoring their hydration state to obtain an average weekly ROH of < 15%.

Results: Implementation of a Fluid Management Program using the BCM resulted in an increment of patients with controlled hydration state from 37% in February 2012 to 55% in February 2013. The BCM programs have demonstrated the importance of efficient training to obtain correct position of the electrodes, the correct way to evaluate results and how to organize a fluid management program. In a period of one year, all patients underwent BCM analysis every month, monitoring their hydration state to obtain an average weekly ROH of < 15%.

Conclusions: Continuous monitoring of patients’ hydration state with proper training in use of the BCM and subsequent adaptation of dialysis prescription helps achieve dry weight.

RELIABLE ESTIMATION OF DRY WEIGHT IN HAEMODIALYSIS PATIENTS BY THE BIOELECTRICAL IMPEDANCE ANALYSIS

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Introduction and Aims: There were significant differences in the slopes of the ultrafiltration (UF) amount removed during haemodialysis (HD) sessions versus the percentage change in the extracellular fluid/total body water ratio for the right lower extremity (ECF/TBWright leg) plot in normohydrated (NH) and overhydrated states. The purpose of this study was to develop and validate a method for predicting dry weight (DW) using these results.

Methods: It was hypothesized that for patients to become NH, the slope of the UF amount versus the percentage changes in ECF/TBWright leg should be the same as that of NH patients and a method for predicting DW was developed. To validate the accuracy of this method, the ECF/TBWright leg was measured by eight-point tactile-electrode bioelectrical impedance analysis before and after HD in 17 newly enrolled NH patients. Using the current DW (cDW) of subjects as a reference, we compared the accuracies of pdDW1 (our devised method) and pdDW2 (the normovolaemia/hypervolaemia slope method).

Results: The mean pdDW, pDW1 and pDW2 values were 56.8 ± 7.9, 56.4 ± 7.7 and 56.3 ± 8.0 kg, respectively. No significant differences existed between cDW, pDW1 and pDW2. pDW1 had a lower root mean square error than pDW2 (1.12 ± 8.0 kg, respectively. No significant differences existed between cDW, pDW1 and pDW2 and pDW2. pDW1 had a lower root mean square error than pDW2 (1.12 ± 8.0 kg). The Bland-Altman plot, differences between pdDW1 and cDW was closer to zero than between pdDW2 and cDW.

Conclusions: A new method was developed of predicting the DW using the relationship between the UF amount and the percentage change in the ECF/TBW ratio of the lower extremities after HD. The devised method appears to be as accurate as the normovolaemia/hypervolaemia slope method.

SALT AND WATER BALANCE IN HEMODIALYSIS

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Introduction and Aims: Most unwanted side effects of hemodialysis therapy are caused by shifts of water and sodium. Balance of salt and water in maintenance hemodialysis therapy is influenced by ingestion of salt and water by the patient as well as by dialysis induced ultrafiltration and changes in plasma sodium concentration. Dialysis induced increase of sodium concentration may induce thirst whereas its decrease may induce symptoms of dysequilibrium syndrome.

Methods: In order to investigate patients response to constant sodium concentration in the dialyzing fluid 290 patients have been included into the study. Dialysis was performed three times per week for 4-6 hrs, Qb 280 ml/min. Sodium concentration in dialyzing fluid was always 138 mmol/l using the same proportioning system and dialyzer (A 2008, A 4008, A 5008, Fx60, Fresenius Medical Care). Patients were treated in one center up to 20 years by the same doctors. Body weight, ultrafiltrate, pre-dialysis and post-dialysis body weights were recorded.
plasma sodium concentration were collected every three months and measured using the same measuring device. There were no injections of sodium chloride during treatment. Sodium balance was calculated using a kinetic model.

**Results:** Mean inter-dialysis increase of body weight was 2.5 kg which is removed by ultrafiltration. Pre-post dialysis sodium concentration is $\pm 0.2$ mmol/l (range: -5.8 +8 mmol/l). Sodium balance by convection (93.8%) is always negative: mean 22.5 g NaCl/60 kg (range: 4-34 g NaCl/60 kg). Diffusive sodium balance (61.6%) may be positive or negative $\pm 4$ g NaCl/60 kg (range: $\pm 12$ g NaCl/60 kg). During the first two years of regular dialysis therapy most patients change their diffusive sodium balance from slightly negative to slightly positive by about 15 mmol corresponding to 1.5 g NaCl.

**Conclusions:** Patients having high convective sodium removal during dialysis exhibit positive diffusive sodium balance. By drinking and eating salt and water most patients accommodate to the sodium concentration of the dialyzing fluid to make dialysis more comfortable and less affected with unwanted side effects.

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**Abstracts**

**WHAT VOLUME EXCESS, TOTAL BODY WATER (TBW), EXTRACELLULAR BODY WATER (ECW) AND INTRACELLULAR BODY WATER (ICW) DEPEND ON IN CRITICALLY ILL PATIENTS?**

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**Introduction and Aims:** Pathological distribution of body water is a serious problem in critically ill patients. Several have underlined the correlation between severity of infection and body water content. Unfortunately, none of them have presented the aim of the present study was to analyse the correlation between volume excess (VE), total body water (TBW), extracellular body water (ECW), intracellular body water (ICW) and plasma interleukin 1 (IL1β), 6, 10, 17α, tumour necrosis factor (TNFα), vascular endothelial growth factor (VEGF), histamine and E-selectin in adult critically ill patients.

**Methods:** Sepsi or septic shock patients treated for acute renal insufficiency were enrolled. All parameters were measured at three consecutive days: the day of admission into Intensive Care Unit (ICU), 24 and 48 hours after the admission into ICU. According to kind of treatment, patients were divided into: treated with continuous venous-fumose infusion (fenoside group) and treated with continuous venous-venous haemofiltration (CVVHF) group. VE, TBW, ECW and ICW were measured using whole body bioimpedance.

**Results:** Forty patients – 25 male and 15 female, aged 53 ± 15 were studied. In all participants, TBW and ECW correlated with VEGF ($p < 0.001$, $r = 0.53$ and $p < 0.001$, $r = 0.51$, respectively). Moreover, TBW moderately correlated with interleukin-6 ($p < 0.001$, $r = 0.42$) and ECW moderately correlated with interleukin-1β, interleukin-6 and histamine ($p < 0.001$, $r = 0.44$; $p < 0.001$, $r = 0.48$ and $p < 0.001$, $r = 0.41$, respectively). In fenoside group, VE strongly correlated with interleukin-17α ($p < 0.001$, $r = 0.43$). TBW strongly correlated with VEGF ($p < 0.001$, $r = 0.53$) and moderately with interleukin-6 ($p < 0.001$, $r = 0.41$), ECW correlated with VEGF and interleukin-17α ($p < 0.001$, $r = 0.46$ and $p < 0.001$, $r = 0.42$, respectively) and ICW strongly correlated with VEGF ($p < 0.001$, $r = 0.57$). In CVVHF group, VE correlated with TNFα ($p < 0.001$, $r = 0.45$), TBW correlated with VEGF ($p < 0.001$, $r = 0.41$) and ECW correlated with VEGF and TNFα ($p < 0.001$, $r = 0.47$ and $p < 0.001$, $r = 0.43$, respectively).

**Conclusions:** 1. TBW strongly depend on plasma VEGF concentration. 2. ECW depend on plasma VEGF and proinflammatory cytokine concentrations. 3. ICW depend on plasma VEGF concentration, particularly in patients treated without artificial renal replacement therapy.

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**FLUID MANAGEMENT IN HEMODIALYSIS: CONVENTIONAL CLINICAL MANAGEMENT VS. BODY COMPOSITION MONITORING (BCM) SUPPORTED MANAGEMENT OF OVERHYDRATED PATIENTS**

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**Introduction and Aims:** Patients who undergo hemodialysis treatment are frequently and inconspicuously fluid overloaded. Chronic fluid retention and overhydration (OH) are associated with left ventricular hypertrophy and according to recent publications a risk factor for morbidity and mortality. Our aim was to compare the management of the hydration status of dialysis patients by assessing their dry weight with bio-impedence spectroscopy (Body Composition Monitor - BCM, Fresenius - Bad Homburg) versus the conventional clinical methods over one year.

**Methods:** Multicenter prospective controlled trial, including 189 incident and prevalent patients on online haemodialfiltration (online-HDF) recruited in 23 portuguese dialysis units. Inclusion criteria were relative predialytic overhydration (OH, relative OH [%] = OH [L] / extracellular water [L]/100) of >15% as assessed by the BCM, and online-HDF treatment three times per week, at least 4 hours per session. Once per month the hydration status was assessed by the BCM in all patients. The participants were allocated in an open-access BCM group (n=101; 53.4%) in which dry weight is tentatively prescribed according to BCM results and a blinded to BCM results group (n=88; 46.7%) in which nephrologists continue to prescribe dry weight according to their clinical judgment. In addition pre- and post-dialysis blood pressure, intradialytic hypotension, interdialytic weight gain, morbidity and mortality, were assessed.

**Results:** At baseline 92 patients (91.1%) of the open access and 79 patients (89.8%) of the blinded group had OH > 2.5L. At study end the rate of patients with OH > 2.5L was reduced in the open access group to 52.5% and in the blinded group to 65.9%. Roughly, patients of both groups started with a similar OH of 3.81 at baseline. After 1 year, a significant reduction of OH was achieved in both groups: 2.92 ± 1.47 L in the open group and 3.36 ± 1.75 L in the blinded group. There was a trend for a difference in OH reduction between groups after 12 months (p=0.06). Relative OH decreased from 20.65 ± 6.48% to 15.40 ± 6.36% in the blinded group from 20.73 ± 5.73% to 16.26 ± 8.48%. Both groups started with a similar pre- and post-dialytic systolic and diastolic blood pressure, and in both cohorts the values could be reduced at month 12. In diabetic systolic blood pressure, the mean systolic blood pressure was reduced from 144.8 ± 24.1 mmHg to 134.6 ± 27.3 mmHg in the blinded group: from 145.9 ± 26.8 mmHg to 136.5 ± 24.7 mmHg. The hospitalization and survival rate was not different between the two groups after 1 year, or when comparing patients with persistent overhydration vs corrected fluid status.

**Conclusions:** In this study it could be shown that hydration status can be improved by tight control. The results suggest that the BCM is a helpful tool to support fluid management of HD patients. We could not find a correlation between blood pressure and hydration status, indicating that blood pressure is not a sound indicator of the hydration status.

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**PRELIMINARY RESULTS OF HIGH-EFFICIENCY ON-LINE MIXED HEMODIAFILTRATION IN A DIALYSIS CENTRE NETWORK IN ITALY (Nephrocare)**

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**Introduction and Aims:** Recent large trials have strongly suggested that survival of chronic dialysis patients may be improved on post-dilution haemodiafiltration (post-HDF) provided that large amount of volume exchange is achieved. However, post-HDF may be of difficult application in a cohort of "critical" patients due to haemoconcentration, low blood flow rate, central catheter use or, in general, scarce plasma refilling. On-line mixed HDF is a new HDF technique in which substitution fluid is infused simultaneously in the inlet and outlet of the dialyzer at the site and partition modulated by a feedback system sensitive to the patient and operating conditions (flow rates, haemoconcentration, membrane surface and permeability).

**Methods:** Mixed HDF was recently implemented in several facilities of an international Dialysis Centre Network. Pilot studies (Pedrini et al. Kidney Int. 2000-2003-2006), have shown that this technique may achieve high convective removal of small and middle molecular uremic toxins while avoiding the drawbacks of the more traditional post- and pre-HDF. Preliminary results of its application in 125 dialysis patients of 13 Centres, are presented here. Efficiency of the technique was evaluated for small toxins, with urea Kt/V calculated from on-line ionis dialysance, effective treatment time, and urea volume measured with bio-impedence method, and for middle molecules toxins (beta2-microglobulin level and reduction rates, B2-M RR).

**Results:** Mean age of the patients was 63.1 ± 13.2 years, (range 26-87), mean dry body weight 74.8 ± 14.4 kg. Ten out of 125 patients had central venous catheter. The remaining had native or prosthetic A-V fistula. High-flux heimoneylizers 1.8-2.1 sqm were used. Results of Mixed HDF, as a mean of a 3-month period compared with those previously obtained on post-HDF are shown. Session time was 239 ± 7 ± 234 ± 14 min,P=0.04, Haematocrit 36.7 ± 4.2 vs 35.4 ± 4%, P=0.02.

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**Comparison of 57 available paired data. Multiple linear regression, adjusted for age,sex, body weight, haematocrit and time that showed the main predictors of lower basal P levels and B2-M RR were blood flow and amount of infusion.**
Conclusions: These promising preliminary results indicate that Mixed HDF may be the most efficient and versatile technique to achieve the highest removal of toxic uremic substances. The feedback system working in Mixed HDF adapts infusion flow and filtration pressure to the patient- and operating conditions, thus allowing to perform HDF and extend its benefits also to critical patients who cannot be treated on post-HDF for different reasons. More extensive application of Mixed HDF will probably provide new insight in the potential of this technique.

Methods: Since October 2010 we routinely use the combination of Evodial® (Gambro) with Citrasate® (a 0.80 mmol/L of citric acid dialysate, Advanced Renal Technologies Inc.) for critically ill patients with an increased bleeding risk and requiring HD. As an internal quality control, we conducted a retrospective analysis to assess efficacy of these HDF. Medical records and nursing plans of all HD performed at the Intensive Care Unit of Universitair Ziekenhuis Brussels between October 2010 and March 2012 were screened for type of dialyzer and dialysate, circuit coagulation, prescribed and effective treatment duration, processed blood volume, ultrafiltration rate and type of access.

Results: During the 18-month study period, a total of 316 treatments in 96 patients combining Evodial® and Citrasate® were performed. The scheduled treatment time was reached in 81.5% (95% CI 77.2% to 85.9%) of dialysis sessions and in 164/210 (78%) of treatments with a prescribed length of ≥240 minutes. Various degrees of circuit coagulation occurred in 171 out of 210 treatments (81.5%, 95% CI 77.2% to 85.9%) of treatments, requiring shortening of scheduled treatment time in 47/54 of cases by a median of 42 minutes (IQR 10 to 70 minutes). In 13/54 of treatments with coagulation the dialysis session had to be interrupted without possibility to reestablish blood of the extracorporeal circuit.

Conclusions: The combination of Evodial® and Citrasate® allows successful hemodialysis without systemic anticoagulation for treatment times of ≥240 minutes in about 80% of patients. In spite of the absence of systemic anticoagulation circuit clotting occurred in only 18% of treatments and had limited although statistically significant repercussions on treatment length and dialysis efficacy.

**Abstracts**

**MP381**

### A RETROSPECTIVE COHORT STUDY OF HEPARIN-FREE INTERMITTENT HEMODIALYSIS (HD) COMBINING EPD-COATED ANIST MEMBRANES (EVDIAL®) AND CITRATE-ENRICHED DIALYSATE (CITRASATE®) IN AN INTENSIVE CARE SETTING

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**Introduction and Aims:** Critically ill patients requiring renal replacement therapy for acute kidney injury are often at increased bleeding risk. This requires anticoagulation strategies which minimize bleeding risk while efficiently preventing clotting of the extracorporeal circuit during hemodialysis.

**Methods:** Since October 2010 we routinely use the combination of Evodial® (Gambro) with Citrasate® (a 0.80 mmol/L of citric acid dialysate, Advanced Renal Technologies Inc.) for critically ill patients with an increased bleeding risk and requiring HD. As an internal quality control, we conducted a retrospective analysis to assess efficacy of these HDF. Medical records and nursing plans of all HD performed at the Intensive Care Unit of Universitair Ziekenhuis Brussels between October 2010 and March 2012 were screened for type of dialyzer and dialysate, circuit coagulation, prescribed and effective treatment duration, processed blood volume, ultrafiltration rate and type of access.

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**Conclusions:** The combination of Evodial® and Citrasate® allows successful hemodialysis without systemic anticoagulation for treatment times of ≥240 minutes in about 80% of patients. In spite of the absence of systemic anticoagulation circuit clotting occurred in only 18% of treatments and had limited although statistically significant repercussions on treatment length and dialysis efficacy.

**MP382**

### DRY WEIGHT, SYSTOLIC BLOOD PRESSURE AND INTIMA-MEDIA THICKNESS PREDICT BRAIN NATRIURETIC PEPTIDE LEVELS IN HEMODIALYSIS PATIENTS

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**Introduction and Aims:** Type natriuretic peptide (BNP) is an emerging marker of cardiac distress in patients with volume overload. High BNP levels in hemodialysis (HD) patients are strongly correlated with development of pathological cardiovascular findings, including left ventricular hypertrophy, hypertension and increased end-diastolic volume, and with increased cardiovascular and overall mortality. Intima-media thickness (IMT) is a marker of vascular dysfunction well correlated with the cardiovascular risk. We supposed that BNP levels are dependent not only to the interdiabetic weight variation (Δ) but also to the vascular dysfunction. Aim: To determine the factors associated with high BNP in chronic HD patients.

**Methods:** 74 subjects were enrolled. Hematological and biochemical variables were obtained by a pre-HD blood draw. We defined Pre-HD BNP≥183 pg/mL as high BNP (were 183 is the median of BNP in our population). Δ weight was defined as [pre-HD weight - dry weight]/ dry weight. In all patients IMT of the common carotid artery was measured. Student t-test and chi-square test were used in this analysis.

**Results:** A total of 74 chronic HD patients were enrolled. The age was 63 ± 13 years, males 54%, BNP 183 pg/mL (range IQ 91-499 pg/mL), IMT 1.76 ± 0.39 mm. Δ weight (1%, OR 1.28, 95%CI 1.01-1.63; P<0.05), Systolic blood pressure (SBP) pre-HD (10mmHg, OR 1.28, 95%CI 1.01-1.61;P<0.05) and IMT (0.1mm, OR 1.22, 95% CI 1.05-1.43;P<0.01) were associated with high BNP pre-HD (AUC=0.73, P<0.001).

**Conclusions:** In chronic HD patients, BNP is influenced not only by the interdiabetic weight variation, but also by the vascular function.

**MP383**

### ON-LINE HEMODIAFILTRATION AND ESA RESISTANCE: ROLE OF HEPACTIN. RESULTS FROM THE REDERT STUDY

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Introduction and Aims: In hemodialytic (HD) patients, anaemia is associated with a reduced survival. Despite treatment with erythropoiesis-stimulating agents (ESAs), a vast majority of patients with chronic kidney disease (CKD) show resistance to this therapy. Anaemia is linked to inflammation and oxidant stress is associated to the uraemic syndrome; recent studies demonstrated that Hepcidin (Hep) may mediate ESAs resistance. High-efficiency on-line hemodiafiltration (OL-HDF) has been shown to improve anaemia and to reduce the need for ESAs in HD patients. This effect is associated with a reduced inflammatory state in these patients. The aim of this study was to investigate the effect of different dialytic techniques on ESAs resistance in chronic dialytic patients.

Methods: A single cross-over, prospective and randomized multicentre study (A-B or B-A) was designed. Forty (40) HD patients from six different dialysis units (male 65%, mean age 67.6 ± 14.7 years and mean dialytic age 48 ± 10 months) were enrolled. Patients were randomized to BHD with low flux polysulphone (PS) membrane group or OL-HDF group with high flux PS membranes and exchange volume > 20 litres. After six months patients were shifted in the other dialytic group for further six months. Clinical data, Hb, ESAs doses, inflammatory markers, b2-microglobulin (b2M) were recorded every two months. HEP was determined bimonthly by ELISA (DRG Instruments GmbH, Germany) and ERI was calculated as the weekly ESAs dose divided by kilograms of body weight divided by haemoglobin level.

Results: A significant reduction of ERI values in patients treated with OL-HDF after 4 months of treatment (from 6.6 ± 1.1 to 5.3 ± 0.86 UI set/kg/Hb) with significant positive correlation between Hep and ERI (r=0.52, p=0.001) were observed. b2M significantly decreased in OL-HDF group (from 42.8 ± 2.5 to 27.1 ± 1.7 mg/L; p<0.001).

Conclusions: A significant reduction of ERI values in patients treated with OL-HDF was observed suggesting a major efficacy of this dialytic technique in reduction of inflammatory status. Furthermore, the positive correlation between ERI and Hep supports a role for this peptide in the development of ESAs resistance in dialytic patients. Finally, the lower b2M in OL-HDF confirms the higher depurative effect of this technique with respect to mid-molecules.

MP385 HEMOCONTROL SYSTEM IN ON-LINE HEMODIAFILTRATION (OL-HDF): "THE SOCRA'THE STUDY" ON SODIUM BALANCE

Alessandro Surace1, Madalena Pieri1, Paolo Rovatti1, Denis Steckiophi2, Emanuele Mambelli3, Elena Mancini3 and Antonio Santoro3
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Introduction and Aims: The HemoControl biofeedback system (HC), which keeps the Blood Volume (BV) with an individualized trajectory, is a recognized strategy for reducing intradialysis hypotension. However, this system has always been used in conventional hemodialysis (HD) alone. The implementation of HC in OL-HDF could be of great clinical interest, considering the benefits of HC with those of the high-volume convective treatments. A crucial aspect for such a system is related to the sodium (Na+) balance.

Methods: A new Na+ model was developed, as compared with the previous one used in HD+HC, to take into account, apart from dialysis Na+, both the Na+ infused and that removed by convective transport. This model was tested in a prospective randomized cross-over pilot study (SOCRATH, NCT01582867). Six patients were treated on 2 different modalities, i.e. HD+HC and OL-HDF with HC (HDF+HC). Each phase consisted of 6 HD (or OL-HDF) treatments without HC followed by 12 treatments with HC. Each patient acted as his/her own control. Plasma Na+ concentrations (NaP, measured by ion selective sodium electrode), Na+ mass balance (NaMB estimated through the model and normalized to the total weight loss, NaMB/TWL), inter-dialytic weight gain (IDWG), blood pressures (BP), PV trends and reported thirst scores (TS, ranged from 5=never to 25=always thirsty) were collected. The HC prescription was the same in both the phases.

Results: The main results are summarized in Table 1: The convective volume achieved in HDF+HC was comparable with that in OL-HDF (22.2 ± 0.5 vs 22.3 ± 0.7 l, p=0.845). No significant difference was found in relative BV changes between the two treatments (p=0.46, figure 1).

Conclusions: The Na+ model implemented in OL-HDF integrated with the HC system resulted able to well control the Na+ mass balance, with non-significant differences in terms of blood pressure, interdialytic weight gain as well as post-dialysis plasma Na+ concentration compared to conventional HD treatment with HemoControl. Further studies are necessary to demonstrate if such a system is able to produce relevant clinical benefits in the long term.

MP385 HIGH CUT-OFF HEMODIALYZERS EFFICIENTLY REMOVE IMMUNOGLOBULIN FREE LIGHT CHAINS AND REDUCE TUBULAR INJURY INDUCED BY PLASMA OF PATIENTS WITH MULTIPLE MYELOMA

Vincenzo Cantaluppi1, Davide Medica1, Alessandro D. Quercia1, Massimo Gal1, Gianluca Leonardi1, Patrizia Anania1, Cesare Guerra1, Gloria Giovannazzo1, Martina Ferraresi1, Ilaria Merito1, Ilaria Dearnbrissi1, Fulvia Giaretta1, Luigi Biancone1 and Giuseppe P. Segoloni1
1Nephrology, Dialysis and Kidney Transplantation Unit, University of Torino, Torino, Italy

Introduction and Aims: Patients with multiple myeloma (MM) develop acute kidney injury (AKI) due to free light chains (FLC) deposition in tubular epithelial cells (TEC) with formation of tubular casts and triggering of apoptosis. High-cut-off (HCO) hemodialyzers have been shown to remove FLC allowing renal recovery. The aim of this study was to investigate FLC removal by HCO filters with established markers of tubular injury such as urine NGAL, retinoid binding protein (RBP), α1-microglobulin (α1-M) and with the pro-apoptotic effect of plasma of patients with MM on cultured TEC.

Methods: We selected 5 MM patients (IgGk or IgGk type) with AKI (RIFLE criteria) requiring dialysis (HCO Gambro Therazile, 18 sessions of 6 hr, blood flow 300 ml/min, dialysate flow 500 ml/min). Plasma FLC and urine NGAL were analyzed by nephelometry. Urine immunoelectrophoresis was also performed. In vitro on isolated human TEC, we evaluated FLC binding by FACS/immunofluorescence, MM plasma-induced apoptosis (TUNEL, caspase-3-8-9 activities), mitochondrial function (Mitotracker) and NGAL mRNA/protein expression.

Results: At study admission, MM patients showed mean serum creatinine 6.74 ± 1.12 mg/dl, plasma FLC 102465.53 ± 2269.38 ng/ml, urine NGAL 226.73 ± 41.85 ng/ml, urine RBP 62.82 ± 12.64 mg/g creatinine, urine α1-M 287.28 ± 39.75 mg/g creatinine. At day 28 from the inclusion in the study, we found that 4/5 (80%) of MM patients recovered renal function after HCO treatment. After 5 days, we observed the removal of more than 50% FLC and a significant decrease of urine NGAL, RBP and α1-M. Serum albumin levels remained stable during the study period. In vitro, MM plasma induced dose-dependent TEC apoptosis via mitochondrial dysfunction, caspase-3-8-9 activation and an increase of NGAL mRNA/protein expression. HCO treatment significantly reduced FLC binding to TEC, MM plasma-induced apoptosis and NGAL up-regulation.

Conclusions: The results of the present study suggest that HCO hemodialyzers efficiently remove FLC and reduced MM plasma-induced TEC apoptosis. Urine NGAL, RBP or α1-M and in vitro TEC apoptosis may be new potential biomarkers to evaluate FLC removal by HCO filters, tubular injury and renal recovery.

Table 1: Comparison of the main results among treatments

<table>
<thead>
<tr>
<th>Treatment</th>
<th>IDWG [Kg]</th>
<th>NaMB/TWL [mmol/Kg]</th>
<th>Pre dialysis BP [mmHg]</th>
<th>Post dialysis BP [mmHg]</th>
<th>Thirst Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD+HC</td>
<td>3.19 ± 0.70</td>
<td>146 ± 24</td>
<td>Systolic (S): 146.78 ± 19.68</td>
<td>S: 127.58 ± 11.81</td>
<td>10.6 ± 2.03</td>
</tr>
<tr>
<td>HDF+HC</td>
<td>3.20 ± 0.89</td>
<td>150 ± 31</td>
<td>Diastolic (D): 68.58 ± 19.75</td>
<td>D: 65.53 ± 18.76</td>
<td>8.27 ± 3.28</td>
</tr>
<tr>
<td>p (ANOVA)</td>
<td>p=0.97</td>
<td>p=0.59</td>
<td>S: 139.58 ± 18.05</td>
<td>S: 126.22 ± 14.68</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>D: 66.7 ± 15.55</td>
<td>D: 61.55 ± 13.13</td>
<td>p=0.026</td>
</tr>
</tbody>
</table>
Introduction and Aims: Protein bound toxins are poorly removed by conventional extracorporeal therapies. Aim of the present study was to quantitatively describe the binding of indoxyl sulfate (IS) in healthy and uremic plasma under different ionic strengths. Furthermore, a physiological set-up for the application of higher ionic strength in plasma for plasma hemodiafiltration therapy was developed.

Methods: Binding experiments were performed by ultrafiltration of 1:2-diluted, IS-added normal human plasma (n=3) applying different ionic strengths: 0.15, 0.30, 0.50, and 0.75 M NaCl. Total and free toxin concentrations were measured by HPLC. The dissociation constant Kd and the number of binding sites Bn were determined by nonlinear regression with a one site specific binding equation. Apart from not adding IS, similar experimental conditions were studied in plasma of 15 patients on hemodialysis. In a miniaturized ex vivo set-up (n=3), the removal rate (RR) of IS was compared between hemodiafiltration (HDF), pre-dilutional hemodiafiltration (HDFP), and modified pre-dilutional HDF (mHDF; substitution fluid: 1.0 M NaCl) in normal and uremic plasma at different flow rates (Q=300 and 400 mL/min). Finally, mHDF was upscaled to a standard HDF machine. The ex vivo hemocompatibility of higher ionic strength (0.15, 0.3, 0.5, 1.2 M NaCl during dialysis therapy was developed.

Results: Scatchard plot and best-fit analysis revealed IS binding to a single site in both normal plasma, Kd of IS positively correlated (r²=0.98, P<0.05) with the NaCl concentration. In normal plasma, Kd: 301 ± 105, 439 ± 19, 562 ± 2.0 µM at 0.15, 0.30, 0.50, and 0.75 M NaCl. The protein bound fraction (PBF) of IS decreased (>0.05) with higher ionic strength in both normal (PBF=93.4 ± 3.1, 89.7 ± 3.4, 85.8 ± 3.8, and 82.6 ± 3.4 %, resp.) and uremic plasma (PBF=92.9 ± 2.7, 96.1 ± 2.7, 93.2 ± 3.8, and 89.6 ± 3.4 %, resp.). RR of IS in normal plasma was similar between HD (RR=3.1 ± 1.5 and 2.5 ± 0.4 %/run, resp.) and HDF (RR=3.7 ± 2.1 and 2.9 ± 0.4 %/run, resp.). Compared to HDF, the RR of IS was higher with mHDF at Q=300 mL/min (RR=6.1 ± 2.9 and 4.3 ± 1.3 %/run; P=0.05 and P=0.22, resp.). In uremic plasma at Q=300 mL/min, no difference was found between HDF and mHDF (RR=4.5 ± 3.1 %/run vs. 6.6 ± 1.3 %/run; P=0.20). Increasing ionic strength in mHDF up to 0.75 M NaCl did not induce hemolysis. Significant hemolysis was only observed at 120 min after further increase of NaCl to 1.00 M (3.1 ± 1.5 %) and 1.20 M (17.6 ± 7.2 %). Post-dialysis hemolysis correlated with NaCl concentration in both blood and substitute (r²=0.47, P<0.05; and r²=0.43, P<0.05, resp.). Red blood cell and platelet counts, complement C5a and thrombin-antithrombin III concentrations were always unchanged but the white blood cell count decreased (P<0.05) already after 60 min with 1.20 M NaCl (post-dialysis: 577 ± 20.4 %). Conclusions: Increasing plasma ionic strength is effective to reduce the PBF of IS in both normal and uremic plasma. Furthermore, mHDF is suited to enhance the removal of IS.

Results: A partial or massive clotting of the dialyzer occurred in less than 1% of sessions in phase 1; 10% and 7% in phase 2; and in 1% and 2% in phase 3. Clotting limited to the drip chambers was observed in 13%, 34% and 12% respectively. The studied coagulation parameters showed a better profile when LMWH was used in association with HeprAN membrane, with aPTT < 40 s and anti-factor Xa activity < 0.3 IU/ml at the end of dialysis, while the generation of TAT complexes did not differ from that observed with the standard anticoagulation modality used in phase 1.

Conclusions: Our results suggest that the HeprAN membrane can be used safely in routine post-dilution hemodiafiltration with reduced doses of LMWH at the beginning of session.

Results: We observed that microvesicles in plasma samples derived from patients undergoing renal replacement therapy and treated with two different dialytic therapies, Bicarbonate Hemodialysis (BED) and On-line Hemodiafiltration (On HDF). A blood sample from patients (n=2 for conditions) was collected at the beginning (10 minutes from the start of the session, pre-dialysis) and at the end of the session (10 minutes before the conclusion of the session, post-dialysis) and MVs were isolated by ultracenrifugation. RNA from microvesicles was isolated and microRNA expression levels were analyzed using Comprehensive coverage of Sanger miRBase v14, TaqMan Array MicroRNA Cards (Card A) for a total of 375 unique assays specific to human mature miRNAs.

Results: We observed that plasma microvesicles exhibit significant differences in their miRNA content from pre and post dialysis. Hierarchical clustering of the data indicated that 15 miRNAs were increased in patients undergoing BED and 21 miRNAs in On-HDF, moreover, 13 and 10 miRNAs were decreased after BED and On-HDF respectively. The crossmatch between post dialysis samples showed an increase after On-HDF and a reduction after 4 of 4 miRNAs (miR-190, miR-205, miR-219, miR-516a-5p) involved in the regulation of proliferation, differentiation, angiogenesis and apoptosis.

Conclusions: The miRNA pattern differences observed between the beginning and the end of the dialysis session suggest that dialysis procedure might influence the circulating plasma microvesicles and that could lead to important implications in the study of the effects of dialysis techniques. Moreover, differentially expressed microRNAs might be used as biomarkers for monitoring disease and dialysis procedure.

Conclusions: The calcium mass balance during hemodialysis was shown to be frequently positive (absorption of calcium from dialysis fluid) for dialysis fluids with high calcium of 1.25 mmol/L or more (Gotch, 2008). We present a quantitative assessment of calcium kinetics and mass balance during the weekly cycle of three hemodialysis sessions in patients undergoing continuous renal replacement therapy. In the end of the study, the removal of calcium was calculated from the measurements in inlet and outlet dialysate fluid and dialysis fluid flow rate. The average values of calcium concentration were calculated from the weekly profiles of calcium in serum. Dialysis equivalent continuous clearance, ECC, was calculated as the ratio of the difference between the total calcium load and the final serum calcium concentration to the total dialysis time.
removed mass per dialysis cycle time (one week) per the time average solute concentration in serum.

Results: The time average concentration of calcium in plasma was 8.90 ± 0.53 mg/dL (range 7.80-10.50 SD). Calcium concentration in serum increased during dialysis sessions from 8.7 ± 0.7 to 9.4 ± 0.6 mg/dL (p < 0.0001), and later on slightly decreased to 9.1 ± 0.6 mg/dL (p < 0.0003) at 45 min after the end of the dialysis. The removed calcium mass was on average 156 ± 486 mg, with 670 ± 291 mg removed from patients on negative (removal) dialysis, and -113 ± 315 mg from patients with calcium absorption from dialysis fluid; in two patients the mass balance was close to zero. The dialysis equivalent continuous clearance for calcium was 0.9 ± 0.55 mL/min (0.3 ± 0.26 mL/min in 10 patients with positive ECC, 0.49 ± 0.35 min/mL in 5 patients with negative ECC, and close to zero in 2 patients), compared to the healthy kidney clearance of 1.5 mL/min.

Conclusions: We conclude that in hemodialysis patients on low calcium dialysis fluid of 1.25 mmol/L, calcium is removed by dialysis on average 10 times slower than by the normal kidneys, and some patients are on positive calcium dialysis calcium mass balance due to absorption of calcium from dialysis fluid. The dialysis treatment stimulates physiological processes that increase calcium concentration in plasma during dialysis in spite of a moderate calcium removal.

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**Abstracts**

**MP390**

**ELIMINATION OF THE MIDDLE SIZE MOLECULES BY THE FXCORDIA 60 IN RELATION TO THE FX 60-DIALYZER**

Francisco Maduell1, Paul Wieneke2, Manel Vera1, Nestor Fontserre1, Raquel Ojeda1, Montserrat Carrera1, Aleix Cases1, and Josep Campistol1

1Nephrology and Renal Transplantation, Hospital Clinic Barcelona, Barcelona, Spain; 2Fresenius Medical Care, Deutschl and GmbH, Bad Homburg, Germany

**Introduction and Aims:** The incorporation of nano-controlled spinning technology in the design of dialyzers allowed to create a new generation of dialyzers with the goal of moving the sieving coefficient curve (vs. molecule size) to the right and increase the steepness in order to get an optimal cut-off point. The aim of this study was to compare two 1.4 m² polysulfone dialyzers, current and new generation with respect to the efficiency in the elimination of a broader spectrum of uremic toxins.

**Methods:** In an open, randomized, cross-over, monocentric, controlled, prospective clinical study 30 adult chronic hemodialysis patients were treated by post-dilution on-line hemodiafiltration once with the FX 60 or FX Cordia 60 (both produced by Fresenius Medical Care) dialyzer type. The remaining dialysis parameters did not vary: dialyzer (ALL, type of dialyzer, iCa (7.5 ± 0.5 mmol/l), blood flow 408 ± 31 ml/min, 300-320ml/min, dialysate flow 500 ml/min. The treatments were performed with FMC 4008 machines and high-flux dialyzers (FX600, FX80 and PS1800).

**Results:** In agreement with previous results the stepwise reduction of the Heparin dose did not lead to any clotting in the extracorporeal circuit or dialyzers, despite the mean post-treatment values of ACT decreased by approx. 20%. After a reduction of the total Heparin dose by 50% there was no drop of the efficacy judged by spKt/V. Ionized Ca (iCa) and total Ca were slightly reduced by about 5-7%. A Ca²⁺ decrease to unchanged balance, and -113 ± 315 mg from patients with calcium absorption from dialysis fluid; in two patients the mass balance was close to zero. The dialysis equivalent continuous clearance for calcium was 0.9 ± 0.55 mL/min (0.3 ± 0.26 mL/min in 10 patients with positive ECC, 0.49 ± 0.35 min/mL in 5 patients with negative ECC, and close to zero in 2 patients), compared to the healthy kidney clearance of 1.5 mL/min.

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**Sample abstract with highlighting:**

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Introduction and Aims: A 59 yr old kidney recipient was admitted in ICU with a flu-like syndrome with myalgia, fever and hypotension. Biological parameters showed an increased CRP, a severe rhabdomyolysis (Creatine Kinase peak value 244900UI/L) with acute kidney injury – AKIN 3 (creatinine peak value 8.3mg/dl from a basal level of 1.9 mg/dl). Considering the rapid onset of anuria and the risk of intra-tubular myoglobin precipitation, renal replacement therapy was required. We decided to evaluate the eurapation capacity of the Super High-Flux (SHF) filter Theratone (Gambro, cut-off point 45 kDa) on myoglobin (MW11.8 kDa) and to compare it to other middle molecules such as β2-microglobulin (MW11.8 kDa) and Interleukin-6 (MW21-28kDa), reflecting the pro-inflammatory status.

Methods: Plasma concentrations of Myoglobin (Chemoluminescence immunoassay), IL-6 (Quantikine – ELISA) and β2-microglobulin (Liaison kit) were determined during the first 3 HD sessions at baseline (T0) and after 1, 2 and 3 hrs, respectively.

Results: A dramatic reduction of all parameters was observed after each HD session, leading to a significant extraction of circulating myoglobin (Table). After 4 sessions with Theratone, the clinical status quickly improved and the patient recovered diuresis. However, conventional HD was needed during two additional weeks. Up to now, renal function has reached the steady state recorded before the acute episode.

Conclusions: SHF membrane may be useful in renal transplanted patients with severe AKI due to rhabdomyolysis.

<table>
<thead>
<tr>
<th>Time</th>
<th>Myoglobin (µg/L)</th>
<th>IL-6 (pg/ml)</th>
<th>β2-microglobulin (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0-session</td>
<td>13,416</td>
<td>6.1</td>
<td>4.9</td>
</tr>
<tr>
<td>T1h</td>
<td>6,704</td>
<td>4.6</td>
<td>3.2</td>
</tr>
<tr>
<td>T2h</td>
<td>5,688</td>
<td>3.8</td>
<td>2.5</td>
</tr>
<tr>
<td>T3h</td>
<td>5,186 (61%)*</td>
<td>3.2 (48%)*</td>
<td>2.2 (55%)*</td>
</tr>
<tr>
<td>T0-session2</td>
<td>13,422</td>
<td>19.9</td>
<td>9.3</td>
</tr>
<tr>
<td>T1h</td>
<td>6,958</td>
<td>15.5</td>
<td>5.2</td>
</tr>
<tr>
<td>T2h</td>
<td>5,178</td>
<td>12.4</td>
<td>3.9</td>
</tr>
<tr>
<td>T3h</td>
<td>4,64 (65%)*</td>
<td>13.8 (30%)*</td>
<td>3.3 (64%)*</td>
</tr>
<tr>
<td>T0-session3</td>
<td>6,187</td>
<td>9.2</td>
<td>13.9</td>
</tr>
<tr>
<td>T1h</td>
<td>3,408</td>
<td>2.8</td>
<td>7.6</td>
</tr>
<tr>
<td>T2h</td>
<td>2,378</td>
<td>2.1</td>
<td>5.1</td>
</tr>
<tr>
<td>T3h</td>
<td>1,776 (71%)*</td>
<td>3.3 (64%)*</td>
<td>3.9 (71%)*</td>
</tr>
</tbody>
</table>

*Extraction coefficients calculated at time 3h of each HD session and expressed in % of basal values.

In-vivo 2 Microglobulin Clearance in High-Flux HD & HDF

E. von Albertini1, C. Mathieu1, A. Cherplid1, A. Boesch1 and M. Romo2
1Clinique Cecil, Lausanne, Switzerland. 2Unilabs, Lausanne, Switzerland

Introduction and Aims: Hemodiafiltration (HDF), with forced filtration by external substitution of plasma water, remains the pre-eminent convective RRT for enhanced removal of large solutes with putative uremic toxicity. Highly permeable dialyzers, available now for use in high-flux hemodialysis (HF-HD), are effectively narrowing the gap from HDF. Primarily due to decreased hollow-fiber inner diameter, resistance to blood flow increases hydrostatic pressure across the membrane. Within the dialyzer, this results in enhanced internal filtration with convection of solutes from blood, with backfiltration of fresh dialysate occurring simultaneously under volumetric control of the equipment. The magnitude of such “internal dialfiltration” is not readily measurable, but can be deducted from evidence of transport of large, poorly diffusible solutes. Aim of the study was to measure in-vivo clearance for β2-microglobulin (β-2M, 11.812 Da) in HF-HD and compare it to HDF.

Methods: Studies were carried out in 12 consenting ESRD patients (9 M, age 70 ± 12, ESRD-vintage 8.1 ± 9.3 yrs, plasma β-2M 27.6 ± 4.5 mg/l) during routine clinical treatments with HF-HD or HDF, performed in the online postdilution autotransfusion mode (Fresenius 5008). Two dialyzers with high hydraulic permeability (UF-Coeff. ≥60 ml/H/m²/Hg) were used: a) Fresenius FX CorDiax 80 (PS-Helixone®plus membrane, 1.8 m²) and b) Gambro Revaclear MAX (polaryethersulfone, 1.8 m²), both containing hollow fibers with reduced inner diameter (185, resp. 190 µm). From measurement of blood and dialysate samples obtained during treatment at various blood flow rates, in-vivo extracorporeal plasma clearance for β-2M (Kfβ2M) was calculated, derived from both mass removal from blood and mass recovery in the dialysate; means were used for analysis. Patients’ overall β-2M reduction rate was estimated from pre- to post-treatment changes of patients’ plasma level in relation to extracellular water volume.

Results: Characteristics & quantification of studied treatments:
- In-vivo measured Kfβ2M
- Conclusions: The demonstrated high in-vivo Kfβ2M obtained in HF-HD with the studied dialyzers, suggests primarily convective transport of large solutes by internal filtration & backfiltration, approximating in magnitude that of HDF.

IN-VIVO 2 MICROGLOBULIN CLEARANCE IN HIGH-FLUX HD & HDF

Described in detail in the above.

AN IMMUNOADSORPTION DEVICE FOR MYOGLOBIN REMOVAL

Jianhui Zhou1, Li Tang1, Deyang Kong1, Li Zhang1, Suozhu Shi1, YangLv1 and Xiangmei Chen1
1Department of Nephrology, State Key Laboratory of Kidney Disease, Beijing, China

Introduction and Aims: Myoglobin is the key element in rhabdomyolysis induced acute kidney injury, which can be removed by hemodialysis or hemofiltration. When emergent catastrophic events happen, i.e., earthquake, flood, the electricity and water supply systems are often damaged so that the hemodialysis machines cannot work. The present study constructed a device based on immunoadsorption to remove myoglobin effectively.

Methods: We screened out 2 pieces of antigentic peptides which were named D-12 and L-12, then we got 2 kinds of polyclonal antibodies by immunizing rabbits. And we chose anti D-12 antibody as ligand to couple resin carrier because its higher titer and affinity. The resin carrying anti D-12 antibody incubated sample, no bands were found in anti L-12 antibody incubated sample. We connected tubes with the device to form a circulation system. Then we test the removal capability of this device.

Results: Only one band appeared near 50k by reduced SDS-PAGE, no minor bands appeared, that means the antibodies had high purity. Indirect ELISA was used to determine antibody titer. The titer of anti D-12 antibody was 1:64000, while titer of anti L-12 antibody was 1:8000. Anti D-12 and anti L-12 antibodies were used respectively as primary antibody, to incubate with myoglobin sample. A 16kD band appeared in anti D-12 antibody incubated sample and anti L-12 antibody incubated sample. The secondary antibodies were used respectively as primary antibody, to incubate with sectioned kidney tissue from rhabdomyolysis model rats. Some areas were found positive stained in anti D-12 antibody incubated tissue, while anti L-12 antibody incubated tissue showed no stained area. We chose anti D-12 antibody as ligand to couple resin carrier and the resin was filled into a glass column to make an adsorption device. Then we connected the adsorption device with some tubes to set up a circulation system. A sample solution of 4000ug myoglobin was added into the system. When the solution pass through this system, a total of 909.2ug myoglobin was removed, the clearance rate was 22.73%. Meanwhile, the blank control device (filled with resin without antibody) can only remove 83.9ug myoglobin with a clearance of only 2.02%. Sample solution of myoglobin and other two common proteins (albumin and lysozyme) were added into fast protein liquid chromatograph (FPLC) to determine the adsorption rate. We found adsorption rate of myoglobin was higher than that of albumin (%) and lysozyme (%), p<0.01 respectively.

AN IMMUNOADSORPTION DEVICE FOR MYOGLOBIN REMOVAL

Described in detail in the above.
Abstracts

Conclusions: In this study, we obtained the polyclonal antibody through screening antigenic epitope, producing antigenic peptides, immunizing, purifying. By coupling the antibody with rasin, we constructed an immunoadsorption device. This device can remove myoglobin effectively.

MP396 WHAT IS THE MOST SUITABLE BIOMARKER FOR EVALUATION OF CHARACTERISTICS AND BENEFITS OF HDF?

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Introduction and Aims: Hemodialfiltration (HDF) can effectively remove uremic toxins, from small to large molecule substances by combination of diffusion and convection. β2-Microglobulin (β2-MG, MW=11.8kDa) is removed mainly by diffusion and α1-Microglobulin (α1-MG, MW=33kDa) is removed only by convection. In the present study we investigated whether α1-MG is the most suitable biomarker for evaluating the characteristics and benefits of HDF based on actual cases. We also evaluated the resolved uremic toxins performance of three hemodiafilters by HDF, and assessed the importance of α1-MG as a biomarker.

Methods: We conducted the dialysis conditions in 17 cases that had stabilized by HDF. The results one month after changing the conditions showed that the symptoms had worsened in 13 of the 17 cases. We changed the conditions again in the 13 cases in which the symptoms had worsened. The results one month after the changes showed that patient quality of life had returned to its previous state. We then investigated the fluctuations in dialysis efficiency associated with these changes in symptoms based on small molecule substances removal and low molecular weight proteins (LMPWs).

Results: 1) In the 13 cases in which the symptoms changed from “stable,” to “worse,” and then to “improved,” α1-MG removal rate (RR) changed significantly from 35.5%, to 31.7%, and then to 32.3% in tandem with the changes in symptoms, but the Kt/V values (1.59 ± 1.65) and β2-MG RR (78.2% - 75.2% - 77.3%) fluctuated within narrow ranges. 2) Under these conditions, the β2-MG RR was a favorable 80% with all three types of hemodiafilters. However, there were significant differences in the α1-MG RR and amounts removed. TDF:18.2%,93mg, ABH:25.9%,126mg, MFX:37.5%,179mg.

Conclusions: There was a close correlation between the changes in symptoms and the RR and amounts removed: TDF:18.2%,93mg, ABH:25.9%,126mg, MFX:37.5%,179mg.}

MP397 HIGH FLUX HEMODIALYSIS WITH NEW MEMBRANES IS AS EFFECTIVE AS HEMODIAFiltrATION FOR MIDDLE WEIGHT MOLECULES EXTRACTION

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Introduction and Aims: Previous studies suggest that middle molecules (MWM) removal is a determinant factor of dialysis patient’s prognosis. New technologies provide better control of pore size of dialyser membranes allowing greater renal permeability. We have studied MWM removal of 9 high flux (HF) membranes in order to verify their ability to get the same performance for removal of MWM in high flux hemodialysis (HF-HD) as hemodialfiltration (HDF).

Methods: Following HF membranes (ultrafiltration rate > 25 ml/h/mmHg) have been studied in the same conditions (membrane surface = 2.0 to 2.2 m², duration of hemodialfiltration session = 4h, blood flow = 340 to 360 ml/min and dialysate flow = 500 ml/min): Polysulfone, Polypolymer, Héleos, Polysulfone, Purema, Polynephron, Helixone, Polyethylene, Purema, PEPF (2 types: small and high pore size). AN69, PMMA.

Results: 366 sessions with Kt/V > 1.2 have been selected in 131 patients. Considering low molecular weight molecules removal and dialysis dose, Kt/V was significantly higher with HF-HD than with all the other membranes (1.42 ± 0.36 vs values from 1.72 ± 0.29 to 1.57 ± 0.36). Significant differences have been found between studied membranes for beta 2 microglobulin (β2-M) RR and myoglobin RR. Helixone membrane provides the greatest values of β2-M RR (78.5 ± 4.7%) and Polyphenylene those for myoglobin RR (68.4 ± 7.2%). Ranking results are for β2-M RR: Helixone > Polyphenylene > PEPA high pore size > Polynephron > PEPA small pore size > Polysulfone > Purema > AN69 > PMMA and for myoglobin RR. Polysulfone > PEPA high pore size > Polynephron > AN69 > Helixone > Purema > Polysulfone > PMMA. Three profiles can be distinguished: 1- Membranes which remove β2-M and myoglobin (Polyphenylene, PEPA high pore size), 2- Membranes which remove β2-M but not myoglobin (Helixone, Polynephron, PEPA low pore size, Polysulfone, Purema), 3- Membranes which remove β2-M and myoglobin at a lower level (AN69, PMMA).

Conclusions: α1-MG is the most suitable biomarker for evaluating the characteristics and benefits of HDF based on actual cases. We also evaluated the resolved uremic toxins performance of three hemodiafilters by HDF, and assessed the importance of α1-MG as a biomarker.

References:

1MP396 WHAT IS THE MOST SUITABLE BIOMARKER FOR EVALUATION OF CHARACTERISTICS AND BENEFITS OF HDF?

2MP397 HIGH FLUX HEMODIALYSIS WITH NEW MEMBRANES IS AS EFFECTIVE AS HEMODIAFiltrATION FOR MIDDLE WEIGHT MOLECULES EXTRACTION

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Nephrology Dialysis Transplantation
Methods: Using the novel DFB dialyzer (patents pending), total surface area = 3 m², we evaluated the in-vitro K and Uf rates at different Qd and Qb. The testing solution was packed human red blood cells, reconstituted with saline, Hct = 32% ± 2%, albumin > 6 g/dL. The solution was spiked with urea, creatinine, Vitamin B12 and phosphate for K studies. Single pass studies were performed and K calculated for Qd = 600 and 700 mL/min at Qb = 300, 400, 500 and 500 mL/min. Weight loss (machine set Uf) was set to 0 mL/min. AN69 and PMMA were compared with significance at p < 0.05. Uf rates were calculated by measuring the change in Hct and calculating the resultant fluid removed. Filtration Fraction (FF%) is equal to Uf rate/Qb, expressed as a percentage. Results: For Urea and Creatinine were not significantly different between the different Qd, however, the Uf rates differed by up to 20% (Vit B12 and Phosphate are pending). Conclusions: Qd directly affects the Uf rate when using the DFB dialyzer. Clearance values did not significantly differ when Qd was changed from 600 mL/min to 700 mL/min, resulting in URR > 90% at Qb up to 500 mL/min. The DFB dialyzer is capable of providing HDF treatments greater than 17 L exchanged (> 100 mL/min), with commonly used Qb and treatment times on standard dialysis equipment. The volume exchanged during the treatment can be tailored to the individual patient’s needs by altering the Qd.

**Abstracts**

**MP401** LOOKING FURTHER THAN ENDOTOXIN: A COMPARATIVE STUDY OF PYROGEN RETENTION BY ULTRAFILTERS APPLIED FOR PREPARATION OF STERILE DIALYSIS FLUID

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**Introduction and Aims:** Sterile ultrafilters are used for filtration of substitution fluid in patients treated with HDF/HF to improve safety for dialysis-therapy and to avoid incompatibility of the fluid. The objective was to test the performance of a disposable new ultrafilter (NUF) in comparison to reference ultrafilters (RUF1 - RUF4).

**Methods:** NUF comprises a flat sheet membrane made of modified polysulfone with net positive charge. Nominal pore size is 0.2 μm with membrane area of approximately 25 cm². Filter performance was tested with pyrogen-contaminated challenge solutions containing lipopolysaccharides (P. aeruginosa LPS: > 500 EU/mL), peptidoglycans (B. subtilis and S. aureus), 1000 ng/mL) and bacterial lysates (P. aeruginosa: 12500 EU/mL).

The following test methods were applied: LAL Test for LPS and Oligo Green assay for ODN quantification, cell-based cytokine induction assays (CIA: IL-18 mRNA and IL-16) and pattern recognition receptor (PRR) bioassay for the evaluation of the biological activity of the challenge solutions and their filtrates.

**Results:** NUF reduced LPS (LAL-test) and LPS-induced biological activity (CIA (IL-16) and PRR) by 100%, while after filtration with the RUFs, between 6.3 ± 0.9 and 0.013 ± 0.01 EU/mL was still detected with the LAL-test. Peptidoglycan from B. subtilis and S. aureus was retained by both NUF and RUF, resulting in a 100% reduction of biological activity as demonstrated by CIA (IL-16) and PRR bioassays. With respect to DNA, however, NUF demonstrated full retention of ODN whereas the RUFs were fully permeable, both based on Oligo Green assay and CIA (IL-16 mRNA). However, DNA from bacterial lysate showed a trend to decrease in biological activity after filtration with both NUF and RUF based on PRR bioassay (TLR9).

**Conclusions:** Thus, the new ultrafilter showed better retention performance for LPS and equal performance for peptidoglycan compared to the reference filter(s) in spite of a smaller membrane surface and larger pore size. Additionally, the new filter retained biologically active ODN which has for the time being not yet been described for any other device. Hence, the application of this filter in HDF therapy has the potential to further optimize patient safety.
THE EFFECT OF NAFAMOSTAT MESILATE IN PROLONGING FILTER PATENCY WITH PATIENTS ON CONTINUOUS RENAL REPLACEMENT THERAPY

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Introduction and Aims: Continuous renal replacement therapy (CRRT) has been considered as an effective modality for renal replacement therapy in hemodynamically unstable patients within intensive care unit (ICU) except for the necessity of anticoagulation. The severity and peculiarities of ICU patients often make it equivocal to use anticoagulation.

Methods: This is a prospective randomized controlled study to show the difference in filter life span and adverse event between nafamostat mesilate group and heparin-free group. The patients are randomly assigned to each group. Heparin free group use M100 membrane. Baseline characteristics and appropriate laboratory tests were taken from each group.

Results: Seventy-three patients were enrolled in this study, and there were no significant differences between two groups in baseline characteristics [Table 1]. There were no significant differences in transfusion, mortality within 28 days, and platelet count between two groups. There were no serious adverse events related to nafamostat mesilate.

Conclusions: Nafamostat mesilate is an effective and safe anticoagulation method in patients with high risk of bleeding without causing major bleeding complication.

MP403 Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>HF-100group (n=36)</th>
<th>M-100group (n=37)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(years)</td>
<td>52.97±13.94</td>
<td>57.54±13.04</td>
<td>0.152</td>
</tr>
<tr>
<td>Male, N (%)</td>
<td>24 (66.67%)</td>
<td>20 (54.05%)</td>
<td>0.271</td>
</tr>
<tr>
<td>Vital sign</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP(mmHg)</td>
<td>122.42±20.89</td>
<td>121.03±21.33</td>
<td>0.779</td>
</tr>
<tr>
<td>DBP(mmHg)</td>
<td>66.75±15.39</td>
<td>63.68±12.44</td>
<td>0.350</td>
</tr>
<tr>
<td>Pulsate (bpm)</td>
<td>113.36±24.27</td>
<td>113.35±23.10</td>
<td>0.999</td>
</tr>
<tr>
<td>Bodytemperature (°C)</td>
<td>36.68±0.81</td>
<td>36.81±1.14</td>
<td>0.585</td>
</tr>
<tr>
<td>RR/min</td>
<td>19.71±4.58</td>
<td>20.05±6.42</td>
<td>0.755</td>
</tr>
<tr>
<td>Laboratory test at CRRT start</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WBC (10³/l)</td>
<td>12.45±11.11</td>
<td>10.49±9.88</td>
<td>0.427</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td>8.49±1.55</td>
<td>9.07±1.86</td>
<td>0.147</td>
</tr>
<tr>
<td>Platelet(10³/l)</td>
<td>57.44±40.05</td>
<td>90.92±97.39</td>
<td>0.087</td>
</tr>
<tr>
<td>Na(mmol/L)</td>
<td>140.28±8.00</td>
<td>140.81±7.49</td>
<td>0.774</td>
</tr>
<tr>
<td>K(mmol/L)</td>
<td>4.19±0.82</td>
<td>4.24±1.06</td>
<td>0.843</td>
</tr>
<tr>
<td>BUN(mg/dL)</td>
<td>64.09±25.64</td>
<td>61.71±30.16</td>
<td>0.718</td>
</tr>
<tr>
<td>Cr(mg/dL)</td>
<td>3.09±1.09</td>
<td>3.41±1.96</td>
<td>0.385</td>
</tr>
<tr>
<td>Averageduration of CRRT (hours)</td>
<td>5.31±5.03</td>
<td>6.93±5.60</td>
<td>0.249</td>
</tr>
</tbody>
</table>

The filter life span and the number of filters used during CRRT was similar in both group, except the number of filters changed due to clots per 24 hours. (1.90 ± 1.60 in M100 group vs. 1.15 ± 0.81 in HF 1000 group; p=0.040) However, when the filters were subdivided into filters used less than 12 hours and over 12 hours, filters used over 12 hours were significantly higher in HF1000 group. (p=0.037, odd ratio 1.840) [table 2].

MP403 Table 2. The distribution of filter life span

<table>
<thead>
<tr>
<th></th>
<th>M100 group</th>
<th>HF1000 group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤12hrs</td>
<td>57 (41.3%)</td>
<td>26 (27.7%)</td>
<td>83 (35.8%)</td>
</tr>
<tr>
<td>&gt;12hrs</td>
<td>81 (58.7%)</td>
<td>68 (72.3%)</td>
<td>62 (64.2%)</td>
</tr>
<tr>
<td>Total</td>
<td>138</td>
<td>94</td>
<td>232</td>
</tr>
</tbody>
</table>

There were no significant differences in transfusion, mortality within 28 days, and survival between two groups. There were no serious adverse events related to nafamostat mesilate.

IS ON-LINE HDF THE BEST STRATEGY FOR RESTLESS LEGS SYNDROME IN DIALYSIS PATIENTS?

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Introduction and Aims: Restless legs syndrome (RLS) is one of the intractable complications in dialysis patients. Prevalence of RLS among dialysis patients from 12 to 35% is reported. In hemodialysis (HD) patients, RLS has been related to uremic toxins with MW of 30kDa or more. Setting dialysis condition removing uremic toxins with MW of 30kDa or more is important to treat RLS. Since setting this condition for on-line HDF is easy, it is the best strategy for the treatment of RLS.

Methods: The study involved 131 patients undergoing hemodialysis (HD) or HDF at our clinic (August 2011 - July 2012). The incidence of RLS was assessed using the diagnostic criteria of the International RLS Study Group. In dialysis patients with RLS, the dialysis methods were changed and the effects of treatment and removal efficiency of LMWP were examined. The severity of RLS symptoms was evaluated using the International RLS Rating Scale score (IRLS). The removal efficiency was evaluated by measuring KiTV and the removal rates (RR) of β₂-microglobulin (β₂-MG) and α₁-microglobulin (α₁-MG).

Results: RLS was observed in 7 patients (5.3%). Case 1 developed RLS during HD (IRLS:32; α₁-MG RR:31.6%). The dialysis method was changed to pre-dilution HDF, and her symptoms resolved within 3 weeks (α₁-MG RR:24.7%). Case 2 developed RLS during HD (IRLS:30; α₁-MG RR:28.8%). Her symptoms resolved within 2 weeks after the dialysis method was changed to pre-dilution HDF (α₁-MG RR:41.9%). Case 3 developed RLS after the dialysis method was changed from pre-dilution HDF to HD (IRLS:32; α₁-MG RR:29.9%). After the dialysis method was switched back to HDF, her symptoms resolved (α₁-MG RR:41.9%). Case 4 developed RLS during HD (IRLS:37; α₁-MG RR:26.2%). After the dialysis method was changed to pre-dilution HDF, his symptoms were relieved (IRLS:31; α₁-MG RR:34.6%). Case 5 was receiving post-dilution HDF (α₁-MG RR:30.7%). After the dialysis method was changed to HDF using the different hemodiafilter, he developed RLS (IRLS:32; α₁-MG RR:26.6%). His RLS resolved 3 weeks after the dialysis method was switched back to HDF using the previous dialyzer (α₁-MG RR:44.2%). Case 6 developed RLS during HDF (IRLS:25; α₁-MG RR:23.8%). His symptoms resolved within 4 weeks after the dialysis method was switched to pre-dilution HDF (α₁-MG RR:41.5%). Case 7 developed RLS during HDF (IRLS:32; α₁-MG RR:24.0%). His symptoms resolved within 3 weeks after the dialysis method was switched to pre-dilution HDF (α₁-MG RR:44.3%). The patients’ symptoms of RLS persisted when the α₁-MG RR was under 35%, while they resolved when the RR was 40%.

Conclusions: According to our cases, there is a relationship between solute removal and RLS. Both the onset and relief of RLS symptoms were strongly correlated with α₁-MG RR. RLS may occur at α₁-MG RR of 30%. RLS can be cured at 40% or more of α₁-MG RR. This may indicate that RLS is caused by the accumulation of uremic substances with MW of around 30kDa or more. Setting dialysis condition removing uremic toxins with MW of 30kDa or more is important to treat RLS. Since setting this condition for on-line HDF is easy, it is the best strategy for the treatment of RLS.
HEMODIALYSIS DURATION, DIALYSIS MODALITY AND PARAMETERS OF ADEQUACY AND CARDIOVASCULAR MORBIDITY

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Introduction and Aims: Weekly duration of hemodialysis is traditionally 12 hours, and randomized controlled HEMO trial found no advantage in survival with higher dialysis dose or using high-flux dialysis membrane. However, experiences of French authors show that the length of hemodialysis treatment is associated with benefits concerning morbidity and mortality of dialysis patients. The aim of study was to compare the parameters of anemia, malnutrition, inflammation, mineral metabolism and cardiovascular comorbidity score, depending on the duration and the type of hemodialysis treatment.

Methods: A total of 206 hemodialysis patients were divided into 3 groups according to the total weekly duration of dialysis treatment: group I (≤12 h), group II (12.5–15 h) and group III (≥17.5 h weekly HD). Also, patients were divided into group A (low flux membranes, group B (high flux membranes) and group C (hemofiltration). Cardiovascular score was determined so that one point was given for: cardiomyopathy, ischemic heart disease, peripheral vascular disease and stroke.

Results: Patients with longer duration of dialysis had significantly higher Hb level (despite of less frequent use of ESA), S-albumin level and S-calci um level. They also had lower ESA resistance index, iPTH value, less frequent use of Prokinetics and VitD metabolites and lower CV morbidity score. Patient on HDF had significantly higher Kt/V than patients on LF- and HF- dialysis (1.41 vs. 1.32 and 1.33). Compared to patients on LF-dialysis, patients on HDF and standard HF-dialysis had significantly higher hemoglobin value (11.2 and 10.9 vs. 10.2 g/dL), less frequent ESA use (62.5% and 67.4% vs. 97.2%) and lower CV morbidity score (1.00 ± 0.97 vs. 0.97 ± 1.03).

Conclusions: Our data support the statement about beneficial effect of longer hemodialysis and high-flux membranes / HDF on anemia indices and CV morbidity.

HYPOPHOSPHATEMIC EFFECT OF BICARBONATE BUFFERED DIALYSIS FLUID CONTAINING SUCCINATE AND HYDROCHLORIC ACID

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Introduction and Aims: As we reported earlier (ERA-EDTA Congress 2012, abstract FP 423), application of bicarbonate buffered dialysis fluid containing 0.44 mmol/L of succinate and 2.12 mmol/L of acetate resulted in significant decrease of predialysis blood level of inorganic phosphate (1.77 ± 0.05 vs. 2.03 ± 0.05 mmol/L in control group, p<0.001) and of the value of calcium-phosphorus product (3.84 ± 0.12 vs. 4.74 ± 1.12 mmol/L2 in control group, p<0.001). We found also definite increase of serum albumin (34.8 ± 0.46 vs 33.2 ± 0.45 g/l in control group, p=0.18). Hypophosphatemic effect of citric acid dialyze, presumably due to increased dialysis efficiency, was noted in some published reports. The replacement of acetate to hydrochloric acid, however, did not cause such an effect. We supposed that decrease of inorganic phosphate (Pi) and increase of serum albumin in our study are the result of succinate’s metabolic action mainly, but not of the lesser acetic burden. To verify this assumption we developed and applied acetate-free bicarbonate buffered dialysis fluid containing succinate and hydrochloric acid.

Methods: 26 clinically stable patients on thrice weekly hemodialysis with predialysis serum Pi >1.78 mmol/l were enrolled in the study. All of them were switched for 4 weeks from standard bicarbonate dialysis fluid containing 3 mmol/L of acetate to acetate-free bicarbonate buffered dialysis solution acidified with succinate (0.5 mmol/L) and hydrochloric acid (2.0 mmol/L). Dialysis and drug prescriptions of patients and their diet remained unchanged. Blood samples were taken immediately before the start of the study and after 4 weeks of treatment with alternative dialysis fluid.

Results: As a result of application of dialysis fluid containing succinate and hydrochloric acid, we found decrease of predialysis levels of serum Pi (2.24 ± 0.64 before and 2.09 ± 0.64 mmol/L after 4 weeks of the study, p=0.08), and of total calcium (2.26 ± 0.17 before the study and 2.21 ± 0.19 mmol/L after 4 weeks of treatment, p<0.001). Respectively, the value of calcium-phosphorus product decreased from 5.14 ± 1.48 to 4.62 ± 1.38 mmol/L2, p<0.036. Serum albumin increased from 34.0 ± 3.1 to 35.0 ± 2.7 g/L, p=0.006. Application of acetate-free dialysis fluid has not caused significant changes of acid-base status, both before and after hemodialysis session.

Conclusions: Application of succinate-containing dialysis solutions improves control of hyperphosphatemia in chronic hemodialysis patients. Hypophosphatemic effect is probably due to succinate’s metabolic action. Succinate accelerates the turnover of the bicarbonic acid cycle, increased consumption of phosphate for the synthesis of ATP. Increased production of ATP improves energy supply of cells and, ultimately, leads to the normalization and improvement of biosynthetic processes, that also contributes to the binding of free inorganic phosphate.
of CRRT was due to effective diuresis in nine cases and due to death in four cases. The death was related to severe disease and MODS. The survival at discharge from the hospital was 46%. At the time of discharge renal function was normal and no patients required dialysis.

**Conclusions:** RCA-CRRT is effective and simple method of extracorporeal blood purification even in neonates. The complications of CRRT in neonates are relatively low. For using potential benefit of RCA-CRRT in neonates, further observations are needed.

**MP408 USE OF LOW MOLECULAR WEIGHT HEPARINS IN LONG NOCTURNAL HAEMODIALYSIS**

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**Introduction and Aims:** Nocturnal haemodialysis presents unique anticoagulation issues compared with traditional haemodialysis due to a longer duration of treatment - 6-8 hours vs 4 hours, longer dialysis lines, single needle techniques using double pump and slower pump speeds. Anticoagulation during long nocturnal haemodialysis could be problematic due to increased risk of haemorrhagic events and prolonged bleeding times post dialysis. Unfractionated heparin (UFH) is the traditional anticoagulant used for anticoagulation of the extracorporeal circuit however due to adverse effects and rising acquisition costs low molecular weight heparins (LMWHs) are increasing being used in standard haemodialysis. **Aim:** we evaluated the introduction of LMWHs for the management of the extracorporeal circuit in patients on long nocturnal haemodialysis. Nine patients currently on the nocturnal dialysis were evaluated, four of which had previously complained of marked hair loss possibly attributable to UFH.

**Methods:** Tinzaparin was selected because of the short half-life (2.5 hours), lower acquisition costs, and in use on the haemodialysis unit. Dosing information was sourced from the product literature, however there was no information regarding acquisition costs, and in use on the haemodialysis unit. Furthermore, tinzaparin was chosen due to its relative ease of use via the dialysis machine. Doses were amended accordingly depending on the signs of clotting, bleeding and the dose was reduced. One patient's tinzaparin dose was reduced due to prolonged bleeding times normal. Three patients experienced slightly prolonged bleeding times post dialysis. Unfractionated heparin (UFH) is the traditional anticoagulant used for anticoagulation of the extracorporeal circuit however due to adverse effects and rising acquisition costs low molecular weight heparins (LMWHs) are increasing being used in standard haemodialysis. **Aim:** we evaluated the introduction of LMWHs for the management of the extracorporeal circuit in patients on long nocturnal haemodialysis.

**Results:** Eight patients are using tinzaparin to anticoagulate the extracorporeal circuit. Three patients remained on the starting dose, the dialysis circuits were clear and bleeding times normal. Three patients experienced slightly prolonged bleeding times and the dose was reduced. One patient's tinzaparin dose was reduced due to subconjunctival haemorrhage not thought to be connected with tinzaparin. One patient showed signs of clotting and the dose was increased. No adverse effects other than prolonged bleeding were noted. Hair loss abated and new hair growth occurred. Switching from UFH to tinzaparin achieved at least a 30% cost saving.

**Conclusions:** Tinzaparin is an effective, cost efficient agent for anticoagulation of the nocturnal dialysis circuit. No additional clotting or bleeding was seen compared with UFH and no accumulation occurred with daily usage. Patient satisfaction improved due to lack of hair loss and ease of manipulation of tinzaparin vials rather than UFH ampoules.

**MP409 CALCIUM MASS BALANCES IN ON-LINE HDF USING CITRATE-CONTAINING ACETATE-FREE AND REGULAR DIALYSIS CONCENTRATES**

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**Introduction and Aims:** Citrate-containing acetate-free haemodialysis concentrate may potentially improve removal efficiency and reduce the inflammatory impact of dialysis, but the propensity of citrate to form complexes with calcium (Ca) is likely to affect the Ca transport. We evaluated the mass balance of Ca (CaMB) and Citrate (CitMB) during haemodiafiltration (HDF) with a new citrate containing acetate-free dialysis fluid versus a regular dialysis fluid.

**Methods:** This randomized cross-over study enrolled 18 stable ESRD pts (71 ± 11 yrs) regularly on 4.5 hours on-line postdilution HDF treatments. Dialysis fluid prepared from SelectBag® Citrate concentrate (1.5 mM Ca, 1 mM citrate, 0 acetate; Ca-) was compared to regular dialysis fluid (1.5 mM Ca, 0 citrate, 3 mM acetate; Ac-). Each patient was treated for one week with Ac-HDF and then switched to Cit-HDF for another week, or vice versa. All patients were treated with 2.1 m2 Polyflux dialyzers (Gambro). In the mid-week session of each period Ca (total and ionized) and citrate levels were measured in plasma and dialysis fluid at start, at 60 and 120 minutes, after start, and at end of treatment. CaMB and CitMB were calculated from total Ca and citrate levels in dialysis fluid. Citrate in plasma and dialysis fluid was analysed by suppressed-conductivity anion-chromatography. Anion-separator: 0.3x25 cm IonPac Fast Anion IIIA (Dionex Corp., U.S.A.); mobile phase: 20 mmol/L NaOH aqueous solution; flow-rate: 1.0 mL/min.

**Results:** The convective volume, set automatically by TMP biofeedback (UltraControl, Gambro), was 26.3 ± 3.3 in Ac-HDF and 26.0 ± 3.9 L in Cit-HDF (p=0.73). Using 1.5 mM Ca in dialysis fluid, the plasma total Ca level was stable during Cit-HDF (from 2.37 ± 0.14 to 2.42 ± 0.11 mM, p=0.13), while it increased during Ac-HDF (from 2.31 ± 0.12 to 2.63 ± 0.16 mM, p<0.001). The plasma ionized Ca level decreased during Cit-HDF (from 1.12 ± 0.07 to 1.07 ± 0.03 mM, p<0.001) whereas it increased in Ac-HDF (from 1.13 ± 0.05 to 1.22 ± 0.03 mM, p<0.0001). CaMB was different between the two periods (p<0.0001): removal of 274 ± 260 mg Ca in Cit-HDF versus delivery of 125 ± 174 mg Ca in Ac-HDF. Plasma citrate level increased in Cit-HDF (from 0.12 ± 0.05 to 0.40 ± 0.10 mM, p<0.001), while it was stable during Ac-HDF (from 0.13 ± 0.02 to 0.12 ± 0.05 mM, p<0.24). CitMB indicated that Cit-HDF was associated with a delivery of 5.3 ± 3.8 g citrate, while Ac-HDF a removal of 0.8 ± 0.4 g (p<0.0001). **Conclusions:** With the same Ca concentration as in regular dialysis fluid the use of 1 mM citrate dialysis fluid in on-line postdilution HDF resulted in a different Ca mass balance and a delivery of 5g of citrate. Our results suggest a need to reevaluate the prescription of Ca in dialysis fluid when shifting to citrate-containing HD concentrates.
PERITONEAL DIALYSIS II

MP410 CRP AS AN INDICATOR OF INFAMMATION IN PATIENTS WITH LOW AND HIGH PERITONEAL PERMEABILITY AND ITS RELATION WITH CAROTID ATHEROSCLEROSIS

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Introduction and Aims: High permeability in peritoneal dialysis (PD) patients had been reported to be associated with increased mortality. Cardiovascular disease is the most important cause of morbidity and mortality in patients with end-stage renal disease. The inflammation is thought to take part in development of atherosclerosis. The aim of this study is to investigate the relationship of peritoneal permeability type with carotid intima media thickness (CIMT) in PD patients.

Methods: Based on the standard peritoneal equilibration test, 56 PD patients (28 male/28 female) were divided in two transporter groups: LOW (Low average) and HIGH (High average) permeability. C-reactive protein (CRP) was measured as a marker of inflammation and CIMT was evaluated by high-resolution B-mode ultrasonography.

Results: 21 patients were LOW and 35 were HIGH transporters. Mean CRP level was significantly higher in the HIGH permeability group compared to LOW group (1.62 ± 1.7 mg/L vs. 0.84 ± 1.00 mg/L respectively, p=0.006). CIMT was found to be higher in the HIGH transporter group although it was not statistically significant. One of the causes of increased mortality rate in this group of patients may be explained by inflammation and atherosclerosis.

Conclusions: CRP, an indicator of inflammation, was found to be higher in the high transporter group. CIMT was found to be higher in high transporter group although it was not statistically significant. One of the causes of increased mortality rate in this group of patients may be explained by inflammation and atherosclerosis.

MP411 RADIOLOGICAL INSERTION OF TENCKHOFF CATHETERS FOR PERITONEAL DIALYSIS: A ONE YEAR SINGLE CENTRE EXPERIENCE

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Introduction and Aims: Peritoneal dialysis is an important home based dialysis modality in patients with end stage kidney disease. The initiation of peritoneal dialysis requires the timely insertion of a reliable Tenckhoff catheter. Traditionally at our centre, Tenckhoff catheters were inserted laparoscopically by surgeons, under a general anaesthetic. This may often be a time consuming process requiring prior surgical and anaesthetic review, as well as operating theatre time and inpatient bed availability. Radiological insertion of Tenckhoff catheters potentially allows for improved access to the procedure as it can be performed as a day case (ie. same day admission) under local anaesthetic and sedation. We report our one year experience following the introduction of this technique to our dialysis programme.

Methods: We performed a retrospective review of all Tenckhoff catheters inserted in the radiology department over a twelve month period. The procedure was first introduced in December 2011. Catheters were inserted percutaneously with the assistance of ultrasound and fluoroscopy. We recorded patient demographics including age, gender, body mass index, previous abdominal surgery and cause of end stage kidney disease. Details of the insertion procedure were also obtained including anaesthetic and sedation. We report our one year experience following the introduction of this technique to our dialysis programme.

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Results: A total of 30 Argyle swan neck Tenckhoff catheters were inserted until the end of December 2012. Mean (+/-SD) age of patients was 56 years (+/-14). Male to female ratio was 2:1. Mean BMI was 25.2 kg/m2 (+/- 4.8). Peritoneal dialysis was the initial dialysis modality in 22 (73.3%) patients. Of the 30 patients, 14 (46.7%) had previously undergone extraperitoneal abdominal surgery. All catheters were inserted successfully and were performed as a day case. Catheters were left for at least 10 days to reduce the risk of leakage: in two cases the catheters were used within five days, both without leaking. There were no cases of peritonitis or exit site infection. Catheter migration occurred in four patients (13.3%) but only one required surgical intervention. Minor pain issues were noted in six patients (20%) and bleeding around the exit site requiring suture in two patients (6.7%).

Conclusions: Radiological insertion of Tenckhoff catheters for peritoneal dialysis potentially provides improved access to catheter placement in a timely manner. It has a high technical success rate even in patients with prior abdominal surgery and can be performed safely as a day procedure. Establishing Tenckhoff catheters this way also has the potential to improve the uptake and initiation of this important home based dialysis modality.

MP412 VIDEOLAPAROSCOPIC REVISION OF MALFUNCTIONING PERITONEAL CATHETERS IS COST-EFFECTIVE IN CONFRONT TO HAEMODIALYSIS

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Introduction and Aims: Videolaparoscopy is the gold standard for revision of persistent malfunctioning peritoneal catheters. The surgical intervention aims to regain effective catheter function in order to proceed with peritoneal dialysis (PD). The aim of the study is to analyze the cost-effectiveness of videolaparoscopy revision based on a simulation of reimbursement costs.

Methods: Reimbursement costs of catheter malfunction management, based on diagnosis related groups and catheter malfunction interventions in the German national health system, are calculated for the following two simulations: Hospitalization for videolaparoscopic revision and follow up in daily automated home PD versus termination of PD, placement of a temporary central venous catheter, creation of an arterio-venous fistula and in-center bicarbonate haemodialysis (HD) with highly biocompatible membranes three times a week. The break-even point of the two strategies, indicating the time after intervention at equivalence of costs, is calculated. Videolaparoscopy interventions for catheter malfunction, performed between 2002 and 2011, were analyzed and followed up to 2012 with regard to permanence on PD and drop out.

Results: The break-even point of the two strategies (videolaparoscopy intervention 8597 Euro + PD 383 Euros/week versus vascular access 4551 Euro + HD 496 Euros/week) was determined at 36 weeks after intervention. Forty-three videolaparoscopy revisions were performed during the observation period. Twelve patients were still on PD at the end of the observation period (prolongation of catheter function: median 87 weeks), whereas the remaining 31 cases terminated PD in median 43 weeks after intervention. The total number of weeks remaining on PD after intervention was 4068 weeks, in confront to 1548 weeks (43 cases x 36 weeks) needed to reach break-even, corresponding to a gain in favor of videolaparoscopy of 2520 weeks. Theoretical savings amount to 284.760 Euro (3520 weeks x difference of costs between HD and PD 113 Euro/week) during the observation period of ten years. This is equivalent to annual reimbursement costs of 14 patients on automated PD, respectively 16 patients on continuous ambulatory PD.

Conclusions: PD is generating minor costs in confront to HD from the view point of the national health system. The need of videolaparoscopy revision at persisting catheter malfunction annuls this economic advantage. A cost-effective videolaparoscopy intervention has to result in a prolongation of catheter function and stay on PD of at least 36 weeks. The retrospective analysis of our videolaparoscopy program confirms the cost-effectiveness of the procedure.

MP413 CREATININE TRANSPORT ACROSS CHEMICAL MODIFIED PERITONEAL MEMBRANE IN VITRO - INFUENCE OF HYALURONAN

Teresa Grzelak1, Marta Kramkowska1, Marcellina Waczk1 and Krystyna Czczewska1

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Introduction and Aims: Hyaluronan is an essential component of peritoneal extracellular matrix. Its molecular function is to provide space for resident peritoneal cells and to maintain peritoneal integrity and remodeling of peritoneum, which have been changed by prolonged peritoneal dialysis and returning incidents of peritonitis.

Methods: We performed in vitro experiments with the isolated rabbit parietal peritoneum (placed inside a modified Ussing-type chamber), taking into account the anterior abdominal wall of white Hyplus 59 rabbits to evaluate the importance of chemical modification of mesothelium and interstitium to the peritoneal transport of creatinine in the present or absent of exogenous high molecular hyaluronan. Values for transfer from the intestinal (I) to the mesothelial (M) side of membrane (I→M) and in the opposite direction (M→I) were calculated using the mathematical model of mass
transport and are expressed as a coefficient of diffusive permeability [P (in centimeters per second)]. Two separate series of experiments were done with the applying chemical modified tissues (due to three minutes long 0.104 g/dL deoxycholate sodium acting on the mesothelial side of peritoneal membrane. In the first series, we examined creatinine (0.1 g/dL) across chemically modified tissue (for 120 minutes). In the second series, transport of this uremic toxin was measured before (15-60 min) and after (75-120 min) hyaluronan (0.1 g/dL, molecular weight 2000 kDa) application in to the experimental system from mesothelial side of membrane.

**Results:** In the first series, the rate of creatinine transfer remained constant, and no differences were observed for I-M transport and in the opposite direction (M-I). The mean value of P (± standard error of the mean) was 2.667 ± 0.162 (± 0.0001, cm/s) for bidirectional translocation (n=15). Application of hyaluronan sodium on the mesothelial side of membrane (n=14) lowered I-M transfer of creatinine by a mean of 27% (P < 0.003) and in the opposite direction by a mean of 18% (p < 0.03).

**Conclusions:** These results show that, in vitro, high molecular fractions of hyaluronan decrease bidirectional creatinine transport across the chemical modification peritoneal membrane. These observations may have clinical importance, especially in patients with disorders of peritoneal permeability, such as peritonitis.

**MP414 TECHNICAL SURVIVAL IN PERITONEAL DIALYSIS PATIENTS: QUALITY OF LIFE AND OTHER RELATED FACTORS**

İbrahim Güney1, Kültügin Türkmern2, Raziye Yazıcı1, Sevket Arslan1, Lütfüallah Altınepe1 and Mehdi Yeksan1

1Nephrology Department, Konya Research and Training Hospital, Konya, Turkey, 2Nephrology Department, Menguçel Gazı Training and Research Hospital, Erzincan University, Erzincan, Turkey, 3Nephrology Department, University of Nenehmet Erbakan, Meram Medical Faculty, Konya, Turkey

**Introduction and Aims:** Despite the improvements in peritoneal dialysis (PD), the impairment of both HRQoL and depression were found to be associated with technical survival in this population. We aimed to investigate the association between HRQoL, depression, other factors and technical survival in PD patients who were followed for 7 years.

**Methods:** One-hundred and five PD patients were included and followed for 7 years in this prospective study.

**Results:** Of 105 PD patients, 18 (17.1%) maintained PD, 87 (82.9%) shifted to hemodialysis (HD). The etiology of patients who shifted to HD were PD failure (41, 47.1%), peritonitis (33, 37.9%), leakage (6, 6.9%), catheter dysfunction (4, 4.6%). The main reason why patients couldn't achieve technical survival in PD patients in terms of age, gender, body mass index, hemoglobin, serum albumin, calcium, phosphorus, cholesterol, triglycerides, parathormone levels and education (p=0.05 for all). There were statistically significant difference between two groups in terms of PD duration, residual urine, co-morbidity and employment status (p=0.007, p=0.0018, p=0.0039, p=0.0001, p=0.028, p=0.008, respectively). When the groups were compared regarding health related quality of life (HRQoL) scores, HD patients who shifted from PD had lower physical functioning (58.73 ± 30.4 vs 81.71 ± 21.4, p=0.001), role physical (22.41 ± 33.5 vs 43.12 ± 27, p=0.0039), physical component scale (PCS) (47.98 ± 20.7 vs 62.61 ± 19.9, p=0.007). BD1 scores of PD and HD patients were not found to be statistically significant (p=0.05 for all). Employment status, age, PD duration, residual urine, diabetes, creatinine, urea, Kt/V and PCS were entered in the model of Cox-regression analysis. Among these factors, increase of 1 point in PCS (increase of 1% in Kt/V) and first point in employment status were found to be the independent predictors of technical survival.

**Conclusions:** We conclude that increase in PCS, decrease in serum creatinine and employment status were associated with higher technical survival in PD patients after 7 years of follow-up period.

**MP415 PERITONEAL DIALYSIS - RISK FACTOR FOR GLYCEMIC VARIABILITY**

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**Introduction and Aims:** In patients with chronic kidney disease insulin resistance is a quasi-permanent associated condition which is a fundamental cause of type 2 diabetes mellitus and atherosclerotic vascular disease. Glucose daily load in peritoneal dialysis (PD) patients is an additional risk factor for metabolic disorders more emphasized compared with healthy subjects, these differences can be explained at least in part by daily intake of glucose.

**Methods:** This was a single-centre, retrospective cohort study involving patients who were initiated on PD as the treatment modality for end stage kidney disease from 1st January 2006 until 31st December 2011 (n=209). 1 year all-cause mortality was determined as death between 3 months and 12 months of PD initiation and was retrieved from the hospital records. Those who died or transferred out or converted to HD within 3 months of PD were excluded (n=37). The serum sodium was taken as a single laboratory reading 3-6 months after initiation of PD. Those with serum sodium <135 mmol/L were categorized as hyponatraemic. Cox proportional hazard regression was used to calculate the hazard ratio (HR with 95% confidence interval (CI)) of 1-year mortality in the cohort of PD patients with hyponatraemia compared to those with normal serum sodium values, Age, gender, diabetes status and biochemical parameters (renal function test, bone profiles and full blood count) were adjusted as covariates.

**Results:** 172 patients were included in the final analysis (55% males, mean age 57.9 ± 15.2 years). 20% (n=36) of patients died within 1 year of PD initiation (50% males, mean age 61.4 ± 17.2 years). Mean serum sodium was 137 ± 5 mmol/L. 28% of patients were categorized as hyponatraemic. 35% 1-year mortality was observed in the hyponatraemic group compared to 15% in those with normal sodium (p=0.003). There was a significant increased risk of 1-year mortality in those with hyponatraemia compared to those with normal serum levels in PD (adjusted hazard ratio=3.75 (95% CI 1.47-9.47), p=0.003). No other factors were found to be significantly associated with 1-year mortality in our cohort of PD patients.

**Conclusions:** Hyponatraemia in stable peritoneal dialysis patients is associated with higher mortality at 1 year.

**MP416 HYPONATRAEMIA PREDICTS 1-YEAR MORTALITY IN STABLE PERITONEAL DIALYSIS PATIENTS**

Wan Ahmad Hafiz Wan Md Achnan1 and Nur Lisa Zaharan2

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**Introduction and Aims:** Hyponatraemia has been associated with increased mortality in patients with heart failure and liver failure, as well as those who were hospitalised. The link between death and hyponatraemia in patients with kidney disease is not well established, especially in peritoneal dialysis (PD) cohort. The aim of this study is to determine whether hyponatraemia independently predicts 1-year all cause mortality in patients on PD.

**Methods:** We retrospectively evaluated all PD patients who were initiated on PD as the treatment modality for end stage kidney disease from 1st January 2006 until 31st December 2011 (n=209). 1 year all-cause mortality was determined as death between 3 months and 12 months of PD initiation and was retrieved from the hospital records. Those who died or transferred out or converted to HD within 3 months of PD initiation were excluded (n=37). The serum sodium was taken as a single laboratory reading 3-6 months after initiation of PD. Those with serum sodium <135 mmol/L were categorized as hyponatraemic. Cox proportional hazard regression was used to calculate the hazard ratio (HR with 95% confidence interval (CI)) of 1-year mortality in the cohort of PD patients with hyponatraemia compared to those with normal serum sodium values, Age, gender, diabetes status and biochemical parameters (renal function test, bone profiles and full blood count) were adjusted as covariates.

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**Conclusions:** Hyponatraemia in stable peritoneal dialysis patients is associated with higher mortality at 1 year.
connector of the extension tubing is inserted into the indwelling catheter until the catheter abuts the plastic hub of the connector. (FIGURE 1b) - the clamp is opened to allow drainage of some mL of dialysate for washing out any contaminants, and then, a new peritoneal dialysis transfer tube is connected to beta-cap adapter - the glue mold is wrapped around the connector and secured with the locking ring (FIGURE 1c) - the sterile silicone glue is applied through the locking ring and the mold is filled (FIGURE 1d) - The glue mold must be removed after 48-72 hours - instructions from the fabricant say that routine peritoneal dialysis can be performed while the adhesive is curing.

Results: We presented here 4 salvage procedures on 4 silicon damaged peritoneal catheters. The catheters had been in situ for one month, 6 years, 6 years, and 5 years respectively before the damage. In patients 1 and 3, the broken catheter was repaired using the kit under prophylactic antibiotic therapy. The kit was used in patient 2, with an incomplete catheter perforation, for preventing future complications. A personal application was used in patient 4 for alleviating his problems with the cycler. None of the patients suffered peritonitis or had dialysate leakage after several months of follow up.

Conclusions: - The breakage of the catheter enhances the risk of contamination and peritonitis and may lead to discontinuate the technique and to remove the catheter. - Repair of the damaged catheter using the Peri-path Repair Kit extends catheter life and prevents its replacement, allowing the patient to continue on PD.

Abstracts

**MP419**

**METABOLITE PROFILING OF PRETONEAL DIALYSIS EFFLUENT BETWEEN LOW AND HIGH-AVERAGE TRANSFER PATIENTS - A PILOT STUDY**

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**Introduction and Aims:** It is known that outcome of peritoneal dialysis (PD) patient is associated with the capacity of solutes and water clearance. However the high molecular weight solutes in peritoneal dialysis effluent (PDF) and their clinical consequences have not been well studied. This study aims to explore the endogenous metabolite remove by PD, especially under different characteristics of peritoneal membrane transport.

**Methods:** A pilot study collected PDF from no-diabetic continuous ambulatory peritoneal dialysis patients underwent fast peritoneal equilibration test in a single centre from March 2012 to November 2012. Among patients with characteristic of high-average transport (HA) and low-average transport (LA), paired cases were selected, based on the gender, age, PTD/Kt/V, residual renal function (RRF) and duration of treatment. Ultra-performance liquid chromatography (UPLC) coupled with Q-TOF mass spectrometry were performed to investigated the metabolic profile in the PDF sample. After raw data acquisition and transformation by Agilent Masshunter Qualitative Analysis software, paired t-test and fold change analysis were conducted to screen feature differences. The different metabolites were defined by Agilent Mass Profiler Pro software finally.

**Table: MP419**

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**Conclusions:** Even normalizing PNA by IBW, values under 1g/kg per day as recommended, are widely prevalent in our patients, but levels under 0.8 g/kg per day were present in only 9%. As most of our patients were overweight or obese by measuring fat mass (anabolic state), we hypothesize that maybe some patients need lower values of nPNA than the recommended to achieve positive nitrogen balance.
Results: Twenty paired PDF samples from cases (female/male, 8/12; age, 58.4±16.3 years; dialysis duration, 14.3±5.6 months) with feature of HA and LA were defined. The metabolomics analysis indicated that distribution of 14 metabolites from 6 metabolic pathway (energy metabolism, lipid metabolism, carbohydrate metabolism, tricarboxylic acid cycle and amino acids metabolism) between HA and LA group had significant difference (p<0.05). Different Metabolites and involved pathway between HA and LA group. 3D PCA plots with the scores of principal components between HA (red) and LA (blue) group.

Conclusions: Current metabonomics results provided new insight into the effect of solutes remove by PD in clinical outcome.

**MP422 ANURIA: THE VILLAIN IN QUALITY OF LIFE AND SEXUAL DYSFUNCTION IN PERITONEAL DIALYSIS PATIENTS?**

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Introduction and Aims: There are several studies that address the quality of life of patients on peritoneal dialysis. Sexual dysfunction, anxiety and depression are highly prevalent in patients undergoing peritoneal dialysis (PD), but studies focusing these particular issues are scarce, especially, in an integrated approach to the patient with anuria. This study aims to evaluate sexual dysfunction and anxiety factors among PD patients, particularly in patients without residual renal function.

Methods: In this observational, cross-sectional study, all chronic PD patients in our Center were asked to complete a self-reported questionnaire: the International Index of Erectile Function (IIEF) for men and the Index of Female Sexual Function (IFSf) for women. Both groups answered the Hospital Anxiety and Depression Scale (HADS) to evaluate the prevalence of depression and anxiety and the EQ5D to measure the health outcome. The data collection consisted in several demographic, clinical and laboratory variables and others related to PD technique. Data analysis was performed in SPSS 20. Mann Whitney U and Chi square tests were used for group comparisons. We assessed confounding variables with multivariate regression analysis.

Results: We evaluated 57 PD patients (50, 9% males), with a mean age of 53, 9±15,7 years and 27, 6% with diabetes. Anuric patients comprised 24, 6% of the total. This risk group had higher C Reactive Protein (p=0,011), lower serum uric acid (p=0,034) and lower nPCR (p=0,002). Sexual dysfunction was present in 78,6% of anuric patients (p=0,036) and 46,5% of non anurics. Anuric males had a worse quality of life (p=0,014) and erectile dysfunction (p=0,04). In a multivariate regression analysis, anuria, diabetes and smoking showed a statistically significant and independent negative contribution to the worse IIEF score (p<0.001), in a model that accounts for 56% of sample variation (adjusted R square). The same was not true with the FSFI score in anuric women. On the other hand we did not find a significant impact of anuria under PD in depression and anxiety scores.

Conclusions: Although PD is feasible in anuric patients, this study emphasizes the importance of addressing sexual dysfunction, co-morbidities and the prevention of cardiovascular risk factors, in particular, of the anuric male, in order to provide a better and more dignified quality of life under PD.

**MP425 PERITONEAL DIALYSIS (PD): IS THE AGEING POPULATION REALLY A BARRIER IN EUROPE?**

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Introduction and Aims: PD is associated with significant benefits for patients and healthcare systems, but its usage varies greatly across Europe. Population characteristics (especially age) are often suggested as an explanation of this variation. The aim of this analysis was to verify if age was a limitation to the usage of PD in European countries.

Methods: The age distribution of ESRD patients and PD usage per age group in incident and prevalent patients were extracted from the 2010 ERA-EDTA registry report. Linear regressions were used to assess the association between PD usage per age and compared countries when clustered by their PD usage.

Results: In the 2010 ERA-EDTA registry report, 19.0% of the incident and 13.9% of the prevalent adult dialysis patients were on PD. The usage of PD patients declined with age in a linear way in incident (p=0.0034) and prevalent (p=0.0171) patients. Analysis by clusters (cluster 1: Nordics & Netherlands plus UK for incident patients only; cluster 2: other countries) showed that the usage of PD patients was significantly higher for all age groups in cluster 1 versus cluster 2 (p=0.0001). In older age groups (65-74 & 75+ age groups), PD use was 1.9-2.1 times higher in prevalent and 1.4-1.6 higher in incident patients in cluster 1 than in cluster 2 (vs 1.5-1.8 in other age groups). This creates a potential gap of 617 incident and 5586 prevalent older age group patients in cluster 2 countries (average per country: 88 incident; 696 prevalent) that could receive home treatment.

Conclusions: PD use significantly declines with age in countries submitting to the ERA-EDTA registry. However, data from cluster 1 countries show that PD usage could be significantly higher than what is currently achieved in cluster 2 countries, including in older patient groups, provided the health status of these older patients is similar across countries. Furthermore, as not all European countries are reporting to the ERA-EDTA registry, e.g., Germany where PD usage is low, these estimations are likely to be very conservative.
Nephrology Dialysis Transplantation

**MP424**

**OPTIMIZATION PERITONEAL DIALYSIS TREATMENT**

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**Introduction and Aims:** Conventional regime of continuous ambulatory peritoneal dialysis (CAPD) for most patients includes 4 exchanges with 3 equally short dwell daytime (4-5 hours) and a long dwell time at night (8-9 hours). The majority of patients are treated with glucose-based peritoneal dialysis (PD) fluids. This mode of treatment has the following problems: 1) rapid changes of transport characteristics, 2) difficulties in organizing work for patients, because they have to make exchange at the middle of their workday. We investigate how the new regime exchange (NMRE) - two short dwell times (every 3 hours) and two long dwell times (every 9 hours), which gives patients the opportunity to work, can influence peritoneal transport characteristics and adequacy of treatment.

**Methods:** We examined 30 patients on NMRE during 6 months. Patients were tested weekly for peritoneal KT\(V_{\text{urea}}\), daily ultrafiltration, ratio of the concentration of creatinine in the dialysate to its concentration in the blood (D/P creat) in the PBT test. These parameters were checked every 3 months. The control group had 30 patients on standard regime exchange (SRE) with same ages, sex and time CAPD treatment. All patients used identical concentrations of glucose in PD solutions and fill volume (2L).

**Results:** Index adequacy K\(T_{V_{\text{urea}}}\) in NMRE group was 2.3±0.2 initially and it didn’t change after 3 months. The patients on SRE had K\(T_{V_{\text{urea}}}\) 2.1±0.2 initially and increased after the observation time. Volume ultrafiltration daily (UI) in NMRE group was 1.3±0.4 and it didn’t change, but in SRE group daily UF declined from 1.5±0.3 to 1.3±0.3 (p<0.05) after 3 months and g to 0.7±0.4 after 6 months (p=0.003). Where D/P creat didn’t change in NMRE group.

**Conclusions:** NMRE regime can reduce negative influence glucose–based peritoneal dialysis solutions on the peritoneum. This situation was confirmed by the lack of change in D/P creat in NMRE group compared with the SRE group; it can be explained by decrease in the time exposure of high concentration of glucose. Also NMRE regime gives patients the opportunity to use long dwell daytime for work without exchanging dialysis solution.

**MP425**

**PERITONEAL REABSORPTION WITH THE PROLONGED PERITONEAL TEST FROM 4 TO 8 HOURS WITH GLUTOSE 1.36%, 2.27% AND 3.96%**

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**Introduction and Aims:** The peritoneal ultrafiltration failure (UFF) in peritoneal dialysis (PD) has improved with the determination of the free water transport. However the peritoneal or lymphatic reabsorption does not have a standardized and easy method applicable in clinical practice. The aim of the study was to calculate the peritoneal reabsorption (without distinction between the intestinal or lymphatic) from 4 to 8 hours in a prolonged peritoneal equilibration test (PPT) with 1.36, 2.27 and 3.86% glucose.

**Methods:** Thirty-two stable patients of a tertiary hospital were studied. Age 54.6±16.6 years; Male/female: 19/13; PD vintage: 20.4±18.0 months. ESRD: GN 16%; Interstitial nephropathy 16%, Polycystic Disease 6%, Vascular and nephroangiosclerosis 9%, diabetes mellitus 6%, unknown 34% and other 16%. Charlson index 5.34 ±2.56.

**Modality:** CAPD 18, APD 10, Incremental PD 4 patients. Methods: The night bag previous to the test was 2.27% glucose. The peritoneal tests (1.36%, 2.27%, 3.86% glucose) were done in random order in a period less than one month. During the PPT the peritoneal volume was emptied and refilled at 60' and 240' and finally voided at approximately 480'. A blood sample at 240' and peritoneal samples at 0', 60', 120', 240' and 480' were withdrawn. Urea, creatinine, glucose, Na+, K+ were determined in all samples. B-2-microglobulin, albumin, total protein, IgA and IgG were analysed at 240'. Data were processed in an Excel file. The PD-Adapt was also calculated.

**Results:** Additionnaly a Personal Dialysis Capacities test was carried out.

**Results:** The PPT showed no significant differences in solute transport parameters among the different glucose concentrations except in D/Do Gla (p<0.001), MTC Urea (p<0.001) and MTC K+ (p<0.001). The correlation with PD-Adequest was good, but less with the PDC. Water transport: All parameters were significantly different among the 3 glucose solutions: net UF, Na+, dip small, slow water transport, free water transport at 60' and 240'. However the 4-8 h. volume reabsorption (G1,36%: 265 ml CI 0.60-1.11; G3,86% 1.05 ml/min CI 0.77-1.33) were not significantly different. The paired t-test between the peritoneal reabsorption volumes and rates of the different glucose concentrations were not significantly different. Their respective Spearman's correlation coefficients were good.

**Conclusions:** The peritoneal reabsorption from 4 to 8 hours with different glucose concentrations is not different. 2. The Prolonged Peritoneal Test could be a practical method to standardize the peritoneal reabsorption rates.

**MP426**

**ZINC TRANSPORTER 7 INDUCED BY HIGH GLUTOSE ATTENUATES EPITHELIAL-TO-MESENCHYMAL TRANSITION OF PERITONEAL MESOTHELIAL CELLS**

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**Introduction and Aims:** Zinc (Zn) is an essential micronutrient and cytoprotectant involved in preventing many types of epithelial-to-mesenchymal transition (EMT) driven fibrosis in vivo. The zinc-transporter family SLC30A (ZnT) is a pivotal factor in the regulation of Zn homeostasis. However, its function in EMT in peritoneal mesothelial cells (PMCs) remains unknown. This study explored the regulation of zinc transporters and the role they play in cell EMT, particularly in rat peritoneal mesothelial cells (RPMCs), surrounding glucose concentrations and the molecular mechanism involved.

**Methods:** The effects of high glucose (HG) on zinc transporter gene expression were measured in RPMCs by real-time PCR. We explored ZnT7 (Slc30a7): the effect of ZnT7 over expression and siRNA-mediated knock-down on HG-induced EMT was investigated as well as the underlying molecular mechanisms.

**Results:** Over-expression of ZnT7 resulted in significantly inhibited HG-induced EMT in RPMCs, while inhibition of ZnT7 expression using a considerable siRNA-mediated knock-down of RMPCs increased the levels of EMT. Furthermore, over-expression of ZnT7 is accompanied by down-regulation of TGF-β/Smad pathway, phospho-Smad3,4 and Smad2,3, expression levels. The finding suggests that the zinc-transporting system in RPMCs is instilled by the exposure to HG.

**Conclusions:** The ZnT7 may account for the inhibition of HG-induced EMT in RPMCs, likely through targeting TGF-β/Smad signaling.

**MP427**

**A NEW CONNECTOR DECREASES THE PERITONEAL DIALYSIS RELATED PERITONITIS**

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**Introduction and Aims:** Peritonitis remains the leading cause of technical failure and a significant cause of morbidity in patients with peritoneal dialysis (PD). Contamination during fluid exchange is a common cause of peritonitis. A small lightweight connector for PD transfer set (Staysafe Catheter Extension Luer-Lock, Fresenius Medical Care, Germany) protected by pin and disinfection cap minimizes the risk of contamination has been developed. This study was to determine the new connector could decrease the incidence of PD-related peritonitis.

**Methods:** All incident PD patients (n=30) between May and October 2008 were into the new connector group, was compared with the conventional connector group of all patient months, respectively, p=0.044) and higher 1-year peritonitis free survival rate(55.6 vs. 80.0%, respectively, p=0.013). Exit site infection rate, however, was not different between two groups. The time spent per 51.68 patient months vs. one per 113.03 patient months, respectively, p=0.147). There were no differences in basic characteristics, causative microorganisms, prescribed antibiotics and managements between two groups.

**Conclusions:** This study suggests that the use of the new connector system decrease the rate of PD-related peritonitis.

**MP428**

**APD DOES NOT GIVE SUPERIOR MASS REMOVAL COMPARED TO CAPD DESPITE THE HIGHER NUMBER OF DWELLS IN APD**

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**Introduction and Aims:** Two observational studies showed more solute removal of protein bound solutes with hemodialysis, while time averaged plasma concentrations were not strikingly higher or even markedly lower in peritoneal dialysis (PD) patients. Furthermore, analogous discrepancies were found among PD modalities, with equal solute removal but higher time averaged concentrations in automated PD (APD) versus continuous ambulatory PD (CAPD). Next to being contradictory, equal removal between APD and CAPD seems remarkably in view of the higher dialysate volume used with APD, especially in cases of high transporter PD membranes or small solutes. To clarify those discrepancies, a cross-over study of APD and CAPD treatment
was performed investigating solute removal and time averaged concentrations. Methods: Fifteen chronic kidney disease patients on either CAPD (n=8) or APD (n=7) were included in a cross-over study performing ad random once 24h of CAPD(4x2L) and APD (5x2L, over 8 and 21 hours during the day) at midweek. PD effluent and urine were collected and stored at 80°C. A blood sample was taken before each 24h test session and immediately centrifuged, and plasma was stored at -80°C until analysis, to derive the time averaged concentration (TAC). Determinations of concentrations of the small water soluble solutes urea, creatinine (CREA), phosphorus (P), and uric acid (UA), the middle molecule beta-2-microglobulin (β2M), and the protein-bound solutes hippuric acid (HIA), 3-carboxy-4-methyl-5-propyl-2-furanpropionic acid (CMFP), indoxyl sulfate (IS), indole acetic acid (IAA), and p-cresylsulfate (PCS) were performed on all samples. Mass removal (i.e. sum of removal in PD effluent and urine, calculated as concentration times volume) and total clearance K (i.e. sum of dialyser clearance and renal clearance, calculated as mass removal during 24h divided by the TAC) were calculated for each PD modus.

Results: PD drained dwell volume was significantly higher for APD (13.3±3.0L) compared to CAPD (8.5±0.7L) (P<0.001), while urine output was significantly higher for CAPD (1.4±0.6L) compared to APD (1.0±0.5L) (P<0.001). For all solutes, no differences were found for the TAC. Total mass removal, however, was significantly higher in CAPD for the small water soluble solutes CREA (P=0.004) and P (P=0.008), while renal clearance was higher in CAPD for even more solutes: urea (P<0.009), CREA (P=0.005), UA (P=0.005), P (P=0.025), and β2M (P=0.020). Protein-bound solutes and β2M were not found being removed differently by both PD modalities.

Conclusions: Although total volume of used and drained dialysate is higher in case of APD, CAPD showed better mass removal for small water soluble solutes, but no difference for other solutes, and this independent of transport status. High volume APD just to increase clearance should not be recommended.

**EFFECTS OF PROTEIN LOSSES IN PERITONEAL DIALYSIS**

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**Introduction and Aims:** Several studies have shown that a high peritoneal albumin clearance is a risk factor for death in PD patients. This may be causative in that it may lead to increased protein loss, with consequent malnutrition, reduced immune competency, and death. We hypothesised that increased use of "dry" periods would reduce albumin losses, with consequent clinical benefit.

**Methods:** 201 incident PD patients were included in a prospective investigation. Peritoneal characteristics, including the area parameter and large pore clearance (LPC) were determined shortly after initiation using the Personal Dialysis Capacity (PDC) algorithm. High transporters were preferentially treated with APD, slow with CAPD. Every six months standard Kt/V analyses were performed, including determination of peritoneal albumin losses and peritoneal albumin clearance. Factors affecting s-albumin and peritoneal albumin loss, and their effect on prognosis were determined.

**Results:** Factors disposing towards low s-albumin were high age, high comorbidity, a high LPC, and a high albumin clearance. No independent effects of treatment prescription (APD/CAPD, dry/wet days) were seen. The results of this study were not included the patients with poor oral hygiene and had oral malodor depending on any intraoral etiology such as caries, periodontal disease and impacted teeth. Oral hygiene index (OHI) scores of the patients were calculated in order assess oral health. Systemic oral malodor of the patients were evaluated using organoleptic method. All measurements were performed pre-dialysis and post-dialysis (3 months after dialysis therapy) procedures.

**Results:** There were no statistically significant differences between the groups according to OHI scores (p>0.05). The Oral malodor scores were found lower at post-dialysis measurements than the baseline measurements in both group (p<0.05). The results of organoleptic measurements indicated that systemic oral malodor were higher in HD group (2.67±0.81) compared to PD group (1.98±0.57) (p<0.05).

**Conclusions:** This study revealed that PD was more effective than HD in decreasing of systemic oral malodor in ESRD patients.

**THE PRESENCE OF CAREGIVER DOES NOT AFFECT THE OUTCOMES OF PERITONITIS IN PERITONEAL DIALYSIS PATIENTS**

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**Introduction and Aims:** Peritonitis is an important cause of morbidity and mortality in PD patients. A long list of factors was evaluated to discover the possible risk factors of peritonitis, with some studies evaluating the influence of caregivers in peritonitis rate among these factors. Currently no study evaluated the influence of caregiver in the outcome of peritonitis episode. The purpose of the present study was to assess the
difference in term of outcome of peritonitis episodes in the patients who need caregiver help in the management of peritoneal dialysis (caregiver group) and in those patients who provide by themselves (self-care group).

Methods: We performed a retrospective, case-control study between caregiver group and self-care group. We analysed baseline patient conditions such as dialysis issue, comorbidity, residual renal function, BMI, albumin, haemoglobin, CRP. Furthermore, we evaluated the rate of healing and complications, including relapsing, catheter removal, and mortality. To reduce the interference of confounding factors, statistical analysis was performed in two classes of age: below and over 75 years old. All continuous parametric variables were presented as mean and standard deviation, while continuous nonparametric variables were reported as percentage. T Student test, Kruskal Wallis test, and Pearson’s chi-square test were used to compare continuous and categorical variables, as appropriate.

Results: We had 217 episodes of peritonitis in 42 months of observation, 87 (40.1%) occurred in the caregiver group. In <75-yr patients, we found a significant difference between caregiver and self-care patients in terms of dialysis (p=0.001), prevalence of Gram positive bacteria (p=0.028), haemoglobin (p=0.042) and dialysis adequacy (p=0.021), while we found significant difference in type of dialysis (p=0.001) in >75-yr patients. We did not appreciate any significant outcome difference in <75-yr patients, regardless of basal conditions. Conversely, we observed a lower rate of peritoneal catheter removal (p=0.017) in caregiver group for patients older than 75 yrs.

Conclusions: The presence of caregiver to manage peritoneal dialysis does not seem to affect negatively the outcome of peritonitis episode.

# Late Referral to Nephrologists is Associated with Elevated Blood Pressure in Peritoneal Dialysis Patients

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Introduction and Aims: Hypertension is known to be highly prevalent in peritoneal dialysis (PD) patients. Not only fluid overload but several predisposing factors may possibly predispose to elevation in blood pressure. This study was performed to elucidate pathogenesis of and a better approach to the hypertension in PD patients.

Methods: A retrospective cohort study was done including patients that had been followed for 2 years or more after initiation of PD in our Department. Blood pressure (ArMBP) was calculated as an average of mean blood pressure collected at the monthly clinic visit during the whole PD period. Independent variables include baseline laboratory data at the initial nephrology clinic visit, antihypertensive medications, fluid status assessed by echocardiogram and chest X-ray film, and body weight and urinary volume which were averaged during the whole PD period.

Results: Univariate analysis showed significant correlations between ArMBP and the following factors: predialysis followup period by nephrologists (R²=0.27, P=0.027), baseline eGFR (R²=0.23, P=0.0024), predialysis eGFR slope (R²=0.23, P=0.0028) and patients age at initiation of PD (R²=0.51, P<0.001). Fluid status, body weight, urinary volume or a number of anti-hypertensive medications were not found to be significantly correlated with ArMBP. Multivariate analysis showed significant correlation (P=0.003) between ArMBP and the baseline eGFR at the initial visit to nephrologists, where lower initial eGFR was associated with higher ArMBP. Using an ROC curve, a cutoff eGFR of 9.0ml/min/1.73m² had 94% specificity and 100% sensitivity against ArMBP 100mmHg or more.

Conclusions: Patients of late referral to nephrologists, i.e. at the eGFR of 9 ml/min/1.73m² or less, should be considered to carry a high risk for hypertension after PD and need to be aggressively treated to avoid hypertension.

# Added Low Dose of Spironolactone in Managing High Blood Pressure in Continuous Ambulatory Peritoneal Dialysis Patients

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Introduction and Aims: Hypertension and left ventricular hypertrophy contribute significantly to mortality and morbidity in dialysis patients. We studied the aldosterone effect with spironolactone in being used more frequently in the treatment of hypertension. We performed this study to assess the effect of spironolactone on blood pressure and its safety in continuous ambulatory peritoneal dialysis.

Methods: Thirty eight patients on continuous ambulatory peritoneal dialysis were selected for the study. Eligible patients received 25 mg spironolactone daily. Tablets were decreased to 25 mg, three times weekly, according to serum potassium and were discontinued in severe hyperkalemia (>6 mmol/l). No changes were made to regular medications. Biochemical, blood pressure and medication data were collected.

Results: Table 1 below shows controlled blood pressure was achieved after 6 months (p=0.001) and 12 months (p=0.001) compared with the baseline. The mean serum potassium level was 4.34±0.63 mmol/l at baseline and 4.45±0.24 mmol/l at study completion (p=0.24). There was no effect by spironolactone on aldosterone concentration. Congestive heart failure was not observed in one patient.

Conclusions: This study demonstrates that spironolactone therapy is effective in reducing blood pressure without producing hyperkalemia in continuous ambulatory peritoneal dialysis.

# Predictors of Cardiac Troponin T (cTnT) in CAPD Patients

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Introduction and Aims: Dialysis patients show elevated high-sensitivity (hs) cTnT. Peritoneal membrane is more permeable than artificial membranes used for regular extracorporal dialysis treatment. Therefore, loss of cTnT with diuretic tablets daily. Results: 87 (40.1%) cases were classified as having high serum cTnT (>0.010 ng/ml) and low serum cTnT (<0.010 ng/ml). Univariate analysis showed significant correlations between serum cTnT and the following factors: age (β=-0.740, p=0.024), arterial hypertension (β=-0.372, p=0.040) together with age, hypertension, diabetic nephropathy, and bicarbonate concentration, but not total cholesterol and triglycerides. Serum hs-cTnT group was compared with hs-cTnT determined in 54 HDF, 35 HF-HD and 158 LF-HD patients.

Results: Peritoneal loss of cTnT was 91.7 (37.4 - 819) ng/day and correlated with serum cTnT (r=0.823, p<0.001). Clearance was 1.96 (0.64 - 5.0) ml/min. In the best model for the logistic regression analysis (corrected R²=0.94, P=0.01), predictors of serum cTnT in CAPD patients were age (β=0.421, p=0.032), arterial hypertension (β=0.513, p=0.023), diabetic nephropathy (β=0.506, p=0.021), total cholesterol (β=0.554, p=0.013), tracycyclol (β=0.572, p=0.033), and bicarbonate concentration (β=0.740, p=0.024), whereas history of myocardial infarction, CAPD duration, serum albumin, P, PTH, and daily peritoneal cTnT loss was insignificant in this model. In the other model (corrected R²=0.595, p=0.004), significant predictors of serum cTnT were serum albumin (β=0.372, p=0.040) together with age, hypertension, diabetic nephropathy, and bicarbonate concentration, but not total cholesterol and triglycerides. Serum hs-cTnT in extracorporeal dialysis patients. Our aim was to establish predictors of serum hs-cTnT in CAPD patients and to compare hs-cTnT between CAPD, on-line hemodialfiltration (HDF), high-flux hemodialysis (HF-HD) and low flux hemodialysis (LF-HD) patients.

Methods: In multiple regression analyses, demographic, clinical, and laboratory data in various combinations were chosen as possible predictors of hs-cTnT in CAPD patients (n=27), including D/P, peritoneal loss and clearance of hs-cTnT. Serum hs-cTnT of CAPD group was compared with hs-cTnT determined in 54 HDF, 35 HF-HD and 158 LF-HD patients.

Conclusions: The presence of caregiver to manage peritoneal dialysis does not seem to affect negatively the outcome of peritonitis episode.

Blood Pressure (BP) | Baseline | After 6 Months | After 12 Months
--- | --- | --- | ---
Systolic BP Median (Percentiles 25,75) | 151.5 (140,156.2) | 140 (138,143.5)* | 139.5 (136,140)*
Diastolic BP Median (Percentiles 25,75) | 79 (75,83) | 75 (70,80)* | 74.5 (70,76)*
Abstracts

**MP435**
**THE RATE OF CENTER’S RESPONSE TO REGISTRY AND ITS RELATION TO PATIENT AND TECHNIQUE SURVIVAL IN IRANIAN CAPD PATIENTS**

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Introduction and Aims: The essential objective of the registry system is not only establishment of a comprehensive database but also facilitation and improvement the quality of patient management.

Methods: Data on 1472 patients CAPD patients which were monthly collected through questionnaires were analyzed. In 14 eligible center response rate to 08 defined questions was considered. Mean response rate denotes the average of responses to all questions in all patients of a particular center. Cox regression analysis was used to compare patient and technique survival in groups with different percentage of response rate.

Results: The highest mean response rate for the 14 centers was 70%, the lowest was 19%, and the average for all centers was 47%. Cox regression analysis showed that patient survival was significantly higher in the center with the highest response rate in comparison with the lowest one (HR:2.65;P<0.007), similar result was found for technique survival (HR=3.09;P<0.004). Likewise, patient and technique survival for the centers with average response rate of less than 60% was significantly lower compared to centers with more than 60% response rate (HR=1.48, P=0.022 and HR=1.98, P=0.001, respectively). The analyses also disclosed that the better patient and technique survival in the center with highest response rate (the best center) is not due to its’ better patient characteristics in comparison with our overall CAPD patients (P>0.05).

Conclusions: The quality of patient care and survival in a PD center may be accessed through level of response rate to questionnaires. Improvement in patient and technique survival then possibly could be achieved through medical team education and center instructive programs.

**MP436**
**CHARACTERISTICS OF INFECTING PATHOGENS AND THEIR ANTIMICROBIAL SUSCEPTIBILITIES IN PERITONEAL DIALYSIS RELATED PERITONITIS: REPORT OF RELATED EPISODES IN A MEDICAL CENTER OVER TEN YEARS**

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Introduction and Aims: To investigate the characteristics of infecting pathogens, their changes and antimicrobial susceptibilities on CAPD related peritonitis in our peritoneal dialysis center in the past 10 years.

Methods: 103 CAPD related peritonitis episodes in 87 patients from 2008 to 2012 were analyzed and compared with 82 episodes from 2003 to 2007. The causative pathogens, their antimicrobial susceptibilities and outcomes on CAPD related peritonitis from the two periods were retrospectively reviewed and compared.

Results: Culture negative rate decreased from 68.2% in 2003 to 41.5% in the last five years (P=0.021). Among culture positive peritonitis episodes, the incidence of gram positive bacteria peritonitis increased from 24.5% to 39.3% (P=0.052). This was mainly due to a significant increase in coagulase-negative staphylococcus peritonitis, which significantly increased from 5.2% to 34.5% (P=0.009). Gram negative bacteria peritonitis decreased slightly (46.3% vs 35.1%; P=0.295). The incidence of Klebsiella pneumoniae peritonitis significantly decreased (12.8% vs 3.5%; P=0.033), while Pseudomonas aeruginosa and Escherichia coli peritonitis rates slightly increased (4.7% vs 9.3%; P=0.338) and 18.7% (P=0.072). The decrease of fungal peritonitis rate was not significant (30.2% vs 17.6%; P=0.123). The comparison of clinical outcomes showed an improvement of total recovery rate from 68.8% in 2003 to 73.9% for 2008-2012 (P=0.09). The catheter removal rate decreased from 19.2% to 14.3% (P=0.238), and the mortality from 10.1% to 5.4% (P=0.118). In both periods, fungal peritonitis had the poorest results, which all the patients either withdrew from peritoneal dialysis or died.

Conclusions: Compared with that in 2003S, the culture positive rate for CAPD related peritonitis in 2008-2012 has been greatly improved. Coagulase-negative staphylococcus is the most common causative pathogen. The mortality and catheter removal rate have been markedly reduced in the last five years. Fungal peritonitis is the most important reason for patients’ dropout.

**MP437**
**TECHNICAL SURVIVAL OF PERITONEAL DIALYSIS CATHETERS: 16-YEARS EXPERIENCE OF A SINGLE CENTER**

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Introduction and Aims: Bedside percutaneous peritoneal dialysis catheter placement performed by the nephrologists is a well-accepted procedure in the clinical practice. However, in some patients, surgical technique is preferred. In this study, technical survival of peritoneal dialysis catheters was evaluated regarding the mode of insertion.

**MP438**
**THE EFFECTS OF SERUM LEPTIN LEVELS ON THROMBOCYTE AGGREGATIONS IN PERITONEAL DIALYSIS PATIENTS**

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Introduction and Aims: The most important causes of mortality and morbidity in chronic kidney disease (CKD) are cardiovascular diseases. The invention of leptin hormone was not added into the 1st (C1) cell, concentration of 25, 50, 100 ng/ml leptin was added into the 2nd(C2), 3rd(C3), 4th(C4) test cells, respectively. Serum leptin levels were measured by ELISA.

Results: It was determined that the effect of leptin on thrombocyte function. Serum leptin levels of patients with CKD have been detected higher than normal population. Patients receiving peritoneal dialysis (PD) appear to have the levels of serum leptin higher than CKD patients treated with hemodialysis and without dialysis. The aim of this study is to investigate the effects of serum leptin levels on thrombocyte aggregations in PD patients.

Methods: Forty-three PD patients and 15 healthy controls were included into this study. Thrombocyte aggregation was calculated from the whole blood by using Multiplate analyzer, subsequently the effects of different concentrations of human recombinant leptin hormone (25, 50, 100 ng/ml) on thrombocyte aggregations were investigated. Whole leptin hormone was not added into the 1st (C1) cell, concentration of 25, 50, 100 ng/ml leptin was added into the 2nd(C2), 3rd(C3), 4th(C4) test cells, respectively. Serum leptin levels were measured by ELISA.

Results: It was determined that the aggregation of the thrombocytes was inhibited by recombinant leptin hormone in both PD patients and control group. The curve, velocity and aggregation values were found statistically significant in 1st test cell when compared to 2nd, 3rd and 4th test cells in PD patients (P<0.000). When compared 2nd test cell to 3rd and 4th test cells, and 3rd test cell to 4th test cell we could not find any
significant differences for area under the curve, velocity and aggregation mean values statistically in PD patients. Area under the curve, velocity and aggregation values were found statistically significant in 1st test cell when compared to 2nd, 3rd, 4th test cells in control group. P values of ClvC2, ClvC3 and ClvC4 for area under the curve and aggregation values were found 0.001, and p values of velocity value were found 0.016, 0.004 and 0.000 for the same compared test cells respectively. When compared 2nd test cell to 3rd and 4th test cells, and 3rd test cell to 4th test we could not find any significant differences for area under the curve, velocity and aggregation mean values statistically in control group.

Conclusions: The inhibitor effect of recombinant leptin hormone on thrombocyte aggregation were proceeding when leptin concentrations was more than 25 ng/ml however it was not significant statistically. Further researches including more PD patients are required to prove the action of leptin hormone on thrombocyte aggregation or its effects on bleeding tendency.

**MP439**

**RESISTANCE TO STIMULATING ERYTHROPOIESIS IN PATIENTS ON PERITONEAL DIALYSIS**

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Introduction and Aims: Several studies indicate a satisfactory response to treatment of anemia with erythropoiesis-stimulating agents (ESAs) in patients with chronic kidney disease. Resistance to these agents is associated with increased morbidity and mortality. The aim of this study is to identify possible factors involved in resistance to ESAs in patients on peritoneal dialysis.

Methods: A retrospective observational study in one year. Included 53 patients on peritoneal dialysis with minimum of 10 months. Patients with active infection, cancer, surgery or transfusion in the last 3 months were excluded. The study divided the patients into two groups: untreated and treated with ESAs. Treated patients were subdivided, based on the resistance index (RI) in sensitive or resistant to ESAs, being resistant those with RI> 9.

**Results:** The mean age of patients was 50.2 years, 57% were male. 49% were on automated peritoneal dialysis and 51% on manual therapy.

Statistically significant differences were found in the group treated with ESAs versus non treated group. 17% of the patients treated showed resistance to ESAs compared to the sensitive patients. Not appreciate, against that expected, notable differences between groups with respect to degree of hyperparathyroidism, or use of drugs that inhibit the renin angiotensin aldosterone or relating to hematological parameters.

Conclusions: The need to administer ESAs depends on several factors. In our study the time on peritoneal dialysis, proved to be a determining factor in whether or not receiving ESAs, so that patients receiving ESAs remained almost twice as long on a dialysis program than those who are not treated with ESAs. Preserving residual renal function and adequate nutritional status are key factors about not treatment with ESAs and if is necessary, an optimal quality of dialysis as assessed by Kt/V and weekly CCr, will mean that exogenous erythropoietin requirements are lower with the cost of ESAs and if is necessary, an optimal quality of dialysis as assessed by Kt/V and weekly CCr, and if is necessary, an optimal quality of dialysis as assessed by Kt/V and weekly CCr, than those who are not treated with ESAs.

**Methods:** All PD-related infections (both exit site and peritoneal) which occurred between Jan 2008 and Dec 2012 in Malta were retrospectively studied. Mean monthly temperatures were obtained from the Maltese Meteorological Office. The cumulative number of PD related infections were studied in both warm and cold months of the year. The total monthly infections were also correlated with the mean monthly temperatures.

**Results:** The warmest months in Malta are May to October, the coldest being November to April with mean monthly temperatures ranging from 19.6°C-27.1°C and 12.3°C-17.5°C respectively. There were a total of 150 PD related infections (including cause of death and death and negative pneumonia) and 158 exit site infection episodes. 45.6% and 52.0% of the exit site infections and peritoneal infections respectively occurred during the warm period of the year whilst 54.4% and 48.0% of the exit site infection and peritoneal infections respectively occurred during the cold period of the year (p<NS). The correlation coefficient of the cumulative monthly number of infections and the mean monthly temperatures of both the exit site infections and peritoneal infections was -0.36 and -0.03 (p<NS). 48.21% and 51.79% of the gram negative infections occurred in the warm and cold period respectively (p=NS) while 56.21% and 43.79% of gram positive infections occurred in the warm and cold period respectively (p=0.039).

**Conclusions:** There was no overall significant difference in the number of exit site and peritoneal infections between the cold and warm months in Malta. Nevertheless a significant warm period peak was observed with Gram positive organisms and with gram negative organisms. This may be attributed to various factors such as: increased outdoor activities, increased perspiration with consequent transportation of skin commensals to the PD catheter site, and possibly increased virulence of these organisms in warm environments.

**Abstracts**

**NPY440**

**THE EFFECT OF AMBIENT TEMPERATURE ON THE PERITONEAL DIALYSIS RELATED INFECTION RATES IN MALTA**

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Introduction and Aims: There are limited studies involving the effect of ambient temperature and seasons on the rate of Peritoneal Dialysis (PD) related infections especially in the Mediterranean basin. Malta; situated in the middle of the Mediterranean Sea has a typical Mediterranean Climate. To study for any variability in the rate of peritoneal dialysis (PD) related infections with different ambient temperatures and seasons in Malta.

**Methods:** All PD-related infections (both exit site and peritoneal) which occurred between Jan 2008 and Dec 2012 in Malta were retrospectively studied. Mean monthly temperatures were obtained from the Maltese Meteorological Office. The cumulative number of PD related infections were studied in both warm and cold months of the year. The total monthly infections were also correlated with the mean monthly temperatures.

**Results:** The warmest months in Malta are May to October, the coldest being November to April with mean monthly temperatures ranging from 19.6°C-27.1°C and 12.3°C-17.5°C respectively. There were a total of 150 PD related infections (including cause of death and death and negative pneumonia) and 158 exit site infection episodes. 45.6% and 52.0% of the exit site infections and peritoneal infections respectively occurred during the warm period of the year whilst 54.4% and 48.0% of the exit site infection and peritoneal infections respectively occurred during the cold period of the year (p<NS). The correlation coefficient of the cumulative monthly number of infections and the mean monthly temperatures of both the exit site infections and peritoneal infections was -0.36 and -0.03 (p<NS). 48.21% and 51.79% of the gram negative infections occurred in the warm and cold period respectively (p=NS) while 56.21% and 43.79% of gram positive infections occurred in the warm and cold period respectively (p=0.039).

**Conclusions:** There was no overall significant difference in the number of exit site and peritoneal infections between the cold and warm months in Malta. Nevertheless a significant warm period peak was observed with Gram positive organisms and with gram negative organisms. This may be attributed to various factors such as: increased outdoor activities, increased perspiration with consequent transportation of skin commensals to the PD catheter site, and possibly increased virulence of these organisms in warm environments.

**Abstracts**

**NPY441**

**THE INFLUENCE OF PERITONEAL DIALYSIS MODALITY ON THE 1-YEAR RATE OF DECLINE OF RESIDENT RENAL FUNCTION**

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Introduction and Aims: The use of automated peritoneal dialysis (APD) has increased substantially over the last years. However, the influence of different PD modalities on the decline in residual renal function (RRF) is unclear due to inconsistencies among studies. In particular, the effect of APD modalities [continuous cyclic peritoneal dialysis (CCPD) and nightly intermittent peritoneal dialysis (NIPD)] on RRF has not been examined in a large cohort of patients.

**Methods:** We conducted a single-center retrospective study to investigate the association between PD modalities and decline in RRF in 142 incident PD patients (34 on CCPD, 36 on NIPD, and 72 on CAPD). RRF was assessed as the average of the 24-hour urine urea and creatinine clearance measured within 2 months from PD start and at 1 year after PD initiation. We defined 1-year decline rate of RRF as the change in RRF between baseline and the 1-year follow-up.

**Results:** There were no statistically significant differences in baseline characteristics, including baseline RRF (CCPD vs. NIPD vs. CAPD: 5.33 ± 1.92 vs. 5.31 ± 0.9 vs. 4.61 ± 2.54 ml/min/1.73 m², P = 0.149). The RRF at 1 year after PD initiation was 1.98 ± 2.20 ml/min/1.73 m² in CCPD patients and 3.63 ± 1.67 ml/min/1.73 m² in NIPD patients, which were moderately lower than 4.23 ± 5.51 ml/min/1.73 m² in CAPD patients (P = 0.064). Moreover, there was no significant difference in the 1-year rate of decline of RRF between CCPD and NIPD patients, although APD patients had a faster 1-year RRF decline rate than CAPD patients (CCPD and NIPD vs. CAPD: 45.8 ± 36.6 vs. 1.17%/year, P = 0.045). APD was associated with a more rapid decline in RRF in patients with ESRD undergoing PD, although multivariate analysis attenuated the significance of this finding (β = −40.56; 95% CI, −81.80 to 0.80; P = 0.054).

**Conclusions:** Our results suggest that CAPD might be more helpful than APD for preserving RRF during the first year of dialysis therapy, although there was no...
significantly different in the 1-year rate of decline of RRF between the two APD modalities.

**MP442**

**AGE AS A RISK FACTOR OF OVERHYDRATION IN PATIENTS ON PERITONEAL DIALYSIS**

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**Introduction and Aims:** Chronic overhydration is a prevalent problem in patients with end-stage renal disease and is associated with numerous complications. The main aim of this study was to assess the impact of age on overhydration, and its relationship with markers of cardiovascular risk in peritoneal dialysis (PD) patients.

**Methods:** The study was performed on 59 PD patients. The patients were divided into two groups depending on their age (group A, 27 patients, <65 years old, mean age 49.41±11.63 years; group B, 22 patients, ≥65 years old, mean age 67.78±13.98). In both groups, the degree of overhydration was assessed with the use of bioimpedance analysis and clinical criteria. NT-proBNP concentration in the serum and the nutritional status (SGA) were measured. Echocardiography and chest X-ray examination were performed to assess the presence of cardiovascular complications.

**Results:** There was a clear correlation between age with clinical features of overhydration (r=0.26; p=0.04) and with the results of bioimpedance analysis (BIA) (r=0.25; p=0.05). The older group of patients had significantly higher BIA overhydration (1.52±2.59 vs. 1.86±2.12 kg; p<0.05), presented with more aortic atherosclerotic changes (6 vs. 18; p=0.01) and had a reduced ejection fraction (EF 58% vs. 49%; p=0.02). In both groups high comparable NT-proBNP concentration in the serum were observed (3368±1898 vs. 5333±5662 pg/ml; n.s.). A significant relationship between age and nutritional status was demonstrated (r=0.39; p<0.01).

**Conclusions:** Older age seems to be a potential predictor for higher fluid overload. Overhydration may be potential risk factor for the development of cardiovascular complications. In PD patients, bioimpedance analysis seems to be a better method for the assessment of overhydration, dry body weight and cardiovascular risk than with other methods. However, further research in this area is necessary.

**MP444**

**RANDOMISED PROSPECTIVE CLINICAL STUDY ON OUTCOME OF PERITONEAL DIALYSIS IN PATIENTS USING NORMAL VERSUS REDUCED GLUCOSE DIALYSATE SOLUTION**

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**Introduction and Aims:** Patients on peritoneal dialysis have a better survival if residual renal function is preserved. This study was a randomized prospective study to evaluate normal versus reduced glucose content in the dialysate solution. Patients were followed over 12 months.

**Methods:** In this prospective randomized clinical study patients starting with peritoneal dialysis were assigned to a treatment regimen with normal or reduced glucose content in the dialysate solution. Each group contained 10 patients. Baseline characteristics, clinical chemistry, markers of endothelial function (Tie-2, Ang-2) as well as residual renal function were assessed after 3.6, 9 and 12 months.

**Results:** Patients assigned to lower glucose dialysate solution showed less gain of weight over time. Furthermore, this group also showed less decrease of residual renal function compared to the normal glucose group. No difference in blood glucose levels and HbA1c serum lipids, red and white blood cell count and liver function parameters were observed. Tie-2, Ang-2 and ADMA levels did not show significant differences.

**Conclusions:** Our study shows that reduced glucose content in dialysate solutions preserves residual renal function in PD patients. Furthermore, lower glucose dialysate contributes to more stable body weight.

**MP445**

**LONG-CHAIN FATTY ACIDS: A RARE CAUSE OF CHYLOUS ASCITES IN ADULT CONTINUOUS AMBULATORY PERITONEAL DIALYSIS PATIENTS?**

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**Introduction and Aims:** Continuous chyle leak can cause a decrease in immunity and loss of fat, resulting in recurrent infections, malnutrition and even obstruction of the peritoneal catheter among peritoneal dialysis patients. Chylous ascites typically occurs due to congenital anomalies of the lymphatic system or secondary to abdominal trauma or surgery in a child. However, is Long-Chain Fatty Acids a rare cause of chylous ascites in adult continuous ambulatory peritoneal dialysis (CAPD) patients? The literature has not been seen.

**Methods:** A 63-year-old female was treated with CAPD for end-stage renal disease 4 weeks due to chronic glomerulonephritis. Four weeks after catheter insertion via an abdominal operation, she was initiated on an intravenous infusion of 10 % Medium and Long chain Fat Emulsion Injection (produced by Baxter, 250 ml containing long-chain fatty acids 12.5 g IV) and oral administration of Enteral Nutritional Emulsion (TP-HE, 500 ml containing long-chain fatty acids 8 g, orally) once daily. The indication for this was poor nutritional intake. Three days later, the peritoneal effluent became "milky". The milky effluent was most apparent on the first drain of each day.
She had not been prescribed calcium channel blockers and she had no history of liver disease, portal hypertension, nephrotic syndrome or pancreatitis.

Results: Peritoneal effluent cell counts were normal and cultures were negative. Peritoneal effluent triglyceride levels were 220 mg/dl which was higher than the diagnosis criterion of chyloliproteinemia (defined as triglyceride levels > 110 mg/dl). Investigations to detect a cause of chyloliproteinemia were negative. The intravenous infusion of Long-chain fatty acids and the oral administration of Enteral Nutritional Emulsion were stopped and the chyloliproteinemia rapidly resolved. It was decided to transfer the patient from peritoneal dialysis to hemodialysis for two weeks to allow her peritoneum to rest. She subsequently resumed peritoneal dialysis with no recurrence of her chylous ascites. Because of the poor nutritional status of the patient, the two fatty acid products were stopped and then the chyloliproteinemia appeared again. From then on, the two fatty acid agents were not used any more for the patient. The patient did not suffer any side-effects from this and, in particular, did not develop peritonitis, lymphopenia or worsening malnutrition.

Conclusions: We highlight a new cause of chyloliproteinemia in adult CAPD patients. In this case, the etiology was high doses of Long-chain fatty acids. This is supported by the fact that the chyloliproteinemia disappeared after these agents were stopped and recovered when they were re-started because of the poor nutritional status of the patient. To our knowledge, this is the first case of such an occurrence. The conservative treatment is effective enough in chylous ascites in our patient.
Introduction and Aims: Levetiracetam is a frequently used drug in the therapy of partial onset, myoclonic and generalized tonic-clonic seizures. Levetiracetam (molecular weight (170.2 Da) is rapidly absorbed after oral ingestion with bioavailability of close to 100%. The elimination half-life in adults is 7 ± 1 hour. The cumulative renal excretion rate of levetiracetam is 66% in the first 48 hours (1). For open dialysis the package insert suggests a dose of 500–1000 mg once a day. As the small unbound molecule is easily removed by dialysis an supplemental dose of 250–500 mg after is suggested (1). Despite the fact that levetiracetam was approved 13 years ago, there are no data for dosing in peritoneal dialysis patients. We therefore analysed pharmacokinetical data of Levetiracetam in a patient on peritoneal dialysis for treatment of partial seizures.

Methods: Samples were centrifuged at 2800g for 5 min at 4°C and stored at -80°C until analysis. Levetiracetam levels were measured using an HPLC method.

Results: A 73-year-old Caucasian male was admitted to our tertiary care hospital to undergo elective angioplasty due to peripheral artery disease Fontaine’s stage IV. Due to diabetic and hypertensive nephropathy he suffered from chronic kidney disease stage 5 and had been undergoing peritoneal dialysis treatment for two years. On admission the patient complained about fatigue and stupor. A thorough history revealed that this coincided with the start of levetiracetam treatment. The patient received a dose of 500 mg bid due to suspected partial seizures with secondary generalization eight weeks to the recent admission. Due to the severe fatigue fractured his metatarsal bone of digitus V a week prior to admission. As fatigue and drowsiness did not improve over time, we assumed an overdosing of antiepileptic drug Levetiracetam. We found Levetiracetam levels in serum increased at about 29.8 mg/l, though being in therapeutic range of 20 – 65 mg/l. After discontinuing Levetiracetam fatigue and stupor disappeared within 24 hours. In order to establish the assumed accumulation /overdose of levetiracetam we reexposed the patient to the drug. After discontinuing Levetiracetam for 7 days, a single dose of 500 mg Levetiracetam was administered after end of automated peritoneal dialysis (APD). This was the treatment of choice due to a high transporter status in peritoneal equilibration test according to the classification of Twardowski (3). Blood was taken before ingestion and 2.5 h, 5 h, 6 h, 8.5 h, 10.5 h, 20 h and 24 h after ingestion as well as peritoneal fluid before ingestion and 7.5 h and 20 h after ingestion in order to study pharmacokinetics in peritoneal dialysis.

Levetiracetam serum levels were found to be considerably elevated in serum for more than 20 hours after ingestion. Serum levels and peritoneal fluid levels were nearly equivalent over the whole time period.

Conclusions: This case suggests that treatment with levetiracetam in patients undergoing dialysis should be regularly monitored to avoid supratherapeutic levels that could lead to severe sequelae.
INTRODUCTION AND AIMS: The aim of this study was to evaluate the association between the attainment of KDIGO guidelines for mineral and bone disorder (MBD) markers and the presence of various ankle brachial systolic pressure index (ABI) levels in our hemodialysis patients.

METHODS: In a cross-sectional study we analyzed 137 patients (85 male; mean age 55.8 ±14.2 years) dialyzed on average for 91.3±54.7 months. Initially, we evaluated the presence of peripheral arterial disease (PAD) (ABI lower than 0.9) and mediolcerous (ABI higher than 1.3) using ABI measurements. In addition, the serum levels and the proportion of the KDIGO guideline achieved ranges for MBD markers of the last 12 months were recorded between the groups of patients with various ABI (N=group with normal 0.9-1.3 ABI, H=group with high ABI ≥ 1.3, and L=group with low ABI ≤ 0.9) levels were compared.

RESULTS: In total 1294 data for corrected serum calcium (Ca), 1266 data for serum phosphate (P), 1244 data for Ca × P product and 224 data for serum intact parathyroid hormone (iPTH) were analyzed. There was no significant difference in any of the serum MBD marker levels between the groups: Ca (2.28±0.11; 2.34±0.19; 2.38±0.26 mmol/L), P (1.38±0.37; 1.48±0.52; 1.59±0.47 mmol/L), Ca × P product (3.23±0.89; 3.48±1.06; 3.73±1.09 mmol/L) and iPTH (146.1±121.6; 138.8±241.3; 188.4±172.3 pg/ml) in N, H and L group, respectively. In contrast, patients with normal range ABI (n=59) had significantly higher percentages of attained KDIGO recommended levels for corrected serum calcium (398/577; 69.8%), serum P (383/617; 62.1%) and serum Ca × P product (336/571; 58.8%) in comparison with patients (n=70; 53.1%) with lower ABI (<0.9) levels. Similarly, the patients (n=45) with high ABI (1.3-1.9) had significantly higher percentage of attained KDIGO recommendations for corrected serum Ca (442/661; 66.8%) vs 309/689; 44.8%), serum P (383/617; 62.1%) and serum Ca × P product (364/608; 59.8%) vs 274/487; 39.8%). On the other hand, there was no difference in percentages of the attained KDIGO recommended levels for serum iPTH between the groups of patients with various ABI (Ca 390/574; 67.9% vs 312/727; 42.9%), serum Ca (355/583; 60.9% vs 232/727; 31.9%) and serum Ca × P product (336/571; 58.8% vs 267/724; 36.8%). Similarly, the same pattern of significance was observed when the groups with different QTc interval duration were compared. Namely, the patients (n=62) with QTc interval < 430 (414.5 ±55.5) ms in comparison with patients (n=70; 53.1%) with QTc interval > 430 (490.8 ±32.3) ms had higher percentages of attained KDIGO recommended levels for corrected serum Ca (442/661; 66.8%) vs 309/689; 44.8%), serum P (383/617; 62.1%) and serum Ca × P product (364/608; 59.8%) vs 274/487; 39.8%). On the other hand, there was no difference in percentages of the attained KDIGO recommended levels for serum iPTH between the groups of patients with various QT (72/112; 64.3% vs 79/142; 55.1%) and QTc interval (76/118; 64.4% vs 75/136; 55.1%) duration.

CONCLUSIONS: HD patients with a higher percentage of achieved serum Ca and P within the KDIGO suggested levels have shorter post HD QT interval. The greater prevention of cardiac arrhythmias and sudden death in HD patients probably could be managed if a higher proportion of the recommended levels for serum Ca and P are achieved.
Abstracts

SERUM SCLEROSTIN LEVELS ARE ASSOCIATED WITH AORTIC VALVE CALCIFICATION IN PREVALENT HAEMODIALYSIS PATIENTS

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Introduction and Aims: Sclerostin is a protein expressed by osteocytes and has been shown to be a good predictor for bone formation in patients with chronic kidney disease. Sclerostin was only recently identified in the subendothelial layer of the human aortic intima, suggesting a possible role in the pathogenesis of aortic calcification. The aim of this study was to evaluate the relationship between serum sclerostin levels and aortic valve calcification in prevalent haemodialysis patients.

Methods: 101 patients (48 females and 53 males, mean age: 59±12 years, mean haemodialysis vintage: 56±28 months) were included in a cross-sectional study. Serum sclerostin levels were measured by ELISA (R&D Systems, Minneapolis, MN). All patients underwent unenhanced, electrocardiography–triggered dual–source computed tomography of the heart.

Results: Patients with aortic valve calcification had significantly higher serum sclerostin levels as compared to patients without calcified aortic valves (2.89±0.78 pg/mL vs 2.17±0.63 pg/mL, p<0.001). The patients are grouped according to tertiles of serum sclerostin levels as follows: (1st tertile: serum sclerostin levels <2.4 pg/mL, 2nd tertile: 2.4–2.7 pg/mL, 3rd tertile: serum sclerostin levels ≥2.7 pg/mL). The frequencies of aortic valve calcification were 36% (5 in 14 cases), 58% (30 in 53 cases) and 94% (33 in 35 cases), respectively (p<0.001 for the trend). In the multivariable regression analysis, age (B=0.46, p=0.015) and serum sclerostin levels (B=0.35, p=0.044) were independent factors for aortic valve calcification.

Conclusions: Serum sclerostin levels may be used as a predictor for aortic valve calcification in prevalent haemodialysis patients. This finding may be clinically relevant and may contribute to the management of aortic valve disease.
MP448
THE CARDIOVASCULAR EFFECTS OF CINCACALCET IN HEMODIALYSIS PATIENTS WITH SECONDARY HYPERPARATHYROIDISM

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Introduction and Aims: Secondary hyperparathyroidism (SHPT) in patients on hemodialysis is strongly associated with cardiovascular morbidity and mortality. Treatment of SHPT with cinacalcet decreases circulating parathyroid hormone (PTH) concentrations and lowers serum calcium and phosphorus concentrations. Therefore, we investigated the cardiovascular effects of cinacalcet in hemodialysis patients with SHPT.

Methods: We studied 12 hemodialysis patients with SHPT (serum intact PTH (iPTH) >300pg/mL). The study consisted of three phases: an initial run-in period of 16 weeks, including a wash-out period of four weeks (pre-treatment), a cinacalcet treatment period of 20 weeks (treatment), and 20-week follow-up after suspension of cinacalcet treatment (post-treatment).

Results: Cinacalcet significantly decreased serum iPTH (pre-treatment vs. treatment; 628.2±250.8 vs. 251.7±237.4 pg/mL, P<0.01), calcium, phosphorus, and calcium x phosphorus product (P<0.01), all of which returned to baseline levels at post-treatment. There was no change in C-reactive protein during the study period. There were significantly improvement in brachial flow-mediated dilatation (P<0.01) and enhanced cardiac-ankle vascular index (P<0.05) with cinacalcet treatment. Moreover, cinacalcet significantly improved diastolic E/ atrial F ratio (P<0.05) and the left ventricular mass index (P=0.04). Cinacalcet also increased serum NOx (P<0.05) and decreased serum isoprostane (P<0.05) and soluble intercellular adhesion molecule-1 concentrations (P<0.05). All of these values had returned to their pre-treatment concentrations at the end of post-treatment.

Conclusions: The addition of a calcimimetic cinacalcet ameliorates vascular endothelial dysfunction and cardiac diastolic dysfunction and hypertrophy by increasing nitric oxide production and decreasing oxidative stress in patients on hemodialysis with SHPT.

MP459
THE INFLUENCE OF CALCITRIOL TREATMENT ON CIRCULATING SOLUBLE RECEPTOR OF ADVANCED GLYCATION END PRODUC (S-RAGE), S100A12 (EN-RAGE) AND INTRACELLULAR RAGE-BINDING PROTEIN (EN-RAGE) IN HEMODIALYSIS PATIENTS WITH SECONDARY HYPERPARATHYROIDISM

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Introduction and Aims: Hemodialysis (HD) patients with secondary hyperparathyroidism (SHP) suffered from inflammation and vascular complication. The receptor for advanced glycation end products (RAGE) has emerged as a central regulator for vascular inflammation and atherosclerosis. The soluble RAGE (S-RAGE) and extracellular RAGE-binding protein (EN-RAGE) exerts respectively an anti-inflammatory and a pro-inflammatory ligand for RAGE on the development of atherosclerotic vascular complications. However, the influence of vitamin D treatment on RAGEs has been unknown. This study evaluated the influence of vitamin D therapy on RAGEs and inflammatory markers in HD patients with SHP.

Methods: We designed prospective study to investigate whether calcitriol treatment in HD patients with SHP affects inflammatory response and RAGES. Fifty one long-term HD patients (mean age 52.6 ± 14.7, 26 males and 25 females) were enrolled in the study to receive calcitriol treatment. We evaluated changes log-transformed value of S-RAGE, EN-RAGE, and IL-6 before and at the end of 8-weeks calcitriol treatment.

Results: Twenty-nine dialysis patients and 20 healthy controls were included in the present study. Twenty-nine uremic patients (age 78 ± 17 yrs) were enrolled for the study. After 8 weeks, level of serum 25(OH)D3 is significantly decreased (61.6 ± 24.2 ms to 48.2 ± 21.7 ms) in sevalemer (n:37), after one year (p<0.03), on the other hand in calcium acetate group (n:39) QTcmax was significantly increased (454.0 ± 37.4 ms to 465.0 ± 33.6 ms) while there was no significant change QTcD at the end of one year.

Conclusions: We suggest paricalcitol and sevelamer based treatment could be a good choice in MHD patients who are accepted to have a high risk of cardiovascular disease and sudden death. Additionally management of uremic acidosis could play a role for cardiovascular stability in MHD patients.

MP460
DIFFERENTIAL EFFECT OF VITAMIN D RECEPTOR ACTIVATORS AND PHOSPHATE BINDERS ON QT DISPERSION IN MAINTENANCE HEMODIALYSIS PATIENTS

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Introduction and Aims: Cardiovascular diseases are the most common cause of mortality in maintenance hemodialysis (MHD) patients. Secondary hyperparathyroidism (SHPT) and hyperphosphatemia are the major contributing factors for the development of cardiovascular disease. Prolongation of corrected maximal QT interval (QTcmax) and QT dispersion (QTcd) are the risk factors for cardiac arrhythmias and mortality. Aim of this study is to examine the differential effects of vitamin D receptor activators (VDRA) and phosphate-binding agents on QT parameters in MHD patients.

Methods: 149 eligible subjects out of 250 MHD patients were included. Patients were grouped according to type of VDRA and phosphate-binding treatment. Type of VDRA and phosphate-binding agents were kept constant for one year. All patients clinical and laboratory parameters data, cumulative calcium intake were recorded prospectively for one year. 12-lead electrocardiogram were performed in the beginning and at the end of one year. Specifically, we calculated the QT max and QTd. Each QT interval was corrected for the patient’s heart rate using Bazett’s formula. The correlation between QT parameter changes and serum electrolyte and acidbase alterations was analyzed at the end of one year.

Results: When sevelamer based therapy was compared to calcium acetate based therapy, QTcmax was significantly decreased (61.6 ± 24.2 ms to 48.2 ± 21.7 ms). There were no significant improvements in QTcD while in sevelamer group (p=0.003) on the other hand in calcium acetate group (p=0.05) at the end of one year.

Conclusions: Vitamin D receptor deficient patients with CKD and healthy controls(<30 nmol/L).

MP461
EFFECT OF 25-HYDROXYVITAMIN D3 (CHOLECALCIFEROL) ON ENDOTHELIAL DYSFUNCTION IN DIALYSIS PATIENTS

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Introduction and Aims: Cardiovascular event are high in chronic kidney disease compared to the general population. In patients with CKD, 25-hydroxyvitamin D3 (25(OH)D3) low level is known. 25(OH)D3 deficiency patients with CKD have higher incidence of cardiovascular events due to the oxidative stress and endothelial dysfunction (ED). Our aim in this study was to investigate the effect of 25(OH)D3 deficiency and supplementation on endothelial dysfunction in patients with CKD who are treated with dialysis.

Methods: Twenty-nine dialysis patients and 20 healthy controls were included in the present study. Twenty-nine uremic patients (age 58 ± 17 yrs) on dialysis and 20 healthy controls (age 38 ± 17 yrs) were evaluated for ED by using high resolution Doppler ultrasound of brachial artery. Also 25(OH)D3 deficiency patients(<30 nmol/ L) with CKD(n=17) and healthy controls(n=8) were evaluated for ED, before and after 8 weeks of oral calcitifederol (50,000 units) medication. Reactive hyperemia following 5 minutes forearm ischemia was accepted as endothelin-dependent vasodilatation flow mediated dilatation (FMD) and compared to endothelium-independent vasodilatation in response to sublingual glyceryl trinitrate(GTN). Also, in all the participant carotid intima media thickness(CIMT) was measured Serum samples from dialysis patients and healthy patients were examined in terms of 25(OH)D3, iPTH, other biochemical laboratory tests. Also, the same measurements were performed before and after 8 weeks of oral calcitifederol medication in 25(OH)D3 deficiency patients with CKD and healthy controls(<30 nmol/L).

Results: The average 25(OH)D3 levels in control and dialysis groups were 34.26±8.7 nmol/l, 30.01±13.4 nmol/l, respectively. Patients on dialysis had a lower FMD of 6.4±5.9 versus 15.99±8.19 and GTN% of 13.02±6.5 versus 25.48±12.98 of the controls. Level of p<0.05 Patients on dialysis had higher CIMT left of 0.79±0.15 versus 0.60±0.09 and right 0.78±0.14 versus 0.59±0.09 than the controls. Level of p<0.05. The lowest 25
**Abstracts**

**MP462 Cox regression models to predict all-cause and cardiovascular mortality.**

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>All-cause mortality</th>
<th>Cardiovascular mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>HR (95% CI)</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td></td>
<td>0.97 (0.92-1.02)</td>
<td>0.97 (0.92-1.03)</td>
</tr>
<tr>
<td>GFR, ml/1.73</td>
<td>1.00 (0.99-1.00)</td>
<td>1.00 (0.99-1.00)</td>
</tr>
<tr>
<td>OPG, pmol/L</td>
<td>1.08 (0.96-1.22)</td>
<td>0.96 (0.82-1.13)</td>
</tr>
<tr>
<td>CaSc, 100 Agatstone units</td>
<td>1.04 (1.005-1.07)</td>
<td>1.06 (1.02-1.11)</td>
</tr>
</tbody>
</table>

*In case of CaSc HR for the change of 100 Agatstone units is given.

**MP462 Simple correlations of selected variables with CaSc.**

<table>
<thead>
<tr>
<th>Independent variable</th>
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<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
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<td>0.0004</td>
</tr>
<tr>
<td>Dialysis therapy duration</td>
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<td>0.2</td>
</tr>
<tr>
<td>Ca</td>
<td>0.23</td>
<td>0.09</td>
</tr>
<tr>
<td>Pi</td>
<td>0.01</td>
<td>0.9</td>
</tr>
<tr>
<td>Ca x Pi</td>
<td>0.06</td>
<td>0.7</td>
</tr>
<tr>
<td>iPTH</td>
<td>-0.02</td>
<td>0.9</td>
</tr>
<tr>
<td>FGF-23</td>
<td>0.36</td>
<td>0.009</td>
</tr>
<tr>
<td>OPG</td>
<td>0.43</td>
<td>0.001</td>
</tr>
<tr>
<td>OC</td>
<td>-0.14</td>
<td>0.1</td>
</tr>
<tr>
<td>OPG</td>
<td>-0.03</td>
<td>0.8</td>
</tr>
</tbody>
</table>

**Conclusions:** These results show a significantly lower levels of 25(OH)D3 in the blood of dialysis patients compared to that of the controls. Also an increased level CIMT is shown with the dialysis patients. So cholecalciferol treatment could improve the ED and increases the level of FMD in patients on dialysis. The cholecalciferol supplement to dialysis patients may also prevent CVD, but this needs more long-term clinical studies.

**MP464 CALCULUS SCORING AS A NON-INVASIVE, SIGNIFICANT PREDICTOR OF MORTALITY IN DIALYSIS PATIENTS**

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**Introduction and Aims:** The aim of the study was to evaluate factors influencing all-cause and cardiovascular (CV) mortality in a group of peritoneal dialysis (PD) patients during a six year observation period.

**Methods:** The study included 55 patients (25 women, 30 men; mean age of 53 +/- 13 years) treated with PD for a median period of 24 months. Coronary arteries calcification score (CaSc) was measured using multi-row spiral computed tomography (MSCT). The concentrations: osteocalcin (OC), osteoprotegerin (OPG), osteopontin (OPN), fibroblast growth factor 23 (FGF-23), iPTH, total calcium (Ca) and phosphates (Pi) were measured. The data on mortality were collected over a 6 year period.

**Results:** During the six year observation period, 22 patients died (all-cause mortality), including 17 due to CV causes. Median overall survival on PD was 37 months. CaSc was a significant predictor of all-cause and CV mortality in simple analysis (HR=1.03 per 100 Agatstone units, p=0.002 and HR=0.05, p=0.003). In multiple models, CaSc was shown to predict total and CV mortality independently on OPG and FGF-23 levels and age of patients. Age, OPG and FGF-23 concentrations significantly positively correlated with CaSc (Spearman correlation).

**Conclusions:** Osteoprotegerin, FGF-23 concentration and age influenced the severity of coronary arteries calcification score. CaSc is a significant predictor of all-cause and CV mortality in the dialysis patient population.

**MP463 SERUM SCLEROSTIN LEVELS ARE INDEPENDENTLY ASSOCIATED WITH CORONARY SCORE AND CAROTID ARTERY ATHEROSCLEROSIS IN MAINTENANCE HAEMODIALYSIS PATIENTS**

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**Introduction and Aims:** Sclerostin is a protein expressed by osteocytes that has been shown to be expressed at the human aorta at the protein level. Recently, it has been shown that sclerostin was associated with renal osteodystrophy in dialysis patients. The aim of this study was to examine the association of serum sclerostin levels, coronary artery calcification score (CaScs) and carotid artery intima media thickness (CIMT) in maintenance hemodialysis patients.

**Methods:** Seventy two patients (38 females and 34 males) were subjected to 6 slice coronary computed tomography to evaluate coronary artery calcification. Moreover, patients underwent B mode ultrasonography of common carotid artery for measuring CIMT and evaluating the presence of plaques. Serum sclerostin levels were measured by an ELISA (R&D Systems, Minneapolis, MN).

**Results:** Mean serum sclerostin level was higher compared to healthy age and gender matched controls (472±1948 vs. 148±75 pg/ml, p=0.001). Correlations between CaScs and serum sclerostin levels (r=0.394, p=0.004), albumin (r=-0.471, p=0.004) and age (r=0.390, p=0.006) were noted. A negative but insignificant correlation was obtained between serum 25-hydroxy D3 levels and CaScs (r=0.162; p=0.245). Multivariable-adjusted regression analyses revealed that increased serum sclerostin concentrations were independently associated with increased CaScs (21.8% increase per 1 SD increase in sclerostin concentration, P<0.04). On the CIMT analysis, serum sclerostin levels were positively correlated with CIMT (r=0.439; p=0.001) while serum 25-hydroxy D3 levels were negatively correlated (r=-0.368; p=0.002). Patients with plaques on carotid arteries had higher serum sclerostin levels compared to ones with no plaques (2287±1681 vs 1174±917 pg/ml; p=0.016). Multivariable-adjusted regression analyses (also adjusted for serum 25-hydroxy D3 levels and calcitriol use) revealed that increased serum sclerostin concentrations were independently associated with increased CIMT (32% increase per 1 SD increase in sclerostin concentration, p=0.04).

**Conclusions:** In this work, free independent associations of serum sclerostin levels with both CaScs and RCIMT were noted. The pathophysiological impact of these results need further investigations.

**MP464 INFLUENCE OF HYDRATION STATUS ON ARTERIAL STIFFNESS IN HEMODIALYSIS PATIENTS**

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**Introduction and Aims:** Cardiac-aortic pulse wave velocity (PWV), a Fluid Overload (FO) of >15% (defined by bioimpedance spectroscopy, BIS) are considered to be strong predictors of mortality. The carotid-brachial pulse wave velocity (PWVb), although not considered to be a predictor of CV events, is still widely used to characterize the upper limb arterial stiffness. This approach also frequently shows differences between arms when a vascular access (VA) for HD is present. The aim of this study was to correlate both PWVa and PWVb with the hydration status and other biomarkers in HD pts from Argentina. We used a recently BIS-based device (BCM Fresenius) which delivers body composition parameters such as Lean Tissue Index (LTI), Fat Tissue Index (FTI) and hydration status expressed as total body water (TBW), extracellular volume (ECW), intracellular volume (ICW), overhydration (OH) and OH relative percentage ((OH/ECW)*100)/(Rel OH%)

**Methods:** We studied 63 prevalent pts (age=57±15 mean time on HD =61±15 months; women 33%; DBT=22%) Both PWVa and PWVb data were collected in a non-invasive fashion. The PWV data were recorded within 30 days of the BCM measurement in all cases. The Pearson correlation coefficient was used to establish the correlation of PWVa and PWVb with age (years), time on HD, blood pressure (BP), Systolic (Sys) and Diastolic (Dia), presence of Diabetes (DBT) and hydration status parameters delivered by BCM = TBW(L), ECW(L), ECW/ICW relation(E/I), LTI and Rel OH %. Pts were further divided into a high PWVa group and a low PWVa group based on the median PWVa (Median=10.13). To compare the groups we used ANOVA and comparison of proportions.Values are expressed as mean (standard deviation).

**Results:** There was a significant correlation between PWVb and age (r=0.471, p=0.005). PWVa, PWVb and DBT had a significant positive correlation (0.37, DBT(p=0.03). Peri HD and Rel OH% (p=0.32). To avoid the effect of VA on PWVb we selected the measurement of PWVb in arms without history of VA. The PWVb of this subgroup (n=43) showed correlation with Rel OH% (0.50, BPSys(0.42) and E/I
HDL concentrations were biochemically measured and LDL was calculated from the serum bicarbonate levels were measured in gas machine. Total cholesterol, triglycerides, and peritoneal dialysis (PD, n=20). Dialysis adequacy was defined by Kt/V for urea and were: regular haemodialysis (HD, n=34), predilution haemodiafiltration (HDF, n=42) patients on different dialysis modalities.

Results: The patients presented significantly higher values of hsCRP and TNFα than the control group (p<0.001), although HDL concentrations were significantly lower (p<0.001). The patients on peritoneal dialysis presented significantly higher serum bicarbonate levels than other groups of patient (p=0.004 and p=0.01 respectively) and lower ox-LDL levels (p=0.04 and p=0.02 respectively). Serum bicarbonate levels were inversely associated to hsCRP, ox-LDL and TNFα (r=-0.23, p=0.04, r=-0.289, p=0.01 and r=-0.33, p=0.004 respectively). ox-LDL was also inversely correlated to HDL (r=0.237, p=0.02). Logistic regression analysis revealed significant relationship between serum bicarbonate levels and both, HD and PAOD after adjustment for traditional risk factors.

Conclusions: Metabolic acidosis activating the inflammation and lipoprotein oxidation influences the cardiovascular morbidity of patients on renal replacement therapies. Peritoneal dialysis holds a better acidosis level and lower oxidized lipids than hemodialysis or hemodiafiltration.

**High Glucose Does Not Modulate the Formation of Vascular Calcification in Experimental Uremic Rats**

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Introduction and Aims: Vascular calcification is highly prevalent in patients with chronic kidney disease and diabetes, and is a risk factor of cardiovascular disease and mortality. Results of previous studies showed that high glucose-induced phenotypic switching of vascular smooth muscle cells (SMCs) into osteogenic cells plays a critical role in the calcification process.

Methods: We examined whether glucose concentration affects high glucose-induced SMC phenotypic switching and calcification in adenine-fed uremic rats and in cultured SMCs.

Results: First, formation of vascular calcification was compared among 4 groups: adenine-fed uremic rats; streptozotocin-injected hyperglycemic rats; adenine-fed and streptozotocin-injected uremic/hyperglycemic rats; and control rats. Vascular calcification was obvious in uremic rats and uremic/hyperglycemic rats, whereas it was not observed in other rats. Aortic calcium contents were significantly elevated in uremic rats and uremic/hyperglycemic rats, but they were not different between the two groups. Moreover, hyperglycemia had no effects on the reduced expression of SMC differentiation markers including smooth muscle α-actin and SM22α, and on the increased expression of osteogenic markers, such as Runx2 and osteopontin, in uremic rats. Second, cultured aortic SMCs were incubated in the medium with various concentrations of phosphate (0.9, 1.8, 2.7, and 4.5 mM/L) and glucose (5, 25, and 50 mM/L), and calcium deposition was measured. Although high glucose increased calcium contents in cultured SMCs in a dose-dependent manner, glucose concentration did not change the amounts of calcium deposition.

Conclusions: These results suggest that glucose concentration does not directly modulate high glucose-induced SMC phenotypic switching and vascular calcification.

**Metabolic Acidosis and ox-LDL as Risk Factors for Cardiovascular Disease in Patients on Renal Replacement Therapy**

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11St Opt of Medicine - Propaeastic, National & Kapodistrian University of Athens, School of Medicine, General Hospital "LAIKO", Athens, Greece, 1"Opt of Nephrology and Transplantation, General Hospital "LAIKO", Athens, Greece

Introduction and Aims: Metabolic acidosis and lipoprotein oxidation are common conditions in end stage renal disease patients. Maintenance dialysis therapies are often not able to completely correct the base deficit. However, chronic kidney disease (CKD), rather than dialysis treatment itself, may be a high risk condition for cardiovascular disease (CVD). We examined the role of metabolic acidosis and ox-LDL on CVD in patients on different dialysis modalities.

Methods: We studied 96 dialyzed patients, 62 males and 34 females, on mean age 62.1 ± 14.27 years old and 24 healthy controls. The treatment modalities which were applied were: regular haemodialysis (HD, n=34), predilution haemodiafiltration (HDF, n=42) and peritoneal dialysis (PD, n=20). Dialysis adequacy was defined by Kt/V for urea and serum bicarbonate levels were measured in gas machine. Total cholesterol, triglycerides, HDL concentrations were biochemically measured and LDL was calculated from the Friedewald equation. ox-LDL, hsCRP and TNFα concentrations were measured by ELISA. We built a logistic regression analysis to predict coronary disease (CD), heart failure (HF) and peripheral arterial occlusive disease (PAOD).

Results: The patients presented significantly higher values of hsCRP and TNFα than the control group (p<0.001), although HDL concentrations were significantly lower (p<0.001). The patients on peritoneal dialysis presented significantly higher serum bicarbonate levels than other groups of patient (p=0.004 and p=0.01 respectively) and lower ox-LDL levels (p=0.04 and p=0.02 respectively). Serum bicarbonate levels were inversely associated to hsCRP, ox-LDL and TNFα (r=-0.23, p=0.04, r=-0.289, p=0.01 and r=-0.33, p=0.004 respectively). ox-LDL was also inversely correlated to HDL (r=-0.237, p=0.02). Logistic regression analysis revealed significant relationship between serum bicarbonate levels and both, HD and PAOD after adjustment for traditional risk factors.

Conclusions: Metabolic acidosis activating the inflammation and lipoprotein oxidation influences the cardiovascular morbidity of patients on renal replacement therapies. Peritoneal dialysis holds a better acidosis level and lower oxidized lipids than hemodialysis or hemodiafiltration.
**MP468**

**PREDICTORS OF CHANGES IN PRE-DIALYSIS SYSTOLIC BLOOD PRESSURE IN AN INTERNATIONAL COHORT OF HEMODIALYSIS PATIENTS**

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**Introduction and Aims:** Prior studies indicated that hemodialysis (HD) patients from US experience an increase in pre-dialysis systolic blood pressure (preSBP) in the first year of dialysis. In contrast, preSBP declines in patients from Europe, Latin America, and Asia Pacific [Quinsburg, ERA-EDTA 2011]. We aimed to explore factors associated with changes in preSBP in a large international sample of HD patients.

**Methods:** The Monitoring Dialysis Outcome (MONDO) consortium consists of HD databases from Renal Research Institute (RRI) clinics in the US; Fresenius Medical Care (FMC) clinics in Europe, Asia Pacific (AP), Latin America (LA); KfH clinics in Germany; Imperial College, London, UK; Hadassah Medical Center, Jerusalem, Israel; and University of Maastricht, The Netherlands [Usuyuki, Blood Purification 2013]. Databases from RRI, FMC AP, and FMC LA were queried to identify all incident HD patients who survived at least 2 years on HD. We employed simple linear regression to compute pre-patient changes (slopes) of preSBP, post-dialysis weight, weekly erythropoietin (EPO) dose, and serum sodium between mins 12 and 24 from HD start. For each variable, “decline” was defined as a significant (P<0.05) negative slope and “increase” was defined as positive slope (P<0.05). Patients with non-significant slopes (P>0.05) were considered “stable.”

**Results:** We studied 6,883 patients (FMC AP N=1,483; FMC LA N=625; RRI N=4,275). 21% of the patients experienced increase in preSBP, with highest frequency in RRI (25.6%); Cornell (21.4%) and serum sodium between mins 12 and 24 from HD start. For each variable, “decline” was defined as a significant (P<0.05) negative slope and “increase” was defined as positive slope (P<0.05). Patients with non-significant slopes (P>0.05) were considered “stable.”

**Conclusions:** Our multi-national study indicates the existence of a trend towards preSBP increase in the second year on HD in the presence of EPO dose increase. In addition, an increase in serum sodium is associated with a decrease in preSBP. We found no clear relationship between changes in body weight and preSBP.
**MP470**

**OXIDATIVE STRESS BIOMARKERS AS PREDICTORS OF MORTALITY AND CARDIOVASCULAR DISEASE IN A COHORT OF HEMODIALYSIS PATIENTS**

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**Introduction and Aims:** Oxidative stress and inflammation are implicated in the pathogenesis of cardiovascular disease (CVD). Although C-reactive protein (CRP), as one of the markers of inflammation, is an established predictor of CVD and all-cause mortality, there is little evidence showing that serum biomarkers oxidative stress are useful in predicting CVD and/or mortality. The purpose of this study was to test a hypothesis that serum biomarkers of oxidative stress predict poor outcome in hemodialysis patients.

**Methods:** The subjects were 517 hemodialysis patients in a prospective cohort named DREAM that was followed-up from 2004 to 2009. At baseline, we assayed several biomarkers of oxidative stress including derivatives of reactive oxygen metabolites (dROMs), test is one of such biomarkers and predicts total anti-oxidant capacity of serum. We analyzed the association of these biomarkers with mortality and cardiovascular disease (CVD) events. Kaplan-Meier curves indicated that a higher dROMs predicted higher mortality, there is little evidence showing that serum biomarkers oxidative stress are useful in predicting CVD and/or mortality.

**Results:** At the start of HD, ER (>12 months) patients had higher proportion of naïve arteriovenous fistula (n=0.000), higher hemoglobin (g/dl) (82.46 ±1.67 vs 79.20 ±13.97, p=0.048), albumin (g/dl) (39.74 ±0.47 vs 35.78 ±6.31, p=0.000), diuresis (ml) (1325.64 ±672.87 vs 848.49 ±532.18, p=0.000) and lower LVMi (g/m2) (145.79 ±40.77 vs 166.60 ±52.23, p=0.031) than LR patients. During HD treatment until follow-up the study, ER (>12 months) and LR remain significantly different with pulse pressure (mmHg) (52.83 ±12.23 vs 58.14 ±16.06, p=0.023), hemoglobin (107.7 ±12.34 vs 101.05 ±14.36, p=0.005), albumin (39.01 ±2.72 vs 37.74 ±3.98, p=0.024) and Kt/V (1.25 ±0.21 vs 1.18 ±0.21, p=0.026). During follow-up, 27 of 89 patients in the ER (>12months) (30.3%) and 90 of 172 in the LR (47.7%) died, with significant difference in survival between ER (>12 months) and LR groups (log-rank, p=0.0005). All-cause mortality was higher both LR vs ER >6 months (HR 1.68; 95% CI, 1.15-2.45, p=0.007) and LR vs ER >12 months (HR 2.05; 95% CI, 1.33-3.15; p=0.001). Cardiovascular mortality did not differ between LR vs ER >6 months (HR 1.46; 95% CI 0.92-2.34, p=0.11), but was higher for LR vs ER >12 months (HR 2.44; 95% CI, 1.38-4.30, p=0.002).

**Conclusions:** This study showed that early regular nephrology referral above 12 months before initiation of HD was associated with a reduced risk of all-cause and cardiovascular mortality in HD patients.
Abstracts

Nephrology Dialysis Transplantation

MP474
PREDICTORS OF CARDIAC EVENTS IN END-STAGE RENAL DISEASE PATIENTS WITH NORMAL MYOCARDIAL PERFUSION SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY

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Introduction and Aims: Normal myocardial perfusion imaging is closely associated with very low rates of cardiac events and better long-term outcomes. However, little is known about its prognostic value in patients with end-stage renal disease (ESRD). Moreover, it is uncertain whether subsets of these patients are at increased risk for serious cardiac events, even in the presence of a normal perfusion scan.

Methods: A total of 266 incident ESRD patients underwent baseline cardiac evaluation with echocardiography and stress/rest single-photon emission computed tomography (SPECT). A summed stress score (SSS) <4 was considered normal, and 177 (61.9%) patients showed a normal SPECT.

Results: During the 4-year follow-up period, there were a total of 79 cardiac events. Patients with SSS <4 had significantly lower annual rates of cardiac events than those with SSS ≥4 (6.1% versus 13.2%, hazard ratio (HR), 0.60; 95% confidence interval (CI), 0.38–0.94). Among patients with SSS <4, however, cardiac event rates significantly differed according to baseline characteristics such as age, presence of diabetes and coronary artery disease, C-reactive protein levels. Regarding the echocardiographic parameters, left ventricular (LV) hypertrophy (LVH), decreased LV ejection fraction (LVEF), and increased LV mass index (LVMI) were closely associated with the development of cardiac events. After adjusting for traditional cardiovascular risk factors, every 10-unit increase in LVMI increased the adjusted hazard of cardiac events by 12% (p < 0.001). Findings were similar in the subgroup with normal SPECT (LVEF), and increased LV mass index (LVMI) were closely associated with the development of cardiac events.

Conclusions: ESRD patients with normal SPECT had a significantly lower risk of cardiovascular disease than those with abnormal SPECT. However, the baseline clinical and echocardiographic parameters strongly influenced the long-term prognosis of these patients. Particularly, increased LVMI was independently associated with cardiac outcomes in patients with normal SPECT.

MP475
CARDIAC HYPERTROPHY IS SUPPRESSED BY REDUCING UREMIC TOXINS AT THE EARLY STAGE OF CHRONIC KIDNEY DISEASE

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Introduction and Aims: Patients with chronic kidney disease (CKD) generally have a high risk of complications including accelerated cardiovascular disease than the general population. Left ventricular hypertrophy is a well-known feature of renal disease, and that mass correlates with survival in renal patients. Blood pressure is currently regarded as a candidate cause of cardiac hypertrophy in CKD. However, it seems unlikely that blood pressure alone causes hypertrophy of the heart. AST-120 is an oral cholesterol absorption inhibitor used for the treatment of CKD. Clinical studies have shown that AST-120 delays the progression of CKD and the initiation of dialysis therapy in pre-dialysis patients. Recently, AST-120 has been reported to prevent the progression of cardiac damage in CKD model rats and patients. In the present study, we confirmed the development of cardiac hypertrophy in CKD rat, and that these changes correlated with serum levels of uremic toxins that are the target of AST-120 action.

Methods: Eleven week-old Sprague Dawley rats were 4/5 nephrectomized and assigned with serum levels of uremic toxins that are the target of AST-120 action. Clinical studies have shown that AST-120- treated groups. We could not find the vascular calcified part in all rats. Among all the biochemical parameters measured in this study, only serum levels of uremic toxins showed significant differences as a result of AST-120 treatment. The relations between the cross sectional area of the heart and serum levels of uremic toxins (indoxyl sulfate (IS), p-cresyl sulfate (PCS), p-cresyl glucuronide (PCG) and hippuric acid (HA)) are evaluated. Overall, a strong and positive correlation was observed between cross-sectional area of the heart and serum levels of uremic toxins (r = 0.7, P < 0.001). These levels were limited only for CKD rats in non-AST-treated, AST-low, and AST-high groups, and particularly, a strong and significant positive correlation was observed for PCS (r = 0.814, P < 0.001) and PCG (r = 0.799, P < 0.001) levels in CKD rats.

Conclusions: We found a possibility that besides blood pressure, some serum uremic toxins (PCS, HA) may be involved in cardiac hypertrophy at the stage of moderate renal function impairment, before vascular calcification begins.

MP476
UREMIC FOOT: A SILENT KILLER AMONG DIALYZED PATIENTS

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Introduction and Aims: Foot ulceration (FU) is a common complication (15-25%) affecting patients with diabetes during their lifetime; it is associated with infections, amputation and death. Diabetes is responsible for 24-45% of incident renal replacement therapy, but Hemodialyzed patients (HDpts) have higher prevalence of other vascular risk factors (inflammation, calciphasis). Thus, the risk of FU is four times higher than in diabetic non HDpts and the risk of amputation is 10 times higher than in general population. We prefer the term “uremic foot” to define the ischemic lower limb chronic ulceration, which affects the quality of life, the mortality rate and the costs of health care. The aim of our retrospective study is to evaluate the prevalence of uremic foot among HDpts referred to our Centre.

Methods: We enrolled 316 prevalent and incident HDpts from January 2006 to December 2011, mean follow-up 34±24 months; mean age 67±14.9 years (65.2%) male, 101 (32.6%) diabetic, 136 (43%) with ischemic heart disease. We evaluated the history of surgical revascularization or percutaneous transluminal angioplasty (PTA), the prevalence of smoking peripheral arterial disease (sPAD), (intermittents claudicatio or no critical ischemia revealed through the Doppler ultrasonography), the presence of chronic FU and amputation (above or below the malleolus). We compared these data among HDpts and among non diabetic pts.

Results: During the 4-year follow-up period, there were a total of 79 cardiac events. Patients with SSS <4 had significantly lower annual rates of cardiac events than those with SSS ≥4 (6.1% versus 13.2%, hazard ratio (HR), 0.60; 95% confidence interval (CI), 0.38–0.94). Among patients with SSS <4, however, cardiac event rates significantly differed according to baseline characteristics such as age, presence of diabetes and coronary artery disease, C-reactive protein levels. Regarding the echocardiographic parameters, left ventricular (LV) hypertrophy (LVH), decreased LV ejection fraction (LVEF), and increased LV mass index (LVMI) were closely associated with the development of cardiac events. After adjusting for traditional cardiovascular risk factors, every 10-unit increase in LVMI increased the adjusted hazard of cardiac events by 12% (p < 0.001). Findings were similar in the subgroup with normal SPECT (LVEF), and increased LV mass index (LVMI) were closely associated with the development of cardiac events.

Conclusions: ESRD patients with normal SPECT had a significantly lower risk of cardiovascular disease than those with abnormal SPECT. However, the baseline clinical and echocardiographic parameters strongly influenced the long-term prognosis of these patients. Particularly, increased LVMI was independently associated with cardiac outcomes in patients with normal SPECT.

MP477
NT-proBNP IS A MORE SIGNIFICANT PROGNOSTIC BIOMARKER OF MORTALITY THAN TROPONIN T IN INCIDENT HEMODIALYSIS PATIENTS

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Introduction and Aims: Numerous previous studies have demonstrated that cardiac and inflammatory biomarkers are significant predictors of cardiovascular (CV) and all-cause mortality in ESRD patients, but most of the studies were retrospective or included small numbers of patients, only prevalent dialysis patients, or only measured one or two biomarkers. The aim of this study was to investigate the association between three cardiac biomarkers and mortality in incident hemodialysis patients.

Methods: A prospective cohort of 864 incident hemodialysis patients was followed for up to 30 months. Based on the median values of baseline NT-proBNP, cTnT, and hsCRP, the patients were divided into ‘high’ and ‘low’ groups, and CV and all-cause mortality were compared between each group.

Results: The CV survival rates were significantly lower in the ‘high’ NT-proBNP and cTnT groups compared to the corresponding ‘low’ groups, while there was no significant difference in CV survival rates between the two hsCRP groups. However, all-cause mortality rates were significantly higher in all three ‘high’ groups compared with each lower group. In multivariate Cox models, natural log of NT-proBNP and cTnT were found to be significant independent predictors of CV and all-cause mortality. Moreover, among the three biomarkers, NT-proBNP had the highest positive predictive values for not only CV mortality (AUC = 0.812, P < 0.001) but also all-cause mortality (AUC = 0.660, P = 0.003).

Conclusions: Although high levels of NT-proBNP and cTnT, but not hsCRP, are independently associated with CV and all-cause mortality in incident hemodialysis patients, the prognostic value of NT-proBNP for mortality is higher than that of cTnT.
THE IMPACT OF CATHETER ABLATION ON DIALYSIS PATIENTS WITH ATRIAL FIBRILLATION

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Introduction and Aims: Atrial fibrillation (AF) occurs significantly more frequently in dialysis patients than in the general population. AF causes significant clinical and hemodynamic deterioration such as low blood pressure during HD. AF is of particular clinical importance mainly because of the increased risk of stroke, and prophylaxis in one-third of hemodialysis patients with AF were reported to have thromboembolic complications within 1 year. Although maintenance of sinus rhythm is the ideal therapeutic goal in AF patients, AF and adverse effects of antiarrhythmic drugs offset the benefits of sinus rhythm. Use of warfarin is not recommended because of high risk of mortality in hemodialysis patients. Up to year 2000, treatment options were limited to medications that regulate the heart’s rhythm, electrical cardioversion to restore sinus rhythm, anti-coagulants therapy, and the Maze procedure. More recently, radiofrequency catheter ablation with pulmonary vein isolation has been developed as a nonsurgical alternative that may be recommended for patients with AF tolerant with medications.

Methods: Among 160 patients receiving dialysis therapy at Yokohama Minami Clinic, 16 (10 males and 6 females; mean age 71.2±11.2, range 50-91 years; mean hemodialysis duration 103.4±74.9 months) with AF (13 paroxysmal, 3 persistent) were enrolled. We performed complete isolation of the whole posterior left atrium including all pulmonary veins, guided by a 3D-mapping system (Ensite NavX) at The Arrhythmia Center, Hayama Heart Center.

Results: Box isolation therapy was performed in all 16 patients. A second session was performed in 6 patients (38%) because of AF recurrence. In two patients with persistent AF, third and fourth sessions were needed to maintain sinus rhythm. At 20.3±13.6 months of follow-up, all patients (100%) with persistent AF were free from recurrent AF or atrial tachycardia, and all patients with paroxysmal AF had no AF during dialysis. One patient developed cervical hematoma due to the patient’s sudden motion during therapy. Mild cerebral infarction occurred in only one patient during the follow-up period. There were no other complications.

Conclusions: In patient on dialysis, the optimal treatment for AF to restore and maintain sinus rhythm has not been established. In this collaborative investigation, radiofrequency catheter ablation in dialysis patients with AF achieved complete maintenance of sinus rhythm. Only one case of cerebral infarction occurred between 16 patients during 20.3±13.6 months of follow-up, compared to the reported incidence of over 30% within one year. Therefore, infarct-related disorders such as cerebral infarction may be reduced by this treatment. The effect of radiofrequency catheter ablation on prognosis should be further investigated.

SPECKLE TRACKING ECHOCARDIOGRAPHY DETECTS UREMIC CARDIOMYOPATHY AND PREDICTS CARDIOVASCULAR AND ALL CAUSE MORTALITY IN ESRD

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Introduction and Aims: Cardiac mortality is dramatically high in end stage renal disease (ESRD). This is mainly driven by sudden cardiac death and recurrent heart failure due to uremic cardiomyopathy. Currently available methods for determination of regional myocardial function are subjective and semi-quantitative. 2-dimensional (2D) strain echocardiography is a recently developed speckle tracking based method to determine myocardial function in a multidimensional fashion. The aim of this study was to test whether 2D strain echocardiography can detect uremic cardiomyopathy and predict cardiovascular mortality in ESRD.

Methods: Two dimensional strain echocardiographic parameters, ejection fraction (EF) and clinical characteristics were assessed in 171 ESRD patients and 44 subjects without known kidney or cardiac disease. Patients were followed up for 2.5 years. In an animal study using two rat models of uremic cardiomyopathy (i.e. 5/6 nephrectomy with high phosphorus diet and ademine nephropathy) we tested whether a)2D strain echocardiography is superior to routine echocardiography to detect early changes in myocardial contractility and b) correlates with hallmarks of uremic cardiomyopathy as interstitial myocardial fibrosis and cardiac hypertrophy.

Results: During the follow-up period of 2.5 years the longitudinal peak systolic and late diastolic strain rates showed the highest correlation variables to predict cardiovascular mortality in ESRD (primary endpoint) in a multivariate cox model (hazard ratios-HR 5.7; 95% confidence interval CI 1.533-21.233; p=0.009 and HR 0.2; 95%-CI 0.006-0.659 p=0.008, respectively). Whereas the strongest predictor for all cause mortality (secondary endpoint) was the circumferential early diastolic strain rate (HR 14.43; 95%-CI 0.256-76.06 p=0.007). Using speckle-tracking echocardiography 90% of the two rat models of uremic cardiomyopathy early i.e. 4-6 weeks and late i.e. 8-10 weeks after induction of kidney disease we observed that various strain parameters were significantly decreased whereas fractional shortening or duplex sonographically calculated cardiac output remained unchanged at the early time-point. Furthermore echocardiographic strain parameters as peak global and systolic circumferential and radial strain and strainrate showed a higher correlation with hallmarks of uremic cardiomyopathy (i.e. grade of interstitial myocardial fibrosis, heart weight and cardiomyocyte cross-sectional area) as routine echocardiographic parameters (fractional shortening or cardiac output).

Conclusions: Speckle tracking echocardiography can detect uremic cardiomyopathy in rats and predicts cardiovascular and all-cause mortality in end-stage renal disease patients.
**Nephrology Dialysis Transplantation**

**Abstracts**

**AGE-DEPENDENT IMPACT OF PULSE WAVE VELOCITY AS A PREDICTOR FOR MORTALITY IN PATIENTS UNDERGOING HEMODIALYSIS**

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**Introduction and Aims:** The incidence of cardiovascular events and mortality is excessively increased in patients treated with hemodialysis (HD). Since aortic media calcification is a major determinant of arterial stiffness, which can be assessed reliably by the noninvasive measurement of aortic pulse wave velocity (aPWV), aPWV is recognized as a strong and independent predictor for all-cause and cardiovascular mortality in HD patients.

**Methods:** aPWV was measured in 75 subjects in 2008. Laboratory and clinical data were collected at the same time. Follow-up of 73 patients could be assessed 4 years later. Statistical analysis included Mann-Whitney U-test, Chi-Square Test, and Cox regression.

**Results:** After 4 years, 37 out of 73 patients had died. In univariate analysis, only aPWV > 11 m/s (HR 2.65; 95 % CI 1.15-6.09) and age per year (HR 1.05; 95 % CI 1.02-1.08) were significantly associated with the risk for all-cause death. When the model was stratified for age (> 66 and ≤ 66 years, according to the median of the cohort), only aPWV remained significantly associated with the risk for all-cause death (HR 3.10; 95 % CI 1.15-8.69). Detailed analysis revealed that aPWV was associated with an almost 10-fold risk of death in patients ≤ 66 years (HR 9.62; 95 % CI 1.99-46.50) whereas in patients > 66 years, aPWV was not significantly associated with the risk of death (HR 1.90; 95 % CI 0.80-4.52).

**Conclusions:** To our knowledge, this is the first study which reveals that the impact of pulse wave velocity as a predictor for all-cause mortality in patients on hemodialysis is age-dependent.

**EFFECTS OF PHYSICAL INACTIVITY ON RISK OF HOSPITALIZATION FOR CARDIO-CEREBROVASCULAR EVENTS IN HEMODIALYSIS PATIENTS**

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**Introduction and Aims:** In hemodialysis patients, physical activity appears to carry many health benefits, such as amelioration of physical deconditioning, hypertension, hyperlipidemia, sleep disorders, and depression. However, the association between physical activity and cardio-cerebrovascular events in these patients remains unclear. We investigated the prognostic significance of physical activity, as evaluated with an accelerometer, in regard to cardio-cerebrovascular events requiring hospitalization among hemodialysis patients.

**Methods:** A total of 209 Japanese outpatients undergoing maintenance hemodialysis 3 times a week at a dialysis treatment center between October 2002 and August 2012 were followed for up to 5 years. At patient entry to the study, physical activity was evaluated with an accelerometer as the number of steps per day for a consecutive 5-day period consisting of 3 non-dialysis days and 2 dialysis days. Patients were categorized into two physical activity groups by using a cutoff value of 5000 steps/day. In addition, clinical characteristics, including age, sex, body mass index, time on hemodialysis, comorbid conditions, and serum albumin and C-reactive protein levels were determined at baseline. A Kaplan-Meter estimate of survival and a Cox proportional hazard regression were used to assess the contribution of physical activity to all-cause hospitalization, cardio-cerebrovascular-related hospitalization, and non-cardio-cerebrovascular-related hospitalization.

**Results:** The median (25th, 75th percentiles) age of the study population was 64 (57, 72) years, 50.7% of the patients were women, and the time on hemodialysis was 39.0 (16.0, 116.0) months at baseline. Seventy-five percent of the patients were placed in the group with <5000 steps/day. During a median follow-up of 44 months there were 46 hospitalizations for cardio-cerebrovascular events and 31 hospitalizations for other causes. After adjustment for the effects of clinical characteristics, the adjusted hazard ratios for hospitalization from all causes, cardio-cerebrovascular events, and non-cardio-cerebrovascular events in the <5000 steps/day group were, respectively, 2.48 (95% CI: 1.20–5.13; P = 0.02), 4.00 (95% CI: 1.39–11.54; P = 0.01), and 1.31 (95% CI: 0.47–3.63; P = 0.61) compared with that in the ≥5000 steps/day group.

**Conclusions:** Physical inactivity seems to be strongly associated with increased risk of hospitalization associated with cardio-cerebrovascular events among hemodialysis patients.

**ROLE ON DIALYSATE MAGNESIUM LEVEL TO INTRADIALYTIC HYPOTENSION**

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**Introduction and Aims:** Intradialytic hypotension (IDH) could induce myocardial stunning & associated with adverse cardiovascular outcomes. Magnesium (Mg) is a critical ion that previously reported to maintain intradialytic blood pressure. The aim of study is to investigate the effect of dMg level to blood pressure during HD.

**Methods:** This study was conducted from July 2011 to April 2012. All of subjects are 18-60 years old who on stable HD procedure at least 3 months (2-3 times weekly, 5 hours per session), and willing to participate. The exclusion criteria were history of myocardial infarction or cardiovascular intervention, symptomatic coronary heart disease, left ventricle EF 40% or less, arrhythmia, diabetes mellitus. The subjects were divided into 3 groups who are dialed in the different dMg level. Group A used low dMg & dCa level (0.2 mmol/L & 1.3 mmol/L), Group B used moderate dMg & dCa level (0.51 mmol/L & 1.54 mmol/L) and Group C used high dMg & dCa level (1.0 mmol/L & 1.9 mmol/L). Group A, B & C respectively enrolled 15, 12 & 15 subjects that were followed within 9 month forward. The following blood pressure was measured at the time of dialysis and at one-hour intervals during the subsequent 5-hour dialysis period. IDH defined as a decrease in blood pressure necessitating fluid replacement therapy and or stopped the dialysis procedure for awhile or terminated dialysis at this time, and or when the SBP or DBP less than 90 and or 60 mmHg respectively, or decreasing SBP more than 40 mmHg below the predialysis SBP.

**Results:** The characteristics of subjects in 3 groups were not different statistically, enclosed age, gender, starting HD, frequency of HD, ultrafiltration per session, sMg, sCa, sAlb, eHb and cardiac status. Group A was found sMg pre-post test, respectively 0.89 ± 0.22 mmol/L & 0.63 ± 0.11 mmol/L, sCa 2.21 ± 0.33 mmol/L & 2.10 ± 0.31 mmol/L, sAlb 3.42 ± 0.46 g/dL & 3.39 ± 0.43 g/dL. Analysis paired sample test, the decreasing sMg level was significant (p<0.05), decreasing sCa level was not significant (p=0.267), Group B was found sMg pre-post test, respectively 0.87 ± 0.21 mmol/L & 0.86 ± 0.17 mmol/L, sCa 2.20 ± 0.36 mmol/L & 2.30 ± 0.25 mmol/L, sAlb 3.33 ± 0.57 g/dL & 3.50 ± 0.44 g/dL. Analysis paired sample test, the decreasing sMg level was not significant (p=0.749), increasing sCa level was not significant (p=0.185), Group C was found sMg pre-post test, respectively 0.87 ± 0.18 mmol/L & 0.90 ± 0.16 mmol/L, sCa 2.22 ± 0.31 mmol/L & 2.43 ± 0.26 mmol/L, sAlb 3.42 ± 0.46 g/dL & 3.44 ± 0.42 g/dL. Analysis paired sample test, the increasing sMg level was significant (p<0.05), increasing sCa level was significant (p=0.05). Mean arterial pressure (MAP) decreased significantly (-5.13±3.63; P<0.05) in group A by 14.7% compared to the other groups. Increasing significantly sMg in group C did not compromise blood pressure by vasodilatation. Inversely, 1.0 mmol/L dMg in group C was superior to the other groups regarding intradialytic morbidity (p<0.05) and blood pressure stability (p<0.05).

**Conclusions:** A low dMg level proved contributing to IDH. Increasing dMg level could prevent IDH. dMg level independently or in dCa combining might has important implications to dialysis tolerance.
MP485  CORONARY ARTERY BYPASS GRAFTING IN DIALYSIS PATIENTS
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Introduction and Aims: To evaluate the outcome after isolated coronary artery bypass grafting (CABG) in patients requiring preoperative chronic dialysis for end stage renal failure (ESRF).

Methods: We retrospectively analyzed data by chart review and questionnaire from 151 patients (pts) (119 male, 32 female) who were operated in our institution between April 1994 and November 2012 and were on maintenance dialysis for at least 1 month preoperatively.

Results: Data from 151 pts. (119 male, 32 female) with a mean age of 64.2 years (range 37-83), who had been on dialysis for a mean of 46.3 months (range 1-1241) preoperatively, were analyzed. 85.4% (129 pts.) suffered from triple vessel disease, 11.3% (17 pts.) had double and 3.3% (5 pts.) had single vessel disease. 2.6% (range 1-6) were performed per operation, thereby using the left internal thoracic artery (LITA) in 78.2% (118 pts) of cases. In 7 pts. (4.6%) the procedure was performed off pump. Mean follow up was 43.2 months (range 3-147). Mean ICU stay was 10.0 days (range 1-80), and patients were discharged after a mean of 22.7 days (range 6-133). 8 pts died within 30 days (5.3%), in hospital mortality was 6.6% (10 patients). Actuarial survival after 1, 3, and 5 years are 80.0, 72.1 and 54.5%, respectively.

Conclusion: Coronary artery bypass grafting can be performed on dialysis patients with acceptable higher perioperative morbidity and mortality, compared to the normal population. Long term survival of ESRF-patients is considerably reduced compared to patients with normal renal function. However, improved postoperative quality of life in the majority of patients, justifies this strategy.

MP486  IN WHAT WAY IS THE SKIN MICROCIRCULATION AFFECTED IN HEMODIALYSIS PATIENTS?
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Introduction and Aims: The interest in the study of skin microcirculation rose from the hypothesis that skin microvascular function can mirror the state of microcirculation in all other vascular beds. Endothelial function is part of the microvascular function that can be examined by the Laser Doppler Fluxmetry (LDF) and is an important cardiovascular risk factor to determine. The LDF is considered a safe and reliable method to study the skin microcirculation. The components of the reactive hyperemia test, namely the peak flux and percent change measurements, are considered good estimates of endothelial function. The so-called novel risk factors for cardiovascular disease (CVD), such as inflammation, endothelial dysfunction, sympathetic over activation, oxidative stress, vascular calcification are highly prevalent in the hemodialysis patients and seem to play an important role in vascular disease progression. Not just the function of the microcirculation, in hemodialysis patients, that can be impaired but also the structure. Structural changes in capillaries have been examined in hemodialysis patients with controversial results.

Methods: 60 subjects were examined, 36 males and 24 females with an age range 35-55 years old. Subjects were divided into three groups: Group A; composed of 20 subjects, on regular maintenance hemodialysis (5-10 years duration ), less than 60 years old, with no diabetes, hypertension or dyslipidemia (factors known to affect endothelial function). Group B; composed of 20 subjects with long standing essential hypertension and Group C; the control group, composed of 20 subject, these were young healthy volunteers. We continued our evaluation and assessed the apparent structural abnormalities in skin microvascular structure using the capilloroscope in the three groups.

Results: Results of the LDF showed a statistically significant difference in the peak flux and the percent change between groups A and C (p<0.001 and 0.002 respectively) between groups B and C (p<0.001 and 0.001). These results denote the presence of endothelial dysfunction in the group of hypertensive patients compared to the control group and as well in the group of hemodialysis patients compared to the control group. Results of the capilloroscope showed a statistically significant difference in the abnormal capillary morphology, capillary rarefaction and the presence of capillary hemorrhage in the hypertensive group compared to the control group but no statistically significant difference between the hemodialysis and the control group in the three studied morphologic parameters.

Conclusions: The study of the microcirculatory changes in patients on maintenance hemodialysis revealed the presence of endothelial dysfunction and that this functional change was not accompanied by any characteristic abnormalities in capillary morphology.

MP487  QTc INTERVAL PREdicts ArTERIAl STIFFNESS and INFLUENCED BY ANEMIA AND VItaMin D SUPPLEMENTATION IN MAINTENANCE HEMODIALYSIS PATIENTS
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Introduction and Aims: Mortality from cardiovascular disease is high in maintenance haemodialysis patients (MHD), accounting for 50% of all-cause deaths. However, as well as the ‘conventional’ atherosclerotic heart disease, there is a greatly increased incidence of sudden death for MHD patients. The QTc interval has been reported to be increased and to be associated with high-risk ventricular arrhythmias and sudden death. There is a direct evidence that in MHD patients increased effect of arterial wave reflections is an independent predictor of all-cause and cardiovascular mortality. We aimed to evaluate the relationship between QT intervals and pulse wave velocity (PWV) and the risk factors for arterial stiffness in maintenance haemodialysis (MHD) patients.

Methods: This is a 12-months prospective study. Eligible 149 MHD patients were enrolled into the study. Electrocardiographic evaluations were performed at the beginning and end of the study. Each QT interval was corrected for the patient’s heart rate using Bazett’s Formula. A QTc interval greater than 440 ms was considered abnormally prolonged. Patients with QTc interval < 440 ms at the beginning and end of the study was defined as Group A (n:48). Patients whose initial QTc interval were >440 ms and/or those whose QTc interval increased >440 ms at the end of follow-up were defined as Group B (n:101). In addition to demographical and laboratory parameters, PWV were assessed at the beginning and end of the study.

Results: Patients in Group B had significantly higher initial and follow-up PWV values, compared to the patients in Group A (7.9 ± 2.8 m/sn to 8.2 ± 3.4 m/sn vs 6.8 ± 2.7 m/sn to 6.5 ± 2.1 m/sn ) values both at the beginning and end of the study (p<0.03 and p<0.001). When the whole patient group was concerned, percentage increase in QTc interval was positively correlated change of PWV during follow-up period (p=0.047). In multivariate analysis revealed that hemoglobin variability was an independent risk factor for the change of PWV (r²: 0.027, p=0.045). Additionally administered equivalent vitamin D dose was significantly higher in Group A compared to Group B (4.1 ± 4.7 mcg/week vs 2.7 ± 3.2 mcg/week, p< 0.05).

Conclusions: Prolonged initial QTc and an increase in follow-up QTc is significantly associated with pulse wave velocity in dialysis patients. We suggest that yearly electrocardiographic evaluation and analysis the changes of QT interval could be a useful guide and a predictor of arterial stiffness of MHD patients. This study also showed that good control of anaemia and vitamin D supplementation have an additive cardiovascular risk reduction in MHD patients.

MP488  CHRONIC SHEAR STRESS and CARBAMYLATED-LDL MODULATE EXPRESSION OF THEIR AGING IN HUMAN CORONARY ARTERY ENDOTHELIUM
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Introduction and Aims: Chronic kidney disease (CKD) patients suffer from accelerated coronary atherosclerosis. Elevated levels of carbamylated LDL induced by uremia and low shear stress resulting from anemia were linked to this process. We investigated how the interplay between LDL receptor family members in human coronary artery endothelial cells, proatherogenic low and atheroprotective high chronic
shear stress and carbamylated LDL contribute to atherosclerosis. **Methods:** First, by means of RT-PCR and Western blotting we explored which LDL-receptor family member was differentially expressed in human coronary artery endothelial cells under control conditions: conventional (static) versus shear stress, both in the presence of native or carbamylated LDL. For shear stress experiments cells were kept on the inner surface of special hollow fiber capillaries where they were exposed either to 2.5 dynes/cm² (low shear stress) or to 25 dynes/cm² (high shear stress) for 24 hours. After identifying the atherogenic LDL receptor relative LR11 (SOLR1) as the differentially expressed molecule in culture, its in vivo expression was examined in human hearts by immunohistochemistry.

**Results:** LR11 was not expressed under static conditions. Chronic low shear stress induced high levels of endothelial LR11 irrespective of the added LDL type (native, carbamylated). Transmembrane as well as soluble LR11 expression was significantly reduced under chronic high shear stress to low levels with carbamylated LDL or non-detectable levels with native LDL. Medium from coronary endothelial cell cultures containing soluble LR11 enhanced vascular smooth muscle cell migration. This was inhibited if blocking antibody against LR11 was added, clearly showing the specific effect of soluble LR11. Expression of LR11 depended on p38MAPK phosphorylation. Finally, in vivo expression LR11 was shown in human coronary artery endothelium.

**Conclusions:** Here we show in vitro and in vivo expression of the atherogenic LR11 in human coronary artery endothelial cells for the first time. Carbamylated LDL and chronic low shear stress, both present in CKD patients, induce expression and shedding of endothelial LR11 through p38MAPK. This leads to pro-atherogenic changes via increased vascular smooth muscle cell migration. High shear stress attenuates these effects. Thus, LR11 and p38MAPK are potential targets for prevention of atherosclerosis in CKD.

**MP489**

**EFFECTS OF AN AEROBIC TRAINING IN PATIENTS ON HEMODIALYSIS PROGRAM**

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**Introduction and Aims:** The Chronic Kidney Disease and the hemodialysis treatment has significant potential in changing negatively the lifestyle of these patients, leading them to a reliance on health care and rehabilitation and, eventually, loss of social roles. Because of the changes mentioned, it’s essential to implement interventions and programs for exercise training, designed to minimize many of the complications of this syndrome and consequently contribute to an improved quality of life. This research aims to evaluate the effects of aerobic training in hemodialysis patients with chronic renal disease.

**Methods:** The study population was composed of 100 patients with Chronic Kidney Disease on regular hemodialysis program in the Nordial hemodialysis Unit, being offered to everyone the same opportunity to participate in the program training. Among those who expressed interest and willingness to participate, after application of the exclusion criteria and taking into account the patients choices, the result was a sample of 43 patients to integrate the Group Training (GT) and 16 patients to establish the Control Group (GC). The aerobic exercise program was implemented in early May of 2012 for 8 consecutive weeks, with a frequency of 3 sessions per week during the dialysis treatment. Before and after the intervention were executed the respective functional and physical assessments and the SF36-v2 questionnaire.

**Results:** The training group is characterized by a mean age of 71.93±11.76 years and in hemodialysis 4.29±3.22 years, after the intervention had significant changes in hemoglobin levels of 11.02±0.88g/dl to 11.30±0.69g/dl and hematocrit of 35.25±6.2% to 33.59±1.9%. In the sit to stand test were observed changes in the number of repetitions of 13.24±4.96 to 18.08±6.23 and in the up and go the time to complete the test went from 15.03±9.10 to 9.96±5.75s. In the quality of life, the change was from 49.93±9.93 to 53.22±7.54s in the component related to mental health.

**Conclusions:** The intradialytic aerobic training implemented had a beneficial effect on aerobic capacity/functional of these patients, as well on the perception of their quality of life, specifically in the component related to mental health. Further investigations are needed to determine the effects of this type of training on blood pressure, glucose and EPO dose administered.

**MP490**

**DIASTOLIC HEART DYSFUNCTION IN PERITONEAL AND HEMODIALYSIS PATIENTS**

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1University Clinic of Nephrology, Skopje, The Former Yugoslav Republic of Macedonia, 2Institute for Heart Diseases, Skopje, The Former Yugoslav Republic of Macedonia

**Introduction and Aims:** Prolonged dialysis treatment time (DTT) have an effect on outcome and survival in haemodialysis (HD) patients. The aim of this study was to elucidate the relationship between DTT with cardiovascular (CV) risk factors in HD patients treated in our Department.

**Methods:** We studied a cohort of 261 patients (mean age at beginning of HD 49.6 ± 15.39 years and HD vintage 99.54 ± 72.15 months) receiving three-times weekly HD treatment. We examined several traditional and non-traditional i.e. uremia and dialysis related CV risk factors. The patients were stratified in three groups according the DTT (DTT <240min, DTT between 240-250min and DTT >250min) and were prospectively followed up for 60 months.

**Results:** Duration of HD ranged from 180 to 300min (median 240min, 32% - DTT <240min, 47% DTT between 240-250min and 21% - DTT >250min). Patients with DTT >250min were younger and had longer HD vintage compared to patients with DTT <240min and DTT between 240-250min. In relation to the traditional and non-traditional CV factors, patients with DTT <240min, DTT >240min and DTT between 240-250min are significantly different with pulse pressure (47.26 ± 9.05mmHg, 58.86 ± 17.26; 54.83 ± 13.71; p=0.001), left ventricular mass index (LVMi) (128.59 ± 59.12g/m²; 158.41 ± 66.58; 137.72 ± 45.73; p=0.0017), C-reactive protein (7.37 ± 8.26mg/L; 25.20 ± 33.33; 15.38 ± 19.33; p=0.000), hemoglobin (113.48 ± 8.74g/L; 100.12 ± 15.17; 105.16 ± 13.23; p=0.0000), albumin (40.08 ± 2.72g/l; 36.94 ± 3.36; 38.48 ± 3.36; p=0.0000), ultrafiltration (3.79 ± 0.83; 2.76 ± 0.60; 3.13 ± 0.81; p=0.0000) and eKt/V (1.5 ± 0.15; 1.03 ± 0.21; 1.08 ± 0.17; p=0.014). During the 5-year follow-up, 117 out of 261 patients (44.8%) had died, most from CV death (63.2%). Patients with DTT <240min and patients with DTT between 240-250min had increase in all-cause (HR 5.85; 95%CI 1.79 -19.09; p=0.003, HR 3.82; 95%CI 1.18-12.41; p=0.025) and cardiovascular mortality (HR 6.40; 95%CI 2.31 -17.74; p=0.000). HR 4.67; 95%CI 1.69-12.85, p=0.003) compared to patients with DTT >250min.

**Conclusions:** This study showed that the better survival in HD patients with longer dialysis session (DTT <240min) is the relationship with better control of important traditional and non-traditional cardiovascular risk factors - blood pressure, LVMi, anaemia, malnutrition, CRP and dialysis prescription.
THE RELATIONSHIP BETWEEN NEUTROPHIL-TO-LYMPHOCYTE RATIO AND CORONARY ARTERY CALCIFICATION IN END-STAGE RENAL DISEASE PATIENTS

Kültigin Türkmen1, Fatih Ozciolk2, Fatih Erdu2, Suleyman Turk1, Mehdi Yekan1 and Halti Tomb2
1Nephrology, Erinaz University Mengucek Gazi Training and Research Hospital Erinaz, Turkey, 2Nephrology, Necmettin Erbakan University Meram School of Medicine, Konya, Turkey, 3Internal Medicine, Erinaz University Mengucek Gazi Training and Research Hospital, Erinaz, Turkey

Introduction and Aims: Cardiovascular (CV) diseases are the most common cause of death in patients with end-stage renal disease (ESRD) receiving hemodialysis (HD) and peritoneal dialysis (PD). Traditional risk factors including diabetes mellitus, hypertension, dyslipidemia, and obesity cannot completely explain this heightened CV risk. Systemic inflammation was found to be correlated with coronary artery disease (CAD) in this population. Neutrophil-to-lymphocyte ratio (NLR) was introduced as a predictor of long-term mortality in patients who underwent percutaneous coronary intervention. Hence, we aimed to investigate the relationship NLR and coronary artery calcification scores (CACS) in HD and PD patients.

Methods: This was a cross-sectional study involving 62 end-stage renal disease (ESRD) patients receiving PD or HD for 36 months in the Dialysis Unit of Necmettin Erbakan University. Complete blood counts with automated differential counts, which included neutrophils, and lymphocytes were obtained. NLR was calculated as the ratio of the neutrophils to lymphocytes. Unenhanced coronary computed tomography (CT) was quantized using electrocardiography-gated cardiac CT scans using 64-slice MDCT. CACS was defined as the presence of more than two contiguous pixels with Hounsfield units greater than 130Statistical differences between two groups were analyzed using the Student’s t test. The Mann–Whitney U test was used to determine differences between nonparametric data. Linear associations between continuous variables were assessed using the Spearman correlation test.

Results: The baseline characteristics of 62 ESRD patients were shown in Table 1. In the bivariate correlation analysis, NLR was positively correlated with CACS (r:0.261, p:0.04), TNF-α (r:0.334, p:0.008), IL-6 (r:0.371, p:0.003) and negatively correlated with albumin (r:−0.244, p:0.05) and hemoglobin (r:−0.324, p:0.01) in ESRD patients.

Conclusions: We concluded that increased NLR is associated with CACS in ESRD patients. Simple calculation of NLR can predict inflammation and CACS in this population.

THE RELATIONSHIP BETWEEN NEUTROPHIL-TO-LYMPHOCYTE RATIO AND CORONARY ARTERY CALCIFICATION IN END-STAGE RENAL DISEASE PATIENTS

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THE RELATIONSHIP BETWEEN NEUTROPHIL-TO-LYMPHOCYTE RATIO AND CORONARY ARTERY CALCIFICATION IN END-STAGE RENAL DISEASE PATIENTS

Kültigin Türkmen1, Fatih Ozciolk2, Fatih Erdu2, Suleyman Turk1, Mehdi Yekan1 and Halti Tomb2
1Nephrology, Erinaz University Mengucek Gazi Training and Research Hospital Erinaz, Turkey, 2Nephrology, Necmettin Erbakan University Meram School of Medicine, Konya, Turkey, 3Internal Medicine, Erinaz University Mengucek Gazi Training and Research Hospital, Erinaz, Turkey

Introduction and Aims: Cardiovascular (CV) diseases are the most common cause of death in patients with end-stage renal disease (ESRD) receiving hemodialysis (HD) and peritoneal dialysis (PD). Traditional risk factors including diabetes mellitus, hypertension, dyslipidemia, and obesity cannot completely explain this heightened CV risk. Systemic inflammation was found to be correlated with coronary artery disease (CAD) in this population. Neutrophil-to-lymphocyte ratio (NLR) was introduced as a predictor of long-term mortality in patients who underwent percutaneous coronary intervention. Hence, we aimed to investigate the relationship NLR and coronary artery calcification scores (CACS) in HD and PD patients.

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Conclusions: We concluded that increased NLR is associated with CACS in ESRD patients. Simple calculation of NLR can predict inflammation and CACS in this population.
Results: Minimscopic and angiographic findings of AVF dysfunction was definitely diagnosed in 90 cases in Group 1 (43\% of Group 1 patients) and finally 11 cases in Group 3 (85\% of Group 3 patients) had higher sclerostin levels than patients free of neuropathic signs and symptoms. Group 2 patients (5.2\% of Group 3 patients) were diagnosed as CTS superimposed to UN (Group 3). No isolated cases with CTS were diagnosed. Patients with neuropathic involvement (Group 2 plus Group 3 patients) had higher sclerostin levels than patients free of neuropathic signs and symptoms (1955\pm1262 vs 1466\pm1384 pg/ml, p=0.03). During 1 year follow-up, AVF dysfunction occurred in 90 cases in Group 1 (43\%), 15 cases in Group 2 (58\%) and finally 11 cases in Group 3 (85\%) respectively (p for the trend=0.029). Cox regression analysis revealed that presence of neuropathy (HR:1.7, 95\% CI: 1.12-2.88, p<0.04) as an independent factor for AVF dysfunction.

Conclusions: The present work links neuropathy to vasculopathy in patients on hemodialysis that should be further studied.

EPICARDIAL FAT THICKNESS PROVIDES INFORMATION ABOUT CARDIOVASCULAR RISK IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Epicardial fat pad (EFP) is a visceral adipose tissue compartment surrounding the heart. It has been defined as a cardiovascular risk predictor in general population. However, its value has not been validated well in patients under hemodialysis (HD). We investigated if EFP thickness was related with total body fat tissue, inflammation, insulin resistance and atherosclerosis in HD patients.

Methods: 50 HD patients (37 male) were enrolled into the study. Patients with diabetes mellitus, atherosclerotic vascular disease, acute infection and/or inflammation and malignancy were excluded. Routine blood examinations, plasma visfatin, insulin levels, lipids, TNF-α, IL-6 and hs-CRP were evaluated. Insulin resistance (IR) was calculated with HOMA-IR formula. EFP thickness, carotis intima media thickness (CIMT) and the fat distribution of the patients using bioimpedence analysis were assessed. The relations of EFP thickness with these parameters were assessed.

Results: The mean age was 45.8 ± 14.6 years of age and the mean EFP thickness was 3.28 ± 1.04 mm for our patients. There were positive correlations of EFP with body mass index (r=0.590, p<0.001), pre dialysis creatinine (r=0.303, p=0.032), HOMA-IR scores (r=0.393, p=0.005), trygyclyceride (TG) (r=0.513, p<0.001), left ventricular mass index (LVMI) (r=0.426, p=0.002), CIMT (r=0.288, p=0.043), fat tissue mass (FTM) (r=0.562, p<0.001), percent FTM (r=0.408, p=0.003) and negative correlations with HDL–cholesterol (r=−0.455, p=0.001), single pool Kt/V urea (r=−0.311, p=0.028) and percent lean tissue mass (LTM) (r=−0.421. p=0.002). EFP thickness had no associations with age, TNF-α, IL-6, hs-CRP and visfatin (for all, p > 0.05). TG/HDL–cholesterol ratio, HOMA-IR scores, LVMI, spKt/V urea, BMI, FTM and percent LTM were determined as independent predictors of EFP thickness in regression models.

Conclusions: Epicardial fat pad thickness has considerable associations with well-known cardiovascular risk predictors in HD patients and could be evaluated by transesophageal echocardiography which is a non-invasive, reproducible and low priced method.
Introduction and Aims: Left Ventricular Hypertrophy (LVH) is the most frequent cardiac alteration in End Stage Renal Disease (ESRD). Although its pathogenesis is considered to be multifactorial, Hypertension (HT), and Fluid Overload (FO) are identified as the major determinants in these patients. Overhydration (OH) is thought to be not only an important cause of HT among haemodialysis (HD) patients, but also an important and independent predictor of mortality in chronic HD. We conducted a cross-sectional study on a population of 59 HD patients in order to find out the associations between derived parameters of FO, measured by BIA, BP and LVH. 36 male and 14 female, age 69±18 years and treated thrice-weekly for 719±126 min per week. All of them had been on HD (HD age) for 34±4.17 months.

Methods: We performed the following tests: BIA measurement with the BCM-Body Composition Monitor-FMC (pre-midweek HD session). We considered OH/EWCW>15%. Blood chemistries at the beginning of the same midweek HD session - A two-dimensional guided M-echochardiography within the two weeks including BCM measurement. LVH was measured according to the ASE guidelines on inter-HD midweek days. Left ventricle internal diastolic diameter (LVDd), diastolic posterior wall thickness (PWTd) and interventricular septum thickness (IVS) were included for LVM calculation (Devereux formula). LVH (males, LVMi_134 g/m; females, LVMi_102 g/m). Relative wall thickness (RWT) was calculated (>0.45 in the presence of LVH suggested concentric LVH). We also collected Antihypertensive medication,Inter & Intra dialytic symptoms. HT (Mean of the monthly office pre HD monitoring) was defined as office BP>140/90.

Results: The overall prevalence of OH was 36%. Although, 70 % of subjects had normal BP values, we found a high prevalence of OH (87%), 51% had eccentric hypertrophy, and 13% had no LVH. OH/EWCW<15% group, had a longer HD-age, lower BP level and the antihypertensive drug use was much lower. Pearson's correlation coefficients showed associations between OH/EWCW and LVDd. On the other hand BP was linked to PWT and IVS. Multiple stepwise linear regression was performed using LVM as the dependent variable and , HD age, Kt/V, hemoglobin, CPR, Albunim, BP and OH/EWCW as independent variables. OH was the most important factor leading to an eccentric LVH while BP influence leads mostly to concentric changes. If HT is present, OH/EWCW influence on LVM and its geometry is even higher.

Discussion: OH/ECW influence on LVM and its geometry is even higher. HD- Age doesn't change any of this links.

Conclusions: LVH was correlated not only with BP but also with OH/EWC. The finding that LVH was eccentric in the majority of patients confirms that the increase in LVM was related to FO which itself is the cause of both hypertension and LVH. Improving Fluid Status is needed to minimize cardiovascular morbidity and mortality.

**Results:** There were significant differences among studied groups in terms of daily diuresis favorable for the “short” and “medium” group ([ml/24 hours] 1278±978 vs 1156±967 vs 737±672, p<0.0001). The duration of hemodialysis treatment ([h], 21.2±7.2 vs 23.3±2.22 vs 3.93±2.58, p<0.02) and HD ultrafiltration volume ([ml] 1818±1322 vs 2152±1308 vs 2950±1141, p<0.007). Patients in the “long” term group presented with the highest values of cardiac dysfunction indicators i.e. NT-proBNP ([pg/ml] 924±12250 vs 6996±14357, p<0.02) and cTnT ([pg/ml] 0.069±0.080 vs 0.079±0.073 vs 0.103±0.081, p<0.03). There were no statistically significant differences between Ca, PO4, and PTH levels. Surprisingly, the osteocalcin concentration was higher in the “short” and “long” term groups (ng/ml 195.68±94.87 vs 127.40±90.67 vs 230.18±98.89, p<0.02). The duration of hemodialysis treatment was strongly and positively correlated with dialysis dose per week (r=0.354, p<0.001) and negatively correlated with residual renal function (r=-0.535, p=0.00001) in the entire study group.

**Conclusions:** The HD time-span exceeding 200 weeks seems to dramatically increase cardiovascular dysfunction. Long-term hemodialysis therapy predictably leads to a decrease of daily residual renal function and to an increase of overhydration requiring a stricter water intake regime which affects the patients’ quality of life. Further studies are necessary to verify relationships between the metabolism of osteocalcin and duration of hemodialysis treatment, overhydration, and cardiovascular risk.

**INTRODUCTION AND AIMS:** Fluid overload is a common problem in hemodialysis (HD) patients. It is associated with cardiovascular risk factors and with higher mortality in HD patients. Our aim was to assess the influence of long-term hemodialysis treatment on a patient’s water balance and cardiac function.

**METHODS:** We studied a total of 62 persons with 31 patients under HD therapy and 31 volunteers included in the study. In all the participants, CIMT was measured and AIP was calculated.
**Abstracts**

**MP501**

<table>
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</table>

**Results:** AIP and CIMT were found significantly higher in the patient group than in the controls (p=0.0001, 0.0001; respectively). There was a significant correlation between AIP and increased CIMT in the patient group (p=0.0001). Among the lipid parameters, the strongest correlation was found between AIP and CIMT.

**Conclusions:** AIP was shown to correlate with a greater number of risk factors, both classical and CKD specific, than CIMT. These data suggest that AIP might be a method which can be used both in diagnosis of subclinical atherosclerosis and in deceleration processes of its progression.

**MP502**

**PULMONARY HYPERTENSION IN CKD PATIENTS**

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**Introduction and Aims:** Systolic blood pressure in heart right ventricle reaching over 30-35 mmHg, assessed by echocardiography on the basis tricuspid regurgitation velocity with the use of Doppler method, is reported in 35% of pre-dialysis patients and in 52% in patients on haemodialysis. Arteriosclerotic fistula, duration of chronic kidney disease (CKD), smoking and female sex are among factors associated with increased pressure in the right ventricle. In patients with pulmonary hypertension (PH), lower values of left ventricular ejection fraction are also observed. It was found that compression closing arteriosclerotic fistula may result in the reduction of PH.

Echocardiographic examination of tricuspid regurgitation velocity may help to identify the cause of breath shortness and in the monitoring of patients' outcomes.

**Methods:** Thirty-one patients undergoing dialysis in the Dialysis Unit in the Department of Nephrology, Hypertension and Family Medicine, WAM University Hospital in Lodz were enrolled into this study. All patients underwent echocardiographic transhoracic examination to determine systolic blood pressure in the pulmonary artery, indices of diastolic function (E, E’, S, L) of left and right chamber and assess the volume of right and left atrium. The study was carried out before and shortly after dialysis. Pulmonary hypertension was defined as systolic blood pressure in the pulmonary artery > 37 mmHg.

**Results:** Mean age of patients was 72.3 years ± 4.5, 30% of them was males. All the patients had impaired diastolic function of left ventricle: E/A = 0.75, E= 9.1 ± 4.0 (before dialysis) and E’ = 9.0 ± 4.7 (after dialysis); E/E’ = 13.5 ± 5.0 (before dialysis), E/E’ = 10.2 ± 4.7 (after dialysis). Diastolic dysfunction of right ventricle: E= 12.5 ± 5.4, E/E’ = 8.0 ± 5.0, S= 15.0 ± 5.0 (before dialysis), S’= 12.5 ± 5.4 (after dialysis). Diastolic pulmonary hypertension – average SPAP = 27.0 ± 17.2 occurred more frequently in women and patients with hypertension (HA). In patients with HA, atrial fibrillation, increased dimensions of the left atrium (LA), increased atrial pressure before dialysis VLA 34.9 ± 21.1, VRA = 31.4 ± 19.6 and decreased after procedure VLA 34.4 ± 20.9, VRA = 30.8 ± 18.0, reduction in early filling velocity (E) and the ejection fraction were more frequent.

**Conclusions:** Pulmonary hypertension occurs in the majority of dialysis patients with diastolic heart failure. Female sex, atrial fibrillation, increased LA volume and reduced velocity of early left ventricular filling (E) are independent predictors of the presence of pulmonary hypertension.

**MP503**

**EFFECTS OF A STRENGTH EXERCISE PROGRAM DURING HEMODIALYSIS**

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**Introduction and Aims:** The present study aims to investigate the effects of an intradialytic program of strength exercises in patients with Chronic Kidney Disease. Individuals who undergo hemodialysis are faced with multiple catabolic processes, including protein and energy level, characterized by loss of muscle mass and decreased visceral proteins. Its pathophysiology becomes so complex, multifactorial and few explanations are encountered. However, it is clear that irregularities in muscle function, exercise performance and physical activity initiated in the early stages of CKD will progressively worsening.

**Methods:** Of the 45 participants, 29 were randomly chosen to join the training group (TG) and 16 control group (CG). The TG conducted a program of strength training during hemodialysis sessions for 8 weeks, 3 times per week, while the CG remained with the usual routine. At the beginning of the program was conducted an assessment period: the Sit-to-Stand Test, the Up- and Go Test, the Hand Grip Test, the Pinch Gauge and anthropometric and laboratory tests, culminating in the application of SF-36 version 2. We repeated this evaluation procedure after completion of training protocol.

**Results:** Taking into account the obtained results, the TG significantly increased the number of repetitions of the Sit-to-Stand Test (12.22±5.37 initial; 15.4±3.27 final), and improved runtime Up- and Go Test (16.74±17.38s initial; 11.33±8.26s end).

Regarding the right handgrip, this group improved significantly (18.79±11.32Kgf initial; 21.92±11.63Kgf end), not even checking the left side (18.5±11.60Kgf initial; 21.0±11.63Kgf final). As for digital right grip strength (5.68±2.14Kgf initial; 6.04±2.88Kgf final) and left (5.21±2.53Kgf initial; 4.88±2.31Kgf end) there is the same situation as in handgrip strength. After completion of training program, in TG the physical component of the SF-36 (version 2) improved significantly (34.178±10.83 initial; 41.52±18.14, final) and the same happened with the mental component (51.43±3.33 initial; 52.74±8.47 final).

**Conclusions:** It’s visible an increase in the number of repetitions of the Sit-to-Stand Test in GT, declaring statistically significant changes. Through these results, it can be said that the program was beneficial, improving the ability of participants to perform a higher number of repetitions in comparison with the results obtained by many authors; It’s clear that the GT had a reduction in the time of execution of the up and go test, with significant statistical differences. These values indicate an improvement in the physical condition of the patients. These results suggest that a program of strength training intradialytic improves functional capacity and quality of life in this debilitated population.

**MP504**

**LOW SERUM MAGNESIUM RELATED WITH ARTERIOESCLEROSIS IN MAINTENANCE HEMODIALYSIS PATIENT BUT NOT IN CHRONIC KIDNEY DISEASE**

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**Introduction and Aims:** Recent clinical studies have shown that lower serum magnesium (Mg) levels are associated with vascular calcification and cardiovascular mortality among patients with hemodialysis (HD). In this study, we evaluated the regulated factors of serum Mg in the patients with chronic kidney disease (CKD) not on dialysis and HD. Furthermore we evaluated the relationship between low serum Mg and arteriosclerosis in these patients.

**Methods:** We measured blood levels of Mg, hemoglobin (Hb), total cholesterol, creatinine (Cr), urea nitrogen (UN), β2-microglobulin (MG), albumin (alb), Calcium (Ca), phosphate (P), intact parathyroid hormone (iPTH), and tumor necrosis factor (TNF)-α in 69 patients with various stage of CKD (not on HD) and 129 patients on maintenance HD. Furthermore, we measured brachial-ankle pulse wave velocity (ba-PWV) and ankle-brachial index (ABI).

**Results:** In HD patients, serum level of Mg was significantly correlated with age (P=0.004, R=0.625), Ca (P=0.02, R=0.21), TNF-α (P<0.005, R=0.25), alb (P=0.001, R=0.21).
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R=0.32) and baPWV (P=0.001, R=0.29). In multiple regression analysis, alb (P=0.001, β=0.31) and Ca (P=0.029, β=0.18) were selected as significant predictors of Mg level in HD patients. Furthermore, serum level of Mg (P=0.012, β=0.22) was selected as significant predictor of baPWV in HD patients. A high level of serum NT-proBNP has been shown to be a risk factor for heart failure and hospitalization for cardiovascular disease in hemodialysis patients. In this study, we examined the relationship between the serum level of NT-proBNP and mortality and also investigated the cut-off value which could predict cardiovascular death.

Methods: A total of 103 patients receiving maintenance hemodialysis at Sangenjiya Hospital were enrolled in this study. A peripheral blood sample was obtained before hemodialysis on a Monday or a Tuesday, and the serum NT-proBNP levels were measured.

Results: The mean follow up period was 1.6 ± 0.6 year. During the follow-up period, 20 deaths were recorded. The cause of death was cardiovascular disease in 10 patients. It was not possible to assess the cut-off point, the area under the ROC curve, and the specificity of the ROC analysis.

Introduction and Aims: The aim of this study was to analyse ACE, MMP 3 and eNOS polymorphism in our group of haemodialysis patients and to correlate the findings with cardiovascular morbidity. ROC analysis revealed 9,412 pg/mL as the cut-off point and the AUC was 0.86, with a sensitivity of 0.90 and specificity of 0.78 over the 2-year follow-up in order for definitive conclusion about importance of this finding in daily clinical practice.

Conclusions: Although our results clearly confirmed association of RAS, MMP3 and eNOS genetic polymorphism with CV co-morbidity, we need more studies and longer follow-up in order for definitive conclusion about importance of this finding in daily clinical practice.


dialysis adequacy calculation and calculation of AKW. AKW was calculated from

R values of 0.17 (P=0.05), 0.18 (P=0.05), 0.19 (P=0.05) and 0.25 (P=0.05). In CKD patients, serum levels of Mg had no significant relation to Cr, UN, β2M, alb, Ca, P, and int-PTH. Moreover, there was no significant correlation between serum levels of Mg and baPWV or ABI in CKD patients. There was no significant difference in serum levels of Mg between CKD (2.19±0.26 mg/dL) and HD patients (2.34±0.35 mg/dL).

Conclusions: Although serum levels of Mg had no clinical significance in CKD patients, in patients on maintenance HD, serum Mg level was regulated by serum levels of Ca and alb. Furthermore, low serum Mg levels in HD patients was associated with the index of vascular stiffness (ba-PWV).

PM505

RELATIONSHIP BETWEEN N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE (NT-proBNP) AND MORTALITY IN MEMOIALYSIS PATIENTS

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Introduction and Aims: N-terminal pro-brain natriuretic peptide (NT-proBNP) is released in blood with an increase in the circulating blood volume or increased ventricular stress. NT-proBNP has been reported to be positively associated with left ventricular mass fraction in hemodialysis patients. A high level of serum NT-proBNP has been shown to be a risk factor for heart failure and hospitalization for cardiovascular disease in hemodialysis patients. In this study, we examined the relationship between the serum level of NT-proBNP and mortality and also investigated the cut-off value which could predict cardiovascular death.

Methods: A total of 103 patients receiving maintenance hemodialysis at Sangenjiya Hospital were enrolled in this study. A peripheral blood sample was obtained before hemodialysis on a Monday or a Tuesday, and the serum NT-proBNP levels were measured. Because of the skewed distribution of NT-proBNP, data were normalized by logarithmic transformation for further statistical analysis. A univariate Cox proportional hazards model for the predictor of survival was examined. A receiver operating characteristic (ROC) analysis was performed to assess the cut-off point, the area under the ROC curve, and the specificity of the ROC analysis.

Results: The mean follow up period was 1.6 ± 0.6 year. During the follow-up period, 20 deaths were recorded. The cause of death was cardiovascular disease in 10 patients. It was not possible to assess the cut-off point, the area under the ROC curve, and the specificity of the ROC analysis.

Introduction and Aims: Accelerated atherosclerosis is very common in haemodialysis (HD) patients and related with morbidity and mortality. Aortic knob width (AKW) which can easily be calculated by chest radiographs has also been found to be related with atherosclerosis in patients with normal renal function. The importance of AKW in HD patients is not known.

Methods: Study participants underwent medical history taking, physical examination, during dialysis and calculation of AKW. AKW was calculated from anteroposterior chest X rays at the end of dialysis session when patients were in their dry weight.

Results: In total 91 HD and 65 patients with normal renal function (as a control group) were included. The mean of the AKW was 35±5.8 mm in HD patients and 26.6±4.3 mm in patients with normal renal function (P<0.0001). In whole group stepwise linear regression analysis revealed that age (P<0.0001), male gender (P<0.0001), systolic BP (P<0.0001), presence of HD treatment (P<0.016) and albumin (P=0.021) were independently related with AKW. On the other hand in HD patients stepwise linear regression showed that age (P<0.0001), predialysis systolic BP (P=0.003), male gender (P=0.001), being non-smoker (P=0.002), total cholesterol (P=0.001), and Intact PTH (P=0.005) were independently associated with AKW.

Conclusions: In HD patients AKW is increased as compared to normal population. Various traditional and non-traditional risk factors were associated with AKW in HD patients. These preliminary findings may enhance the use of chest radiography as a screening method and, if confirmed, can assist risk stratification in HD patients.

PM507

GENETIC POLYMORPHISM AND CARDIOVASCULAR CO-MORBIDITY IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Cardiovascular morbidity is the major concern in dialysis patients and many risk factors have been proposed to be involved in its development. Apart from traditional and non-traditional risk factors, genetic susceptibility may be of importance including renin-angiotensin system (RAS), matrix metalloproteinase 3 (MMP 3) and endothelial nitric oxide synthase (eNOS) polymorphism. The aim of this study was to analyse ACE, MMP 3 and eNOS polymorphism in our group of haemodialysis patients and to correlate the findings with cardiovascular morbidity.

Methods: The study included 200 patients on regular haemodialysis, three times per week on polysulphone membrane for more than six months. Genetic analysis was performed by using polymerase chain reaction – restriction fragment length polymorphism method (PCR-RFLP).

Results: Out of 200 patients 73% had 5A/6A, 21% had 5A/5A and 6% had 6A/6A. MMP 3 genotype was selected as significant predictor of cardiovascular disease in hemodialysis patients. The ROC analysis of the NT-proBNP for death from cardiovascular disease revealed 9,412 pg/mL as the cut-off point and the AUC was 0.86, with a sensitivity of 0.90 and specificity of 0.78 over the 2-year follow-up in order for definitive conclusion about importance of this finding in daily clinical practice.

Conclusions: Although our results confirmed association of RAS, MMP3 and eNOS genetic polymorphism with CV co-morbidity, we need more studies and longer follow-up in order for definite conclusion about importance of this finding in daily clinical practice.

PM508

NEUTROPHIL ACTIVATION IN HEMODIALYSIS IS ASSOCIATED WITH AN INCREASE OF PTX3 PRODUCTION AND WITH VASCULAR DAMAGE

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Introduction and Aims: Neutrophils play a key role in the inflammatory response and in the differentiation of the arteriosclerotic vascular disease. However, neutrophil role in atherothrombosis is less well characterized. Our study is aimed to assess the contribution of neutrophils to inflammatory process in HD patients.

Methods: Neutrophils from 20 healthy subjects were enrolled. Analysis of PTX3 protein expression in freshly isolated neutrophils was evaluated by confocal microscopy. Intracellular staining for PTX3 protein was performed.

Results: The expression of PTX3 in healthy subjects was 0.6±0.2 fold, whereas in HD patients the expression was 1.5±0.3 fold. By using Student’s t-test a statistically significant difference between healthy and HD patients was observed (P<0.05).

Conclusions: The increased expression of PTX3 in HD patients suggests that neutrophils play an important role in inflammation and arteriosclerosis in HD patients. Further studies are necessary to verify these findings and to understand the mechanisms underlying the increased expression of PTX3 in HD patients.
Introduction and Aims: Systemic calcifications are a common finding in chronic renal disease. However, cardiac involvement is especially ominous and leads to conduction defects and arhythmia that may cause sudden death.

Methods: Prospective study screening 52 hemodialysis patients for cardiac arrhythmia using ECG and 24 h holter ECG monitoring including hemodialysis sessions. Patients with symptomatic atrioventricular block (AVB) were treated by permanent pacing to avoid consequent mortality.

Results: Atrioventricular block was found in 4 patients (7,7%) : 4 men, aged mean 61 years with a mean hemodialysis duration of 83,25 months. Two patients were diabetic and hypertensive and one had ischemic cardiomyopathy history. Clinical symptoms were especially fatigue and unconsciousness. One case of reversible cardiopulmonary arrest was noted. ECG/Holter-ECG revealed complete atrioventricular block in all cases. Mitrall valve calcifications were present in 2 patients, 2 subjects had aortic valve calcifications and left ventricular hypertrophy. Systolic function was normal in 3 cases. CCKT demonstrates a high ACC (> 401) in two cases with a special involvement of anterior interventricular artery. No short or long-term complications related to pacemaker implantation were encountered.

Conclusions: Cardiovascular calcifications are associated with several disturbances of the conduction system in maintenance hemodialysis, and leads to substantial morbidity and mortality. Many risk factors are established such as advanced age and duration of dialysis. In our patients, AVB was contributed to metastatic calcifications involving the cardiac valves and the coronary arteries consequent to long-term exposure to imbalances in mineral metabolism and the use of calcium carbonate as phosphate binder and vitamin D to treat secondary hyperparathyroidism. More attention should be focused on screening of conduction defects by Holter ECG in earlier chronic renal disease to avoid consequent mortality.

Introduction and Aims: Prognostic value of CRP has been associated with high mortality in patients with chronic kidney disease without dialysis. This study was conducted to evaluate the clinical characteristics and long-term survival difference of hemodialysis (HD) patients with chronic hypotenison.

Methods: According to the pre-HD systolic blood pressure (sBP) at the last mid-week of January 2004, a total of 407 HD patients at our center were divided into quintiles: group 1: sBP>102±14 mmHg; group 2: sBP>130±57 mmHg; group 3: sBP>147±55 mmHg; group 4: sBP<163±44 mmHg; and group 5: sBP<189±14 mmHg. The final observation period was on the 31st July, 2008.

Results: Compared to the other 4 groups, group 1 has the lowest prevalence of diabetes (groups 2,3,4,5: 12.9±5.6% vs 7.6±4.9%, p<0.001). Group 1 was associated with non-dialysis (OR=0.16, 95%CI = 0.08-0.34), longer HD vintage (OR=1.01, 95%CI=1.00-1.01), and lower serum phosphate concentration (OR=1.80, 95%CI=0.66-0.98) in multiple logistic regression analyses. Mean BP drop after HD showed a positive correlation to pre-HD systolic BP (r=0.501, p<0.001). Mean BP in group 1 was consistently lower than the other groups. However, for those who received HD for less than 37 months in duration, group 1 had a significantly higher long-term mortality rate, but over 37 months, they did not show any difference in mortality rate.

Conclusions: Increased CRP levels were an independent risk factor for endothelial dysfunction and vascular damage progression in this setting. The high risk of mortality in patients with chronic kidney disease such as heart failure in recent years natriuretic peptides have become promising candidates in this respect. In ESRD population the clinical benefit of N-terminus pro-brain natriuretic peptide (NT-proBNP) measurements has not been well established. Aim of this study: To evaluate the role of serum NT-proBNP levels and carotid intima-media thickness in diagnoses and detect the progression of left ventricular dysfunction and left ventricular mass in a sizable cohort of stable patients.
Abstracts

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MP514
THE RELATIONSHIP BETWEEN NEUTROPHIL/LYMPHOCYTE RATIO AND BRAIN NARIUPEPTIDE IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Malnutrition is a common problem in uremic patients. It is unclear whether there is an association between the degree of malnutrition and 24-h ambulatory blood pressure patterns in patients undergoing hemodialysis (HD). In the present study, we observed the relationship between the degree of malnutrition and ambulatory blood pressure patterns, which are both risk factors for cardiovascular morbidity and mortality.

Methods: We observed 148 patients undergoing HD in the Nephrology Department of Celal Bayar University Medical Faculty, Manisa, Turkey. All cases were assessed for body weight alterations, dietary food intake, gastrointestinal symptoms, loss of subcutaneous fat and muscle tissue, presence and severity of comorbidities, and functional capacity. Each parameter was evaluated between 1 and 5 points; thus, a total malnutrition score was calculated for each case (subjective global assessment). Ambulatory blood pressure measurements were performed for all cases on the day between the two HD sessions.

Results: We found that the circadian blood pressure rhythm deteriorated in patients with a high-malnutrition score, and that malnutrition was more common and severe in those subjects with the non-dipper (ND) and reverse-dipper (RD) blood pressure patterns. The malnutrition scores of the patients in the RD group were significantly higher than those of the patients in the ND (p = 0.021) and dipper (D) (p = 0.003) groups. Malnutrition score was positively correlated with the nighttime systolic and nocturnal mean blood pressures and mean 24-h arterial blood pressure (all P<0.01). Serum albumin was significantly lower in the RD group compared with the D and ND groups. Serum albumin was negatively correlated with HD duration (r = -0.21), nighttime systolic blood pressure (p = 0.005, r = -0.28), nighttime mean arterial blood pressure (P = 0.04, r = -0.21), nighttime/nighttime mean systolic blood pressure ratio (p = 0.016, r = -0.36), nighttime/nighttime mean diastolic blood pressure (p = 0.027, r = -0.32), and nighttime/nighttime mean blood pressure (p = 0.012, r = -0.41). The malnutrition index was significantly correlated with the mean nighttime/nighttime systolic blood pressure ratio (p = 0.001, r = 0.42) and mean nighttime/nighttime diastolic blood pressure ratio (p = 0.002, r = 0.40).

Conclusions: This is the first study to investigate the possible association between malnutrition and deterioration of the blood pressure circadian rhythm in a HD population. We suggest that a deteriorated diurnal blood pressure rhythm parallels the malnutrition phenomenon in patients undergoing HD. However, the issue of sympathetic overactivity or volume overload as the main cause of deterioration in circadian blood pressure rhythm in patients with malnutrition remains unclear.

MP513
EFFECTS OF NOCTURNAL BLOOD PRESSURE MEASUREMENTS ON NUTRITIONAL PARAMETERS IN PATIENTS UNDERGOING HEMODIALYSIS

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Introduction and Aims: Malnutrition is a common problem in uremic patients. It is unclear whether there is an association between the degree of malnutrition and 24-h ambulatory blood pressure patterns in patients undergoing hemodialysis (HD). In the present study, we observed the relationship between the degree of malnutrition and ambulatory blood pressure patterns, which are both risk factors for cardiovascular morbidity and mortality.

Methods: We observed 148 patients undergoing HD in the Nephrology Department of Celal Bayar University Medical Faculty, Manisa, Turkey. All cases were assessed for body weight alterations, dietary food intake, gastrointestinal symptoms, loss of subcutaneous fat and muscle tissue, presence and severity of comorbidities, and functional capacity. Each parameter was evaluated between 1 and 5 points; thus, a total malnutrition score was calculated for each case (subjective global assessment). Ambulatory blood pressure measurements were performed for all cases on the day between the two HD sessions.

Results: We found that the circadian blood pressure rhythm deteriorated in patients with a high-malnutrition score, and that malnutrition was more common and severe in those subjects with the non-dipper (ND) and reverse-dipper (RD) blood pressure patterns. The malnutrition scores of the patients in the RD group were significantly higher than those of the patients in the ND (p = 0.021) and dipper (D) (p = 0.003) groups. Malnutrition score was positively correlated with the nighttime systolic and nocturnal mean blood pressures and mean 24-h arterial blood pressure (all P<0.01). Serum albumin was significantly lower in the RD group compared with the D and ND groups. Serum albumin was negatively correlated with HD duration (r = -0.21), nighttime systolic blood pressure (p = 0.005, r = -0.28), nighttime mean arterial blood pressure (P = 0.04, r = -0.21), nighttime/nighttime mean systolic blood pressure ratio (p = 0.016, r = -0.36), nighttime/nighttime mean diastolic blood pressure (p = 0.027, r = -0.32), and nighttime/nighttime mean blood pressure (p = 0.012, r = -0.41). The malnutrition index was significantly correlated with the mean nighttime/nighttime systolic blood pressure ratio (p = 0.001, r = 0.42) and mean nighttime/nighttime diastolic blood pressure ratio (p = 0.002, r = 0.40).

Conclusions: This is the first study to investigate the possible association between malnutrition and deterioration of the blood pressure circadian rhythm in a HD population. We suggest that a deteriorated diurnal blood pressure rhythm parallels the malnutrition phenomenon in patients undergoing HD. However, the issue of sympathetic overactivity or volume overload as the main cause of deterioration in circadian blood pressure rhythm in patients with malnutrition remains unclear.

MP515
HUMORAL AND ECHOCARDIOGRAPHIC PREDICTORS OF MORTALITY IN CHRONIC KIDNEY DISEASE

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Introduction and Aims: Previous studies indicate that several humoral and echocardiographic factors are predictive for cardiovascular mortality in patients with chronic kidney disease (CKD). However, complete quantitative echocardiograms evaluating several parameters in conjuction with humoral factors have not been reported. The aim of this study was to determine humoral and echocardiographic predictors of survival in two groups of patients, predialysed and dialysed.

Methods: Three humoral factors, brain natriuretic peptide (BNP), C-reactive protein (CRP), fibrinogen, and complete echocardiograms were evaluated in 95 CKD patients (56 predialysed, and 45 dialysed). Kaplan-Meier survival analysis and Cox proportional hazards regression analysis were used to determine which variable predicted the all-cause mortality.

Results: In a group of predialysed patients predictors of all-cause mortality were BNP and C-reactive protein. Regarding echocardiography, several parameters appeared to be predictive for all-cause mortality: left ventricular ejection fraction, left atrial volume index, indexes of myocardial deformation, and systolic myocardial velocity by tissue doppler. In the group of hemodialysis patients the only predictor of all-cause mortality were BNP and CRP. Cox proportional hazards regression analysis revealed that in predialysed patients the strongest predictor of mortality were BNP, CRP, and left atrial volume index. For hemodialysis patients the strongest predictor was only CRP.

Conclusions: The results of our study suggest that humoral and echocardiographic markers of left ventricular dysfunction are associated with all-cause mortality in predialysed patients, and humoral biomarkers are more related to survival in dialysed patients.

on chronic HD without clinical signs of progressive heart failure.

Methods: This study was conducted on 100 persons, 55 were known as ESRD patients on regular HD (Dialysis group) and 25 patients with CKD not on HD (CKD group) in addition to 20 healthy volunteers (control group). All participants were thoroughly interrogated and examined clinically and were subjected to plasma NT-proBNP level, carotid Duplex and transonic echocardiography at baseline and after six months.

Results: Mean NT-proBNP showed significantly higher in dialysis group compared to the CKD group (P<0.001), and the control group (P<0.001). There is a significant strong inverse correlation between NT-proBNP and EF (P<0.001). There is also a strong positive correlation between NT-proBNP and change of EF over six months (r=0.01). Also there is a significant strong positive correlation between NT-proBNP and change of LVM & LVMI and change of EF over six months (ΔLVM (P<0.001)). Mean carotid media-thickness showed significantly higher in dialysis group and the CKD group, compared to the control group (P<0.01).

Conclusions: The study recommended that plasma NT-proBNP assessment is an easy and non-invasive test and should be monitored in HD patients owing to its close relation to left ventricular mass, systolic dysfunction and cardiovascular morbidity and mortality in this population. Rising NT-proBNP levels may reflect worsening ventricular stress and may help earlier diagnostic and therapeutic strategies. CIMT can be used to detect an accelerated disease process and subclinical disease.
**PROGNOSTIC VALUE AND LINK TO ATRIAL FIBRILLATION OF CIRCULATING KLOTHO AND FGF23 IN HEMODIALYSIS PATIENTS**

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**Introduction and Aims:** A deranged calcium-phosphate metabolism contributes to the burden of morbidity and mortality in dialysis patients. This study aimed to assess the association of the phosphaturic hormone Fibroblast growth factor 23 (FGF23) and its coreceptor Klotho with morbidity and mortality.

**Methods:** This is a prospective multicenter longitudinal observational study. We measured circulating Klotho and FGF23 levels at enrollment and two weeks later in 239 prevalent hemodialysis patients.

**Results:** Median Klotho levels were similar in non-survivors and in survivors (351 vs 338 pg/ml, P=0.85). Increasing Klotho levels were not associated with mortality in a multivariable adjusted analysis when examined either on a continuous scale (HR 1.24; 95%CI 0.83-1.87 per SD increase) or in tertiles, with the tertile 1 as the reference category (HR for tertile two 0.65; 95%CI 0.26-1.64; HR for tertile three 2.18; 95%CI 0.91-2.23). Kaplan-Meier analysis with long-rank test did not reveal a significant difference between groups stratified according to the Klotho tertiles. Klotho levels were lower among patients with atrial fibrillation than without (307 vs. 350 pg/ml, P=0.03). Increasing Klotho levels were associated with the absence of atrial fibrillation in a multivariable adjusted logistic regression analysis (OR 0.66; 95%CI 0.42-1.02 per SD increase). Median FGF23 levels tended to be higher in non-survivors than in survivors (304 vs 201 reference units/ml, P=0.07). Increasing FGF23 levels were associated with monotonically increasing mortality risk in a multivariable adjusted analysis when examined either on a continuous scale (HR 1.45; 95%CI 1.06-1.98 per SD increase) or in tertiles, with the tertile 1 as the reference category (HR for tertile two 1.57; 95%CI 0.62-3.99; HR for tertile three 3.91; 95%CI 1.26-12.34).

**Conclusions:** FGF23, but not circulating Klotho levels, are associated with mortality in hemodialysis patients. Higher circulating Klotho levels seem to be protective against atrial fibrillation.
CKD-MBD II

**MP516**

**KDIGO-RECOMMENDED PTH LEVEL ACCELERATES AORTIC CALCIFICATION IN PATIENTS NEW TO HEMODIALYSIS**

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**Introduction and Aims:** Vascular calcification is an important factor influencing cardiovascular complications and the vital prognosis in hemodialysis patients. However, a target level of PTH and a guide for medical practice to prevent vascular calcification are not clearly defined in the KDIGO’s guidelines and are controversial. We investigated the development and progression of aortic calcification in the early stage of hemodialysis initiation.

**Methods:** We performed a retrospective cohort study in 102 patients who initiated hemodialysis for end-stage kidney disease between July 2004 and June 2009 and could be followed up for three years in our hospital. We compared the extent of calcification in the aortic arch at the time of hemodialysis initiation and three years later by reviewing postero-anterior chest X-ray. We defined an outcome as an increase in the extent of calcification by 50% and examined the factors related to this outcome using multiple logistic regression analysis.

**Results:** Aortic arch calcification was observed 68% of patients at baseline and increased to 80% during the three-year study period. In addition, forty-eight of the 102 patients achieved the outcome. The mean daily dose of calcium carbonate (1,000-mg units) for three years (odds ratio: 2.2 [95% CI 1.5 - 3.4]), an iPTH level of 180 pg/ml or above (3.9 [1.6 - 10.6]), and age (1.5 [1.0 - 2.3]) were significantly associated with progression of aortic calcification. On the other hand, the presence of diabetes, use of activated vitamin D and statin, mean levels of serum calcium and phosphate and factors related to lipid for three years were not associated with the progression of aortic calcification.

**Conclusions:** The KDIGO’s guideline recommend PTH level is maintained in the range of two to nine times the upper normal limit in patients with CKD stage5D, regarding the relative risk of death. However, in view of vascular calcification, it is important to control the PTH levels more strictly from the early stage of dialysis initiation, in addition to reducing the doses of calcium-containing phosphate binders as far as possible.

**MP517**

**VARIATION IN NHS SERVICES AND ACHIEVEMENT OF TARGETS IN THE MANAGEMENT OF SECONDARY HYPERPARATHYROIDISM IN PATIENTS WITH END-STATE RENAL DISEASE UNDERGOING DIALYSIS IN THE UK NHS**

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**Introduction and Aims:** Secondary hyperparathyroidism (SHPT) is widely prevalent in patients undergoing dialysis and is associated with significant morbidity and mortality. There are several differing target ranges set by the renal association, KDIGO and KDOQI with anecdotal evidence of significant variation in practice across UK renal units. The aim of this study was to examine the achievement of targets for calcium, phosphate and PTH according to the various available guidelines and relate this to staffing and services across 8 UK renal units.

**Methods:** A retrospective multi-centre study was undertaken in 8 UK renal units purposely selected to include a variety of sizes and geographical locations. Calcium, phosphate and PTH results were extracted from renal unit databases and data regarding renal unit service structure and local policies related to SHPT management was obtained through a key informant questionnaire and review of written policies.

**Results:** 2361 patients were included from 8 UK renal Units. Number of dialysis patients from each centre ranged from 110 to 636. Geographical locations ranged from Dundee in Scotland to Exeter in the South of England. Overall achievement of targets was low with 11% of all patients with all 3 biomarkers within the Renal Association and KDOQI targets and 23% within the KDIGO targets. Reported staffing varied between the units ranging from 27 patients per consultant to 91 patients per consultant. Dietician and renal pharmacist input also varied from 55 patients per dietician to 154 patients and 110 patients per renal pharmacist to no renal pharmacist. The 2 units with the highest number of patients achieving target range for calcium, phosphate and PTH differed considerably in staffing (27 vs 91 patients per consultant, 75 vs 195 patients per dietician and 195 vs 636 patients per renal pharmacist for the 2 sites respectively).

**Conclusions:** Achievement of targets for calcium, phosphate and PTH are low across all dialysis centres, not helped by differing target ranges and a lack of consensus as to what constitutes best practice in SHPT management. In line with this observation, this study confirms there to be no clear association between reported staffing levels and achievement of targets.

**MP518**

**THE NUMBER OF OXYPHIL CELLS INCREASES IN SECONDARY HYPERPARATHYROIDISM**

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**Introduction and Aims:** The number of oxyphil cells (OC) increases in the parathyroid glands (PTG) of patients affected by secondary hyperparathyroidism (HPT), especially if they are treated with vitamin D and/or calcium/magnesium. Furthermore, the incubation of PTG with a high calcium medium has been shown to lead to the formation of OC, consistent with the hypothesis that calcium-sensing receptor (CaSR) stimulation may increase the OC number. This hypothesis has been not tested in the clinical setting. Aim of this study was to verify whether the cell populations in the PTG can be influenced by disorders of mineral metabolism as measured before parathyroidectomy (PTx).

**Methods:** A retrospective study on 65 consecutive patients submitted to a first PTx, either total or subtotal, in our hospital in the last 4 years was performed. Biochemical parameters of mineral metabolism, including serum ionized calcium (iCa) and calcitonin (CT), were obtained before PTx. Patients aged < 18 years and patients treated with cinacalcet were excluded from the study. Chief cells (CC), OC and transitional oxyphil cells (TOC) were evaluated by means of a semiquantitative assessment in all the histological specimens; patients were considered positive if OC and/or TOC were present in more than 5% of examined area and at least in one gland.

**Results:** The 65 patients were subdivided into three groups, according to cell distribution: group 1 (only CC), group 2 (CC+OC), and group 3 (CC+OC+TOC). There were no significant differences either in the demographic characteristics or parathyroid hormone (PTH), alkaline phosphatases (ALP), albumin and phosphate (P) serum levels among the three groups. Interestingly, total serum calcium (tCa), iCa and CT serum levels were significantly different and increased steadily from group 1 to group 3 (Table).

**MP518 Table 1. Demographic and biochemical characteristics of the patients**

<table>
<thead>
<tr>
<th></th>
<th>Group1 (CC)</th>
<th>Group2 (CC+OC)</th>
<th>Group3 (CC+OC+TOC)</th>
<th>Statistical significance *</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>number</strong></td>
<td>20</td>
<td>23</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td><strong>Age, years</strong></td>
<td>40±10</td>
<td>52±14</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HDvintage,months</strong></td>
<td>124±82</td>
<td>113±55</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>M/F</strong></td>
<td>12/8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PTH, pg/ml</strong></td>
<td>1690 ± 587</td>
<td>1653 ± 718</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ALP, mU/ml</strong></td>
<td>295 ± 213</td>
<td>291 ± 186</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CT, pg/ml</strong></td>
<td>10.1 ± 5.6</td>
<td>18.4 ± 9.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>iCa, mg/dl</strong></td>
<td>10.2 ± 0.6</td>
<td>10.52 ± 0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Alkaline phosphatases (ALP)</strong></td>
<td>1.21±0.2</td>
<td>1.32±0.1</td>
<td>p &lt;0.01</td>
<td></td>
</tr>
<tr>
<td><strong>Albumin, g/dl</strong></td>
<td>3.99±0.4</td>
<td>3.97±0.38</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>P, mg/dl</strong></td>
<td>6.0 ± 1.5</td>
<td>6.0 ± 1.3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* ANOVA test; NS = not significant
Abstracts

Results:
Ca and P (Ca/P<50). In the case of severe hyperparathyroidism, therapy with vitamin
intradialytic Ca infusion. Dialysis sessions were tailored at normalization of pre-dialysis
schedules of treatment were tested: 1. NxStage (Ca 1.5 mEq/L); 2. and 3. Conventional
hyperparatiroidism was defined as PTH>300 pg/ml for at least 3 months. Four
(PPTH) profiles are collected, 38 in severe hyperparathyroidism (9

Introduction and Aims: Abnormal bone turnover is common in CKD, but its effects
on bone quality remains unclear. The aim of this study was to identify differences in
bone microarchitecture between patients with low vs. high bone turnover by
HR-pQCT.

PARATHYROID HORMONE PROFILING FOR OPTIMIZATION OF CALCIUM CONTENT IN DIALYSE IN SEVERE HYPERPARATHYROIDISM, IN TAILORED, INCREMENTAL HEMODIALYSIS

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Introduction and Aims: Severe hyperparathyroidism is still a challenge in hemodialysis.
The definition of dialysate Calcium (Ca) is a pending issue, coming of age in case of
tailored dialysis schedules and of portable home dialysis machines (NxStage), with low
flow dialyse. Direct measurement of Ca mass transfer is complex; Ca levels at start and
end of dialysis are a poor measure of Ca balance. This study aims at describing
the morphologic prevalence of OC and TOC in HPT was associated

Conclusions:
Thirty healthy volunteers served as controls.

Bone turnover (HBT) iPTH >500 pg/ml (n:15; mean age 51.6 ± 7.9 iPTH 1142 ± 669).

Methods:
Twenty two prevalent hemodialysis (HD) postmenopausal women were
recruited for measurements of bone microarchitecture at the distal radius (DR) and
tibia (TB). HD patients were matched for age, dialysis vintage and time since
menopause and were divided in two groups according to their serum iPTH: Low bone
turnover (LB) iPTH <200 pg/ml (n:2; mean age 52.8 ± 4.7; iPTH 124 ±55) and High
Bone turnover (HBT) iPTH >350 pg/ml (n:15; mean age 51.6 ± 7.9; iPTH 1142 ± 669).
Thirty healthy volunteers served as controls.

Results: In the DR, cancellous bone volume (BV/TV) was greatly decreased in LBT
than HBT (N: 13 ± 2.5%; LBT 6.4 ± 3.8%; HBT 8.6 ± 3.7; p<0.05); trabecular thickness
(TbTh) was slightly decreased in LBT and significantly increased in HBT (N: 0.06
±0.01 mm; LBT: 0.046 ± 0.01; HBT: 0.070 ± 0.01; p<0.01). Cortical Thickness (CtTh)
did not significantly differ from each other (N: 0.69 ± 0.18 mm; LBT: 0.47 ± 0.07;
HBT: 0.36 ± 0.20). Similar trends were seen for all parameters at the tibia except for a
borderline significant difference in cortical volumetric density (LBT: 811 ± 69 mg HA/
cm3; HBT: 719 ± 120 mg HA/cm3, 95%CI-11.4%±9.0% p=0.08).

Conclusions: We conclude that microarchitecture parameters of bone quality varies
albeit by different mechanisms with different levels of bone turnover, trabecular
parameters being more compromised in LBT and cortical parameters in HBT. The
lower cortical volumetric density probably reflects higher bone porosity in the HBT
caucasian patients.


THE IMPORTANCE OF DIFFERENTIATION BETWEEN PARATHYROID HORMONE 1-84 (iPTH) AND NON 1-84 FRAGMENTS IN THE DISORDERS OF BONE AND MINERAL METABOLISM

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Introduction and Aims: Parathyroid hormone (PTH) is one of the important
hormones regulating calcium and phosphate homeostasis in the management of bone
metabolism. Methods that are currently used for its determination can measure both
the complete molecule 1-84 as well as its degradation fragments the non 1-84 (PTH).
Both molecules have different and sometimes opposite effects. This study is performed to

determine whether patients are having a low bone turnover using the marketed
automated methods of the third generation measuring PTH 1-84(iPTHbio).

Methods: The study was performed in 147 patients on hemodialysis with the
determination of PTH, PTHbio, PTH ratio (PTHbio / PTH-PTHbio), Ca, P, FGF23,
25OHvitaminD, before hemodialysis. PTH and PTHbio were measured using roche
detection, FGF23 ImmunoMx.

Results: The mean age of the study population was 66.1 ± 14.59 years, 76 men and 71
women, the mean time on HD was 5.2 ± 4.79 years, 13 patients were on HDF online,
and 134 on standard HD. Other studied mean values were: Ca 9.21±0.74 mg/dl, P 5.34
±2.3 mg/dl, PTH 298±64.3±53 pg/ml, PTHbio 174.94±172.18 pg/ml, PTH1-84/
PTH7-84: 1.72±3±285, FGF23 2853.0±4246.8 RU/ml, 25 OH vitD3 35.55 mg/ml.
There is correlation between FGF23 and PTHbio, PTHbio and the ratio PTH1-84/PTH7
but not with the 25OHvitD. In the univariate model PTH1-84/PTH7-84 ratio correlates
positively with FGF23 (p<0.04) such that a 1% increase in the ratio is an increase of
1.6% of FGF23. PTHbio iPTH and also correlate with FGF23. The ratio does not
correlate with either the Ca or P, years in HD or age. In the univariate analysis
model the PTH1-84/PTH7-84 ratio correlates positively with FGF23 (p<0.04) such that
a 1% increase in the ratio represents an increase of 1.6% of FGF23. PTHbio and iPTH
also correlate with FGF23. The ratio does not correlate with either the Ca or P, years in
HD or age.

Conclusions: 1. It is very important to know the values of 1-84 and non 1-84
fragments our patients 2. - The values of PTH 1-84 are significantly lower than those
used now. 3. - All measured forms of PTH correlate well with each other but indicate
different aspects 4. - The ratio expresses a sample of high turn over bone and correlates
with the FGF23.

THE RELATIONSHIP BETWEEN INTACT PARATHYROID HORMONE LEVELS AND DAILY PHYSICAL ACTIVITY IN HEMODIALYSIS PATIENTS

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Conclusions: The morphologic prevalence of OC and TOC in HPT was associated
with statistically significant increases in serum Ca and iCa serum levels, that could
induce an increase in the CT serum levels. Uremic patients affected by HPT, being
exposed to higher iCa levels, may have a shift in the phenotype of parathyroid cell
populations.

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Introduction and Aims: Poor physical activity and decreased daily activities are commonly seen in hemodialysis (HD) patients. Along with the progression of chronic kidney disease (CKD), various abnormalities of mineral and bone metabolism develop such as osteitis fibrosa and adynamic bone disease which are related with intact parathyroid hormone (Intact-PTH). Surprisingly scarce data exists regarding the relationship between intact PTH and daily physical activity in HD patients.

Methods: This cross sectional included HD patients who regularly attending in a state hospital. Demographics, clinical parameters, laboratory data were recorded for all patients. Depressive symptoms, quality of life and daily activities of HD patients were measured by Beck Depression Inventory, SF-36, and Nottingham Extended Activities of Daily Living Scale (NEADLS) respectively.

Results: In total 114 patients were enrolled. The value of Intact-PTH for <25th (Group 1), <25th-50th (Group 2), 50th-75th (Group 3) and >75th (Group 4) quartiles were <132.5 pg/ml, ≥132.5 <261.0, ≥261.0 <510.4 and ≥510.4 respectively. The NEADLS scores were 25.3±10.8, 35.0±9.4, 27.2±13.9 and 26.4±12.9 as going from Group 1 to Group 4 respectively. Post hoc analysis of these 4 groups revealed that only Group 1 and Group 2 were different with respect to NEADLS (P:0.009). The incorporation of NEADLS and Intact-PTH was inversely associated with daily activities in whole (P:0.012), and Group 2 and Group 4 were different with respect to NEADLS (P:0.034).

Conclusions: Intact-PTH levels were inversely associated with daily activities in whole group. However the post hoc analysis demonstrated that the association between intact PTH and daily activity is not linear and daily physical activity was lower only in patients with lowest and highest quartiles of Intact-PTH.

MP524 TRENDS IN MEDICAL AND SURGICAL MANAGEMENT OF SECONDARY HYPERPARATHYROIDISM (SHPT) AMONG HEMODIALYSIS PATIENTS: RESULTS FROM THE DIALYSIS OUTCOMES AND PRACTICE PATTERNS STUDY (DOPPS)

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Introduction and Aims: SHPT is highly prevalent among patients on chronic hemodialysis (HD), and parathyroid hormone (PTH) levels have risen over the past decade. Treatment options for SHPT include pharmacological agents and surgical removal of parathyroid glands (parathyroidectomy). (PTX). We describe trends in PTH levels and SHPT treatments in the DOPPS, to evaluate the hypothesis that PTX rates have decreased over the time period since the availability of cinacalcet therapy.

Methods: 39,499 participants in DOPPS phase 2-4 (2002-2012) without a prior PTX were included. Incident PTX rates were calculated as the sum of PTX hospitalizations divided by follow-up time. PTX levels, cinacalcet, and vitamin D prescriptions were collected at study enrollment. Poisson, logistic, and linear regressions were used to compare trends over time in PTH level, PTX treatment, and medical prescription respectively.

Results: Trends over time in PTH levels and SHPT treatments are shown in Table 1. In Eur-A/NZ and in N America, median PTH increased but the prevalence of very high PTH (>800 pg/ml) remained stable. In Japan, median PTH remained relatively stable, but the prevalence of PTH>800 increased. PTX rates decreased in Eur-A/NZ and Japan while remaining relatively unchanged in N America. Patients with PTH>800 had a higher PTX rate after adjusting for region and phase (p<0.01). Cinacalcet prescription increased from DOPPS phase 3 to 4 in all regions. During the same time period, vitamin D prescription increased in Eur-A/NZ and North America. In Japan, prescription of any vitamin D remained stable, however use of IV vitamin D became more common in recent years.

Conclusions: In the international DOPPS cohort, SHPT treatment changed over the past decade, with a decrease in PTX and increase in cinacalcet and vitamin D prescription. Given the proven efficacy of calcimimetics, the rise in median PTH levels observed outside of Japan was likely due to higher target PTH levels as reported by medical directors at DOPPS facilities, not shown. The prevalence of very high PTH (>800 pg/ml) has changed little in median PTH and decrease in PTX, probably because cinacalcet is now prescribed for this condition.

MP525 THE CALCIMIMETIC CALINDOL PREVENTS HIGH PHOSPHATE-INDUCED VASCULAR CALCIFICATION BY UPREGULATING MATRIX GLA PROTEIN

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Introduction and Aims: High serum phosphate (Pi) levels represent a major issue in dialysis patients, because associate with secondary hyperparathyroidism (SHPT), vascular calcification (VC), and cardiovascular outcomes. In this population, calcimimetics are used to control SHPT, hyperphosphatemia, and, more recently, to delay the progression of VC. The aim of this in vitro study was to investigate the direct effects of the calcimimetic calindol on the progression of high Pi-induced VC.

Methods: Rat vascular smooth muscle cells (VSMCs) were incubated with high Pi concentrations, and the effects of calindol were investigated on vascular calcium (Ca) deposition and VSMC osteoblastic differentiation.

Results: Calindol inhibited Ca deposition concentration-dependently with a maximal inhibition of 64.0±5.2% achieved at 100 nM. Furthermore, calindol was able to partially prevent the high Pi-induced Bone Morphogenic Protein 2 (BMP-2) expression upregulation (32.4 ± 4.6% of inhibition; p<0.01). Interestingly, the pretreatment with calindol enhanced the Matrix Gla Protein (MGP) gene expression significantly, compared to high Pi-treated cells (40.2 ± 6.6 % of increase, p<0.01).

Conclusions: In conclusion, we demonstrated that the calcimimetic calindol prevents high Pi-induced VC, by affecting osteoblastic differentiation in vitro. In particular, the inhibitory effect of calindol on VC is probably due to its stimulatory role on Ca Sensing Receptor, leading to an increase in the synthesis of MGP by VSMCs.
This multicenter observational study was conducted between July 2011 and August 2012. 146 patients with severe SHPT on chronic hemodialysis were enrolled into the study. Patients with serum calcium ≥ 10.5 mg/dL, Ca × P < 75 and PTH concentrations >= 600 pg/ml were excluded to constitute the study group. The primary endpoint was to compare the effectiveness of paricalcitol and cinacalcet treatment of MHD patients with severe SHPT. The aim of this study is to evaluate and compare the effectiveness of cinacalcet and paricalcitol or calcitriol treatment of MHD patients with severe SHPT. SHPT however, there is no consensus on the most effective type and dose of therapy. The present study was designed to compare the effectiveness of combination therapy in patients with SHPT. A total of 78 patients in group CP and 68 subjects in group CC were evaluated. Demographic and clinical characteristics and laboratory data of two groups were similar at baseline. In group CP, mean PTH values in 1st and 12th month were 1257.6 ± 668.4 pg/ml and 928.8 ± 497.3 whereas in CC group, mean PTH values in 1st and 12th month were 1226.9 ± 595.6 pg/ml and 1210.9 ± 574.8 (p<0.003). At baseline both groups had similar phosphorus levels which were significantly lower than the group CC (p<0.02, respectively). At baseline both groups’ alkaline phosphatase levels were similar however at the end of the study in group CP, ALP levels were significantly lower than the group CC (p<0.002). Both initial and completion cinacalcet doses were similar in both groups. Despite the mean dose of vitamin D administration was significantly higher in paricalcitol group (14.98 ± 9.06 mcg/week/12 months) than the cinacalcit group (10.8 ± 8.85 mcg/week/12 months) we observed less hyperphosphatemia and elevated Ca×P in group CP (p<0.01, p<0.05 respectively). Duration of vitamin D cessation because of high phosphorus levels to combination therapy with paricalcitol and cinacalcit was superior in terms of PTH response to treatment, less hyperphosphatemia and decrease in alkaline phosphate levels to combination therapy with paricalcit and cinacalcit in dialysis patients with severe SHPT. We suggest that paricalcitol and cinacalcit combination should be preferred in resistant cases.

Results: The presence of lymphocytes in the normal parathyroid gland and tissue architecture (nodal in patients with sHPT) allows for discrimination between normal parathyroid glands and parathyroid glands of patients with sHPT. Protein expression of receptor factor (FGFR)/Klotho complexes seem to be involved in its development. The variability of each immunohistochemical variable was high. Therefore correlations between the FGFR3, Klotho, FGFR2, and FGFR1 expression within each tissue slide was high. Therefore correlations between the different immunohistochemical variables were analyzed for each of the nine fields and the results were shown as means and 95% confidence index. Results: Serum calcium and phosphate concentrations were assessed before the first dose of cinacalcit and then after 3 and 6 months of treatment. The results are shown as means and 95% confidence index. Results: Serum PTH concentration was significantly decreased after 3 and 6 months of treatment from 1138 (931-1345) to 772 (551-992); p<0.001 and 635 (430-839) pg/ml; p<0.0001, respectively. Plasma FGF-23 concentration decreased after 3 and 6 months of treatment from 593 (457-730) to 513 (380-645); p=0.099 and 433 (304-561) pg/ml; p=0.015, respectively. Serum calcium and phosphate concentrations were assessed stable during the observation [calcium: 2.15 (2.07-2.22) before treatment, 2.11 (2.04-2.17) after 3 months of treatment and 2.08 (2.0-2.15) mmol/l after 6 months of treatment]; [phosphate: 2.02 (1.87-2.18), 1.97 (1.81-2.14) and 1.9 (1.74-2.05) mmol/l; p<0.20 respectively]. Conclusions: 1. Treatment with cinacalcit decreases plasma FGF-23 concentration in hemodialysed chronic kidney disease patients with secondary hyperparathyroidism. 2. Clinical consequences of decreased plasma FGF-23 during the therapy with cinacalcit need to be elucidated.
SCLEROSTIN AND 1 YEAR SURVIVAL AMONG PATIENTS UNDERGOING HEMODIALYSIS

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Introduction and Aims: Sclerostin, a protein expressed by osteocytes, has recently been shown to be a good predictor for bone formation in chronic kidney disease patients. Serum sclerostin levels are increased in these patients and whether sclerostin affects patient survival is unknown.

Methods: We examined 1 year survival according to serum sclerostin levels in a prospective cohort of 350 prevalent hemodialysis patients (164 males, 186 females, mean age: 57±13 years, mean hemodialysis vintage: 58±32 months).

Results: During follow-up, 26 hemodialysis patients (7.42%) died. Patients who died were older (67.8±9 vs 56.5±13 years, p=0.013), had lower 25-hydroxy vitamin D3 (19.6±9.1 vs 29.8±11 ng/ml, p=0.024) and higher sclerostin levels (2143±1327 vs 1469±1373 pg/ml, p=0.007). Patients with 25-hydroxy vitamin D3 levels greater than median value (21.6 ng/ml; Group 1) were associated with an increase in survival when compared to patients with 25-hydroxy vitamin D3 levels greater than median value and receiving calcitriol therapy (Group 2), patients with 25-hydroxy vitamin D3 levels lower than median value and receiving calcitriol (Group 3) and finally patients with 25-hydroxy vitamin D3 levels lower than median value and not receiving calcitriol therapy (Group 4) (Log-rank: p=0.0049). Increased sclerostin quartiles are associated with decreased survival (Log-rank:p<0.025). Highest sclerostin quartile (>2282 pg/ml) was associated with a 22% increase in the multivariable adjusted risk of death, as compared with the lowest quartile (<757 pg/ml; adjusted also for both calcitriol therapy and serum 25-hydroxy vitamin D3 levels).

Conclusions: Increased sclerostin levels seem to be independently associated with mortality among prevalent hemodialysis patients.

DIETARY TRENDS AND MANAGEMENT OF HYPERPHOSPHATAEMIA AMONG DIALYSIS PATIENTS

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Introduction and Aims: Achieving recommended levels of protein intake while maintaining guideline levels of serum phosphorus (P) is associated with the best outcomes in patients undergoing dialysis. Hyperphosphataemia management (using dietary modification and binders to reduce intestinal P absorption) can be complicated if patients consume drinks and processed food that are rich in P-containing additives. We conducted a survey to examine dietary trends among patients with chronic kidney disease (CKD) and the problems associated with P control.

Methods: Renal care professionals responsible for providing dietary advice in renal units in the Netherlands, Spain, Sweden and the UK were asked to complete an online questionnaire. The information requested included responder demographics, patient numbers, nutritional trends and problems associated with dietary P restriction. Results from the 4 countries were pooled.

Results: The questionnaire was completed by 48 dietitians, 35 nurses and 1 physician (>60% response rate) representing clinics with >15 000 dialysis patients in total. Since entering clinical practice a mean of 15 years ago, 29 (35%) responders had noticed a decrease in the consumption of food prepared from fresh ingredients, 47 (56%) had noticed an increase in consumption of fast food, and 40 (48%) had noticed an increase in consumption of foods rich in P-containing additives: 50 (60%) felt that CKD patients now have greater awareness of the P content of food. Haemodialysis (HD) patients were reported as being most likely to have difficulty restricting P: 32 (40%) responders reported that the majority of their HD patients found it hard to follow advice on P restriction; younger patients (18–45 years) were thought to have the most difficulty. When asked about the relative importance of restricting P and maintaining protein intake in HD patients, 42 (50%) considered them equally important and 30 (36%) favoured maintaining protein intake.

Conclusions: This survey suggests that, despite increased awareness of the P content of food, many patients have problems restricting dietary P. There is a trend towards greater consumption of processed foods in which P-containing additives may be used to extend shelf life, improve colour or flavour, or increase water retention. P from these additives is absorbed more easily than P from natural protein-rich foods. The renal community must lobby for labelling of food and drink to show use of P additives and, ideally, P content per portion. This would enable patients to avoid or limit their intake of unnecessary P from additives and help maintain adequate protein intake within the limits imposed by dialysis and an acceptable binder regimen.
Abstracts

p<0.001 and p<0.05). There was significant (p<0.001) difference in all laboratory (iPTH/Ca/P) target achievement between group AD (15.8%) and OLD (20.2%). Prevalence of type 2 diabetes mellitus (DM) was the highest (p<0.001) in group OLD (30.9%) followed by group VOLD (28.8%) and AD (27.3%). Serum iPTH level was lower in patients with DM compared to pts without DM patients in all age groups (AD: p<0.01; OLD: p<0.001; VOLD: p=0.666). Calcimetic (p<0.001), phosphate binders (p<0.01) and vitamin D (p<0.01) prescription was the highest in the AD group in comparison to OLD and VOLD groups. Percentage of patients without these medications was the highest in group VOLD (38.4%).

Conclusions: In CKD-5D patients laboratory and target achievement of serum iPTH, Ca and P as well as treatment practice of mineral and bone metabolism area significantly different from each other across age groups. Serum iPTH level was continuously and significantly decreased with increasing age and it further decreased in case of T2DM. Further research needs to more elucidate these age related clinical differences in CKD-MBD patients in Hungary.

Methods:

Eighteen stable HD patients, (male/female: 13/5), aged 68.5 (39-89) years, were on PPI, omeprazole, 20 mg once daily, already for 25 (14-48) months (PPI group). Follow-up period was 14 months. No patient was on Mg-containing medication.

Results: Mg levels were lower in PPI group throughout the study compared to no PPI group and this difference was statistically significant in months 1, 5 and 10 (2.19±0.28 vs 2.51±0.54 mg/dL, p=0.002; 1.91±0.33 vs 2.40±0.24 mg/dL, p=0.002 and 2.11±0.26 vs 2.41±0.29 mg/dL, p=0.02, respectively), whereas no significant difference was found in other studied parameters, including Ca and PTH. In both groups, no significant changes were detected during the study in all measured parameters, except for PTH that was sig each other acer by the end (282.50±111.65 vs 551.67±215.18 ng/ml, p=0.002 for PPI group and 178.21±114.14 vs 453.62±288.80 ng/ml, p=0.01 for no PPI group). URR > 75% and spKT/V > 1.5 were found in PPI group, while in no PPI group < 70% and > 1.4, respectively, throughout the study. No significant differences were noted in Mg and the other studied parameters between two groups when analyzed according to sex (male/female), HD modality (conventional HD/HDF) and cinacalcet or paricalcitol use.

Conclusions: Long-term PPI use was associated with variably lower sMg levels in HD patients with no significant differences in serum Ca and P levels. This association appears to be independent of factors such as sex, HD adequacy and modality as well as cinacalcet or paricalcitol use.

Results:

The mean age of patients was 51.8± 16.9 years, 51% male, 49% were female. There were 16 hemodialysis and 25 peritoneal dialysis patients. The ratio of vitamin D level under 15 ng / ml was 87.8%. Sexual dysfunction rate of 85.4%, anxiety rate of 25.6% and depression rate of 11.1% were noted in sMg and the other studied parameters between two groups when analyzed according to sex (male/female), HD modality (conventional HD/HDF) and cinacalcet or paricalcitol use.

Conclusions: Vitamin D deficiency in addition to anemia, may contribute to sexual dysfunction. In hemodialysis patients sexual dysfunction is more common than peritoneal dialysis patients. Advanced age, malnutrition and vitamin D deficiency have negative impact on sexual life.

Introduction and Aims: Sexual dysfunction is very common in dialysis patients. It impairs the quality of life. This work was done in order to assess the relationship between serum vitamin D levels with sexual dysfunction in dialysis patients.

Methods: 25-hydroxyvitamin D level of 41 dialysis patients were evaluated. 25-hydroxyvitamin D level > 30 ng/ml were accepted as vitamin D sufficient patients. Patients were divided into 3 groups according to the level of 25-hydroxyvitamin D: group 1: 25-hydroxyvitamin D level ≤ 5 ng / ml group 2: 5-15 ng / ml group 3: We applied the Hospital Anxiety and Depression Scale (HADS), and Arizona Sexual Experiences Scale (ASEX) to all patients. ASEX for the total score was used as cut-off point 11. Values ≥ 11 were considered as sexual dysfunction. HADS anxiety subscale scores was taken as the cut-off point 10 and HADS depression subscale was taken as the cut-off point 7. Values greater than cut-off point were evaluated as anxiety and depression, respectively.

Results: Vitamin D deficiency in addition to anemia, may contribute to sexual dysfunction. In hemodialysis patients sexual dysfunction is more common than peritoneal dialysis patients. Advanced age, malnutrition and vitamin D deficiency have negative impact on sexual life.

Methods:

Conclusions: In case of T2DM. Further research needs to more elucidate these age related clinical differences in CKD-MBD patients in Hungary.

Results:

Conclusions: Long-term PPI use was associated with variably lower sMg levels in HD patients with no significant differences in serum Ca and P levels. This association appears to be independent of factors such as sex, HD adequacy and modality as well as cinacalcet or paricalcitol use.

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(Mg) containing phosphate binders are effective in controlling serum phosphate. A moderate increase in serum Mg concentration has been observed in patients treated with Mg containing phosphate binders. The impact of a moderate increase in serum Mg in VC is not clear. Previous experimental works have shown that high Mg concentration reduces calcification of vascular smooth muscle cells in vitro. However, there are no in vivo studies where the effects of high concentrations of Mg were evaluated. The present study was designed to evaluate whether a dietary supplementation of Mg can revert VC in rats with renal failure induced by 5/6 nephrectomy (Nx) + calcitriol (CTR) and high phosphorous (P, 1.2%) diet. METHODS: VC was generated in male wistar rats through Nx, CTR administration (80 ng/kg) and high P diet (1.2%) for 2 weeks (control group). The effect of dietary Mg on VC was evaluated by dietary supplementation (0.6% Mg). Rats were distributed in the following groups: Nx + CTR + P 1.2% and Nx + CTR + P 2 ± 2 additional weeks of 0.6% Mg diet. Calcium (Ca) and P contents in plasma, aorta, lung and stomach were analyzed. Plasma levels of creatinine, Mg and PTH were also measured. Finally, van Kossa staining was performed in aorta.

Results: Aortic Ca levels as well as aortic, stomach and plasmatic levels of P decreased after 2 additional weeks with 0.6% Mg supplementation vs. rats without Mg. These levels were similar or lower than in the control group. Mg and CTR levels increased in rats fed with 0.6% Mg diet while PTH levels decreased significantly with respect to the control group. Van Kossa staining and plasmatic levels of P were also lower than those of rats fed without Mg diet or control group. Finally, mortality decreased drastically (50%) after Mg supplementation treatment.

Conclusions: An increase in dietary of Mg promotes the reversion of vascular calcification and hyperparathyroidism.

### Nephrology Dialysis Transplantation

**Abstracts**

**MP535**

**LOWER DIALYSE CALCIUM CONCENTRATION FOR HOME HEMODIALYSIS CAN AFFECT CALCIUM BALANCE DURING DIALYSIS SESSION AND BONE METABOLISM**

Nori Hanafusa1, Ikuto Masakane1, Satoko Ito1, Shigeru Nakai1, Kanenori Maeda1 and Hiroshi Suzuki1

1Working Group for Patient Registry Japanese Society for Home Hemodialysis Yamagata Japan

**Introduction and Aims:** Many clinical reports of frequent or long hemodialysis have recently demonstrated dramatic clinical benefits in terms of morbidity or mortality. Such treatments bring enhanced ultrafiltration capacity due to prolonged treatment period per week, as well as improved solute removal. There is a concern that even subtle differences in dialysate composition can cause larger consequences than ordinary in-center hemodialysis. Above all, negative Ca balance through dietary supplementation of Mg can revert VC in rats with renal failure induced by 5/6 nephrectomy (Nx) + calcitriol (CTR) and high phosphorous (P, 1.2%) diet.

**Methods:** VC was generated in male wistar rats through Nx, CTR administration (80 ng/kg) and high P diet (1.2%) for 2 weeks (control group). The effect of dietary Mg on VC was evaluated by dietary supplementation (0.6% Mg). Rats were distributed in the following groups: Nx + CTR + P 1.2% and Nx + CTR + P 2 ± 2 additional weeks of 0.6% Mg diet. Calcium (Ca) and P contents in plasma, aorta, lung and stomach were analyzed. Plasma levels of creatinine, Mg and PTH were also measured. Finally, van Kossa staining was performed in aorta.

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**Conclusions:** An increase in dietary of Mg promotes the reversion of vascular calcification and hyperparathyroidism.

### Nephrology Dialysis Transplantation

**Abstracts**

**MP536**

**DIFFERENCE IN FACTORS ASSOCIATED WITH BONE FRACTURE BETWEEN MALE AND FEMALE PATIENTS ON HEMODIALYSIS**

Masataka Tsunoda1, Ryota Ikei2, Naomi Sasaki3, Megumi Sato3 and Nobuo Hashimoto4

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**Introduction and Aims:** In the general population, osteoporosis is more frequently found in females, and is commonly evaluated by change of bone mineral density (BMD). In clinical practice of hemodialysis (HD), however, bone fracture sometimes occurs in male patients with normal BMD. The aim of this study was to examine the difference in clinical factors associated with bone fracture between male and female patients on HD.

**Methods:** In this study, we included 54 patients (male: female = 32: 22, age 65 ± 11 years, HD duration 123 ± 105 months) treated with HD for more than 1 year. The patients were classified into 2 groups: one with a history of bone fracture after HD initiation (n=21), and the other without the history (n=33). Between the groups, we compared clinical factors including blood biochemical tests and BMD by dual-energy X-ray absorptiometry in both sexes separately.

**Results:** Nine of the male patients and 12 of the females had a history of bone fracture after HD initiation. In the female patients, there was a significant difference in BMD and the young adult mean (YAM) of lateral lumbar spine between the two groups (Table). In contrast, in the male patients, there was a significant difference in plasma total homocysteine (Hcy) levels but not in BMD between the groups. Multiple logistic regression analysis showed that in females, BMD was independently associated with a history of fracture (p=0.04). In male patients, plasma Hcy level was marginally significantly associated with a history of bone fracture (p=0.07). Table. Comparison between clinical factors with and without fracture.

**Conclusions:** Bone strength depends on both bone quantity and quality, and collagen cross-links are determinants of bone quality. Recent studies have indicated that hyperhomocysteinemia reduced bone strength via a reduction of enzymatic cross-links and an increase of nonenzymatic cross-links. Hyperhomocysteinemia, a frequent complication in HD patients, might play a role in bone fracture in this population.

### Nephrology Dialysis Transplantation

**Abstracts**

**MP537**

**DIFFERENCE IN FACTORS ASSOCIATED WITH BONE FRACTURE BETWEEN MALE AND FEMALE PATIENTS ON HEMODIALYSIS**

Norio Hanafusa1, Ikuto Masakane1, Satoko Ito1, Shigeru Nakai1, Kanenori Maeda1 and Hiroshi Suzuki1

1Working Group for Patient Registry Japanese Society for Home Hemodialysis Yamagata Japan

**Introduction and Aims:** Many clinical reports of frequent or long hemodialysis have recently demonstrated dramatic clinical benefits in terms of morbidity or mortality. Such treatments bring enhanced ultrafiltration capacity due to prolonged treatment period per week, as well as improved solute removal. There is a concern that even subtle differences in dialysate composition can cause larger consequences than ordinary in-center hemodialysis. Above all, negative Ca balance through dietary supplementation of Mg can revert VC in rats with renal failure induced by 5/6 nephrectomy (Nx) + calcitriol (CTR) and high phosphorous (P, 1.2%) diet.

**Methods:** VC was generated in male wistar rats through Nx, CTR administration (80 ng/kg) and high P diet (1.2%) for 2 weeks (control group). The effect of dietary Mg on VC was evaluated by dietary supplementation (0.6% Mg). Rats were distributed in the following groups: Nx + CTR + P 1.2% and Nx + CTR + P 2 ± 2 additional weeks of 0.6% Mg diet. Calcium (Ca) and P contents in plasma, aorta, lung and stomach were analyzed. Plasma levels of creatinine, Mg and PTH were also measured. Finally, van Kossa staining was performed in aorta.

**Results:** Aortic Ca levels as well as aortic, stomach and plasmatic levels of P decreased after 2 additional weeks with 0.6% Mg supplementation vs. rats without Mg. These levels were similar or lower than in the control group. Mg and CTR levels increased in rats fed with 0.6% Mg diet while PTH levels decreased significantly with respect to the control group. Van Kossa staining and plasmatic levels of P were also lower than those of rats fed without Mg diet or control group. Finally, mortality decreased drastically (50%) after Mg supplementation treatment.

**Conclusions:** An increase in dietary of Mg promotes the reversion of vascular calcification and hyperparathyroidism.
MP538  INTERLEUKIN-17 PRODUCING EFFECTOR MEMORY T CELLS AND CD4+CD25+FOX3+ REGULATORY T CELLS CORRELATED WITH PHOSPHATE AND PARATHYROID HORMONE LEVELS IN CHRONIC HEMODIALYSIS PATIENTS

Min-Hui Wang2,3, Kuan-Yu Hung4,5, Ohng-Kang Chiang1,6, Jen-Qi-Wen Huang2,6, Kuo-Cheng Lin2,3, Cheng-Lin Lang1
1Internal Medicine, Cathay General Hospital, Taichung City Taiwan Republic of China, 2Internal Medicine, Cathay General Hospital, Taichung City Taiwan Republic of China, 3Internal Medicine, Far Eastern Memorial Hospital, Taoyuan City Taiwan Republic of China, 4Internal Medicine, China Medical University Hospital, Taichung City Taiwan Republic of China, 5Internal Medicine, National Taiwan University Hospital, Taichung City Taiwan Republic of China, 6Internal Medicine, National Taiwan University Hospital, Taichung City Taiwan Republic of China

Introduction and Aims: T helper (Th) lymphocytes play critical roles in the immune activation and inflammation in the chronic hemodialysis (HD) patients and mineral bone disorders including hyperparathyroidism and hyperphosphatemia contribute to the inflammatory effects. Interleukin-17 producing effector memory T (Th17) cells and CD4+CD25+Fox3+ regulatory T (Treg) cells both come from naive Th cells, share reciprocal development pathways but exhibit opposite effects. Here we investigated the relationship between the Treg and Th17 cells and mineral bone disorder in the chronic HD patients.

Methods: One hundred and five patients (age ≥ 35 years old) on chronic HD over 3 months were enrolled. Patients with systemic infection or malignancy, taking immunosuppressive medication were all excluded. The peripheral blood mononuclear cells were collected, cultured and stimulated by phytohemagglutinin-L (PHA-L), phorbolmyristate acetate (PMA) and ionomycin in different time point. The Treg cells and Th17 cells were then stained and analyzed by flow cytometry. Hematological and biological markers were detected. The relationship was analyzed by statistical analysis. Results: The T cell differentiation were as follows: Th17 cells (mean ± standard deviation (SD): 25.61% ± 10.2%) and Treg cells (8.45% ± 4.3%). In the mineral aspect, the Th17 cell differentiation correlated with phosphate (P) level (r = 0.211, p < 0.05) and intact parathyroid hormone (iPTH) level (r = -0.277, p < 0.05). The Th17 cell differentiation negatively correlated with P and iPTH levels (r = 1.97, p < 0.05 and r = -1.76, p < 0.05). Besides, the Th17/Treg cell ratio also correlated with the age and albumin levels (r = -0.25, p < 0.01 and r = 0.26, p < 0.05) but did not correlated with the calcium, alkaline-P or CRP levels as determined by statistical analysis. In the non-diabetes patients group (n = 53), the Th17 cells differentiation more predominant correlated with P and iPTH levels (r = 0.443, p < 0.001 and r = 0.384, p < 0.005).

Conclusions: The results indicate that the Th17/Treg imbalance in the chronic HD group. Higher phosphate level and intact parathyroid hormone level, and lower albumin level increase the Th17 cell differentiation, especially in the non-diabetes, chronic HD patients.

MP539  SERUM LEVELS OF OSTEOCALCIN ARE ASSOCIATED WITH CEREBRAL AND CARDIAC VASCULAR DISEASES IN HEMODIALYSIS PATIENTS

Kazuhiro Okano1,2, Tetsuri Yamashita2, Yuki Tsuruta2, Asako Hibari, Naoki Miyah, Naoki Kimata, Ken Tsuchiya1,2, Kosaku Nitta3 and Takashi Akiba1
1Department of Blood Purification, Kidney Center Tokyo Women’s Medical University Tokyo Japan, 2Department of Medicine, Kidney Center Tokyo Women’s Medical University Tokyo Japan

Introduction and Aims: Osteocalcin (OC) is known as a bone metabolic marker. Serum OC levels have a better correlation with results of bone biopsies than serum levels of ALP or PTH in hemodialysis (HD)population. Further, OC has been reported to affect vascular calcification. In the present study, we examine correlation of serum OC levels with cerebral and cardiac vascular diseases (CVD) and mortality in maintenance HD patients.

Methods: This study is a longitudinal observational cohort study conducted over a period of 5 years. One hundred twenty-six HD patients were enrolled. We defined CVD events as new onset of fatal or nonfatal myocardial infarction, angina pectoris, cardiac failure, cardiac arrest caused by arrhythmia, cerebral infarction, or cerebral hemorrhage. To evaluate the impact of serum OC levels on CVD events, the participants were divided into two groups based on the median serum OC level of 71.5 ng/ml (low-serum OC group: <71.5 ng/ml, high-serum OC group ≥71.5 ng/ml).

Results: CVD events were observed in 29 out of 126 patients (23.0%). The number of cumulative CVD events in the low-serum OC group was significantly higher than that in the high-serum OC group (p < 0.005). Multivariate Cox proportional hazards analysis demonstrated that a low level of serum OC is a significant predictor of a higher incidence of CVD events (hazard ratio, 2.925; p = 0.0241) after adjustment. There was no significant difference in survival rate between the high and low OC groups in normal Ca × P patients, while significant difference (P < 0.001) was observed in high Ca × P group.

Conclusions: Serum OC levels may be a useful marker for predicting the emergence of new CVD events in maintenance HD patients.

MP540  ELDECALCITOL (ELD) TREATMENT FOR LOW BONE MASS IN POSTMENOPAUSAL WOMEN RECEIVING MAINTENANCE HEMODIALYSIS

Naomi Sasaki1, Masataka Tsunoda2, Ryota Ikese3, Megumi Sato4 and Nobuo Hashimoto5
1Nephrology and Dialysis H.N.Medic Sapporo Japan, 2Nephrology and Dialysis H.N.Medic Sapporo-Higashi Sapporo Japan, 3Nephrology and Dialysis H.N.Medic Kitahirosima Kitahirosima Japan, 4Nephrology and Dialysis Arizanoka Megumi Clinic Sapporo Japan

Introduction and Aims: ELD, a new active vitaminD3 analog developed in Japan, has been recognized as an effective osteoporotic therapeutic drug in primary osteoporosis. We treated postmenopausal women receiving maintenance haemodialysis in our institution with ELD for 1 year, and evaluated the effects on lumbar spine bone mineral density (LS-BMD).

Methods: Twenty-one postmenopausal women receiving haemodialysis in our institution for at least 6 months were enrolled. Patients with two or more previous vertebral fractures, those receiving a metal-containing phosphate binder, and those with a mean serum albumin-corrected calcium (Ca(Alb)) level >9.5mg/dl were excluded. ELD treatment was started at 0.5μg/day. LS-BMD was measured at the lateral aspect of the L1–L4 vertebrae using the dual-energy X ray absorptiometry measurement (DEXA) on a QDR2000 densitometer.

Results: Table 1 shows the changes in mean serum Ca(Alb), P, intact PTH, BAP and TRACP-5b. Data shown as mean (SD). Mean serum Ca(Alb), P, and intact PTH levels were well-controlled before and after ELD treatment. ELD could be used safely without causing severe hypercalcemia. Mean BAP level was significantly decreased throughout this study (reference range; 31 to 123 U/L). Mean TRACP-5b level was significantly decreased after 6 months ELD treatment, however the level had remained higher than normal range throughout this study (reference range;120 to 420 mU/dL). Table 2 shows the changes in mean LS-BMD. Data shown as mean (SD). Mean LS-BMD was significantly increased after 6 months, but then decreased after 1 year ELD treatment. t = 0.05 vs before treatment.

Conclusions: Although our results are observational study at a single institution, they suggest that ELD could be safely used to increase bone mass in dialysis patients. However, ELD treatment may not be enough to improve low bone mass due to severely bone absorption such as postmenopausal women.

MP541  RELATIONSHIP OF OSTEOPROTEGERIN LEVEL AND CHRONIC KIDNEY DISEASE - METABOLIC BONE DISEASE (CKD-MBD)

Lamya Harb1
1Internal Medicine and Nephrology Al-Azhar University Cairo Egypt

Introduction and Aims: The plasma level of Osteoprotegerin (OPG) in combination with intact parathyroid hormone (iPTH) can be used as a marker for noninvasive diagnosis of CKD-MBD (Chronic Kidney Disease - Metabolic Bone Disease) in hemodialysis and predialysis patients. The aim of the study to assess the level of (OPG) in end stage renal disease, and whether there is significant correlations between, iPTH, serum calcium , phosphorus, CaXph product, CRP, cholesterol, triglycerides and BMD (bone mineral density) in Patienten Hemodialysis and Predialysis stages (stage 3&4).

Methods: Eighty one individuals were included in the study, classified into three groups GROUP A:41 patients chronic kidney disease stage 5, GROUP B:30 patients as pre-dialysis group (stage 3&4CKD), Group C:Control group, consists of 10 healthy

MP540

<table>
<thead>
<tr>
<th>Ca(Alb) (mg/dL)</th>
<th>P (mg/dL)</th>
<th>intact-PTH (pg/dL)</th>
<th>BAP (U/L)</th>
<th>TRACP-5b (mU/dL)</th>
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<tr>
<td>8.97 (0.34)</td>
<td>5.06 (0.48)</td>
<td>111.5 (59.2)</td>
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<tr>
<td>9.30 (0.34)</td>
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<td>9.47 (0.48)</td>
<td>5.16 (0.52)</td>
<td>79.0 (42.7)</td>
<td>67.5 (31.4)</td>
<td>459.5 (240.0)</td>
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Acknowledgements: This research was funded by a grant from the Egyptian Ministry of Higher Education and Scientific Research.


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volunteers who are age and sex matched to the patients. All groups were subjected to the following: full medical history, full clinical examination, total serum Calcium and total serum Phosphorus, C-Reactive Protein (CRP), total serum cholesterol and triglycerides, intact parathyroid hormone (iPTH), serum Osteoprotegerin (OPG) and measurement of BMD with DEXA at lumbar spine L2-L4.

Results: There was highly statistical significant increase in OPG level measured for groups A, B compared with group C. In dialysis group, OPG showed a non significant correlation with calcium, but it showed a significant positive correlation with age. On the other hand, it showed a significant positive correlation with age, iPTH, Phosphorus, CaxPh product, CRP, Cholesterol, Triglycerides, and high significant negative correlation with BMD. In pre-dialysis group, OPG showed a non significant correlation with CaxPh product, CRP, Triglycerides and stage 3 & 4 of CKD. But it showed high significant positive correlation with age, iPTH, Phosphorus. On the other hand, it showed a significant negative correlation with Cholesterol. While a highly significant negative correlation was obtained with corrected serum calcium, and high significant negative correlation with BMD.

Conclusions: We conclude that the osteprotegerin increased in patients with CKD even in the stages before the start of renal replacement therapy. We strongly suggest the annual determination of this marker as part of the biologic flow-up of these patients. Serum OPG may be a useful biomarker for early diagnosis of CKD-MBD, also OPG or one of its derivatives may be used in the future in the treatment of CKD-MBD.

MP542 LANTHANUM CARBONATE AND SURVIVAL IN MAINTENANCE HAEMODIALYSIS PATIENTS

Hirotaka Komaba1, Takatoshi Nakata1, Hajime Suzuki2, Takao Suga2 and Masatami Fukagawa1

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Introduction and Aims: Lanthanum carbonate is a non-calcium phosphate binder that is effective for the treatment of hyperphosphatemia in patients undergoing dialysis. However, there are limited data on whether treatment with lanthanum carbonate affects survival.

Methods: We retrospectively collected data on maintenance haemodialysis patients (n = 2,269) beginning in December 2008, a time immediately prior to the commercial availability of lanthanum carbonate in Japan. We compared all-cause mortality among patients who began treatment with lanthanum carbonate (n = 675) with those who remained untreated (n = 1,594). We also compared survival in a subcohort of treated (n = 568) and untreated (n = 568) patients matched by the propensity score of lanthanum carbonate treatment with cinacalcet.

Results: In the unmatched cohort, the lanthanum-treated group had a significantly lower mortality than the untreated group (HR 0.46; 95% CI 0.32 to 0.66; P <0.0001). Multivariate-adjusted analyses showed a non significant association between lanthanum carbonate and survival in the whole cohort (HR 0.72; 95% CI 0.48 to 1.07; P = 0.10) but there was a significant association in a subgroup of patients with baseline serum phosphate >6.0 mg/dl (HR 0.53; 95% CI 0.29 to 0.96; P = 0.035). Similarly, lanthanum carbonate was not associated with a significant survival benefit in the propensity score-matched cohort (HR 0.71; 95% CI 0.46 to 1.09; P = 0.12) but a significant association was found when the analysis was restricted to patients with baseline serum phosphate >6.0 mg/dl (HR 0.50; 95% CI 0.27 to 0.93; P = 0.029).

Conclusions: Treatment with lanthanum carbonate was independently associated with survival benefit in maintenance haemodialysis patients with uncontrolled hyperphosphatemia. Randomized controlled trials are needed to determine whether lanthanum carbonate actually improves survival among patients receiving maintenance haemodialysis.

MP543 EVALUATION OF WEEKLY PHOSPHATE REMOVAL IN HE MODIALYSIS PATIENTS

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Introduction and Aims: Excess of phosphate (iP) is a risk for death in hemodialysis (HD) patients. Estimating the amount of iP absorption (Ap) is important for evaluating effect of diet and phosphate binders. Ap is considered to be equal to the amount of intradialytic iP removal (Rp) because the balance of absorption from intestine and elimination of iP is generally maintained in HD patients. We established a formula for calculating estimated Rp (eRp) and reported in the 49th ERA-EDTA congress. For obtaining an easy method for providing estimated Ap (eAp) per week, we analysed phosphate kinetics of entire week using this formula.

Methods: We studied 29 patients undergoing 4-hour HD thrice a week. Their Blood flow rate (Qb) was between 160-240 ml/min. Their serum iP concentration (Pa) at start of HD was 4.5±1.3 mg/dl. Blood samples were drawn at start and end of HD in consecutive 3 HD sessions (the first (HD1), second (HD2) and third (HD3) HD sessions of the week). We calculated eRp using following formula as reported previously.

\[ eR_p = \frac{Q_b}{UR} \times (P_{a1} + P_{a2} + P_{a3}) \]

Where Qb (dl/min), Un1= serum urea nitrogen concentration at start of HD, Un2= serum urea nitrogen concentration at end of HD, Pa1=Paat at that HD session, Pa2 = Pa at that HD session, Ur = amount of ultrafiltration (dl/session). (1) We compared Pa and UN alteration within a week. (2) The total eRp per week (eRpw) was calculated by sum of eRp in three sessions. eRpw was compared with eRp in HD1 (eRp1). (3) The relationship between eRp and Pa was analyzed in 87 HD sessions.

Results: (1) Eight of 29 patients did not have the highest Pa before HD1 although serum UN concentrations before HD, were the highest in all patients. The removal amount of iP was not associated with that of UN or parathyroid hormone level. (2) eRpw was 2648±579 mg. The percentage of eRp in each HD session was 35.8, 33.7 and 30.5%. Weekly amount of iP removal estimated by data from HD1 (eRp1) was shown as eRp1(weightday/2.793eRp1). This eRp1(weightday) was extremely similar to the sum of Rp from three sessions (y=0.951x+138, R=0.947, P<0.001). (3) In 87 HD sessions, correlation between eRp and pre-HD Pa was observed (y=1753e-102, R=0.800, P<0.001). Stratified analysis did not show that Qb and body weight affect this correlation. These findings show that the eRp decreases by 175 mg when Pa becomes 1 mg lower in conditions of this study. For reducing the Pa before HD, by 1mg, weekly amount of iP absorption should be restricted by 489 mg.

Conclusions: (1) The iP removal was not dependent on protein intake or parathyroid hormone level. (2) The amount of iP absorption per week could be easily estimated. (3) Relationship between serum iP concentration at start of weekly first HD and amount of iP absorption was revealed.

MP544 UNDERCARBOXYLATED OSTEOCALCIN AND SECONDARY HYPERPARATHYROIDISM IN POSTMENOPAUSAL PATIENTS ON HEMODIALYSIS

M. Zhelyazkova-Savova1, D. Gerova1, D. Paskalev1, V. Ikonomov1, R. Zortcheva1 and B. Galunska1

1Medical University of Varna Varna Bulgaria

Introduction and Aims: Osteocalcin (also known as non-collagenous bone matrix gla protein)(OC), is a vitamin K-dependent Ca++-binding protein, produced by osteoblasts. OC biosynthesis is tightly regulated by 1,25-dihydroxy-vitamin D. OC carries three gamma-glutamic acid residues (Gla) at positions 17, 21, and 24, which are target for vitamin K-dependent carboxylation and OC activation. Carboxylated OC is

<table>
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<th>Control group</th>
<th>HD patients without secondary hyperparathyroidism (SHPT)</th>
<th>HD patients with SHPT, not treated with cinacalcet and calcitriol</th>
<th>HD patients with SHPT treated with cinacalcet and calcitriol</th>
</tr>
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<td>3.01±0.36 n=26</td>
<td>12.33±18.106 n=6</td>
<td>14.630±7.824 n=10</td>
<td>23.723±6.917 n=7</td>
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<tr>
<td>2.1±0.01</td>
<td>4.3±0.02</td>
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Abstracts

**Nephrology Dialysis Transplantation**

**MP54**  
**Abstracts**

**PREDIALYSIS IONIZED CALCIUM LEVEL MEASUREMENTS IN PATIENTS ON HAEMODIALYSIS**

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Introduction and Aims: Blood calcium measurement is recommended in patients on haemodialysis (HD). The Kidney Disease: Improving Global Outcomes (KDIGO) foundation recommends the measurement of ionized calcium (iCa) levels, but in clinical setting total calcium (Ca) level concentration is prefered over that of albumin-corrected calcium (Alb-Ca) level. Aim: To identify the factors associated with predialysis levels of iCa and to compare the ability of iCa and Alb-Ca levels in predicting iCa cases.

Methods: The predialysis iCa and Ca levels were measured, at the actual pH, for all patients on HD at a single institution and also underwent usual mid-week biology. The data were analysed using Linear regression and Bland-Altman testing.

Results: A total of 160 HD patients were evaluated, with a mean age of 71.8 ± 14 years; 41.6% were female and the mean duration of dialysis was 67.8 ± 75 months. The treatment involved administration of calcium carbonate (17%), calcium acetate (17%), sevelamer (30%), alfacalcidol (18%), calcitriol (11%), and cholecalciferol (91.5%). The mean diacylactate concentration (DDC) was 1.51 mmol/L. The mean iCa was 2.2 ± 0.14 mmol/L (range, 1.86–2.65 mmol/L) and the mean Alb-Ca was 2.3 ± 0.13 mmol/L (range, 1.9–2.67 mmol/L). Both were correlated with the iCa (mean iCa level: 1.1 ± 0.07 mmol/L; range, 0.93–1.41 mmol/L; (r² = 0.6, p < 0.001; y = 0.55 ± 1.4 and x = 0.53; r = 0.001; y = 0.78 ± 1.3, respectively). The mean ratios of iCa/Alb-Ca and Alb-Ca/iCa were 1.93 and 2.02, respectively. iCa was correct in 84% of patients and Alb-Ca, in 37% of patients, in predicting low iCa levels (<1.12 mmol/L; n = 64). iCa was correct in 82% of patients, and Alb-Ca, in 80% of patients, in predicting normal iCa levels (1.12–1.32 mmol/L; n = 93). Alb-Ca was not a predictive factor for hypercalcemia (IaCa > 1.32 mmol/L, n = 3); Alb-Ca predicted hypercalcemia in 2/3 patients. Sex was associated with iCa values: iCa was 1.12 ± 0.07 mmol/L in males and 1.16 ± 0.06 mmol/L in females (p = 0.008). Serum bone markers, PTH values, aortic calcification scores, and bone mineral density values were not associated with Ca quantities.

Conclusions: Despite vitamin D supplementation and a mean DCC of ≥1.5 mmol/L, predialysis hypercalcemia is highly prevalent in patients on HD (43%); the male predominance of this finding was not unexpected. Insufficient dietary calcium intake or insufficient supplementation may be the main cause for this finding. iCa appears superior to Alb-Ca in predicting hypercalcemia. Hypercalcemia is very uncommon and not predicted by Ca.

**MP546**  
**SERUM 25-HYDROXYVITAMIN D ON CHRONIC KIDNEY DISEASE STAGE 5D- EFFECTS OF SUPPLEMENTATION WITH CALCIFEROL**

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Introduction and Aims: Chronic kidney disease(CKD) shows high incidence of Hypovitaminosis D(Hyd) contributing to the raise of morbi-mortality. Aims: To study evolution of( Hyd) in CKD stage 5D, on patients undergoing Hemodialysis(HD) or Peritoneal Dialysis(PD) supplemented with oral doses individualized(to reach serum levels of 30ng/ml was administered 100IU/0,7mg/ml of calciferol(D3) at times:3:00;6:00;9:00.2- To compare emergence of HyD baseline(BL) and outcome on PD and HD.

Methods: 69 patients were evaluated,45 HD-62.2% male and 24 PD-62.5% male. The mean age on PD was 68.3±1.4 years on HD 53.1±6.5 years. Serum 25-hydroxyvitamin D (25OH D) was normal in 1(4.77%) patient on PD, and in 63(3.3%) on HD. Serum levels of parathormone(PTH), Calcium(Ca), alkaline phosphatase(AP), phosphorus(P) and 25OH D were expressed as percentages. Mineral bone disease(MBD) was present in 39% of patients with high P or PTH.

Results: 25 patients were supplemented; 48, 45±16 years and BL values: 25OH D: 22.6±6.8; Ca: 9.8±0.8; P 5.4±1.5; 25OHD 199.6±105.1; CaP 51.9 ±14.5; PTH 0.5±0.1; iCa 2.02; tCa 2.65±0.84 mmol/L; Alb-Ca was 2.3 ± 0.13 mmol/L. Both were correlated with the iCa (mean iCa level: 1.1 ± 0.07 mmol/L; range, 0.93–1.41 mmol/L; (r² = 0.6, p < 0.001; y = 0.55 ± 1.4 and x = 0.53; r = 0.001; y = 0.78 ± 1.3, respectively). The mean ratios of iCa/Alb-Ca and Alb-Ca/iCa were 1.93 and 2.02, respectively. iCa was correct in 84% of patients and Alb-Ca, in 37% of patients, in predicting low iCa levels (<1.12 mmol/L; n = 64). iCa was correct in 82% of patients, and Alb-Ca, in 80% of patients, in predicting normal iCa levels (1.12–1.32 mmol/L; n = 93). Alb-Ca was not a predictive factor for hypercalcemia (IaCa > 1.32 mmol/L, n = 3); Alb-Ca predicted hypercalcemia in 2/3 patients. Sex was associated with iCa values: iCa was 1.12 ± 0.07 mmol/L in males and 1.16 ± 0.06 mmol/L in females (p = 0.008). Serum bone markers, PTH values, aortic calcification scores, and bone mineral density values were not associated with Ca quantities.

Conclusions: Despite vitamin D supplementation and a mean DCC of ≥1.5 mmol/L, predialysis hypercalcemia is highly prevalent in patients on HD (43%); the male predominance of this finding was not unexpected. Insufficient dietary calcium intake or insufficient supplementation may be the main cause for this finding. iCa appears superior to Alb-Ca in predicting hypercalcemia. Hypercalcemia is very uncommon and not predicted by Ca.
More cost-effective than SC ≥5600 mg/day but not lower SC doses (≤4800 mg/day). Patient chart data (2012) indicated that 40% of patients in Germany receive SC ≥5600 mg/day monotherapy, of which 37% receive doses ≥6400 mg/day. The annual cost saving with a decreasing one patient from SC to LC 3000 mg/day ranged from €274/year (SC 5600 mg/day) to €2520/year (SC 9600 mg/day).

Conclusions: Our analyses indicate that LC 3000 mg/day is more cost-effective than SC doses ≥5600 mg/day, which may account for over 40% of ESRD patients in Germany. For these patients, switching phosphate binder therapy from SC to LC offers potential drug cost savings, a reduced daily tablet burden (3 vs ≥2 tablets/day), and effective serum phosphate control.

MP551

COMPARISON OF SEVELAMER, SEVELAMER CARBONATE AND LANTHANUM CARBONATE IN VITRO AND IN VIVO

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Introduction and Aims: Hyperphosphatemia is common in patients with chronic renal failure (CKD), particularly in advanced stages. The phosphate binders (PB)

N.B. SC:LC dose-relativities from approximately 2.1 have been reported as similar doses.

Abstracts
Sevelamer (S), sevelamer carbonate (SC) and lanthanum carbonate (LC) are the drugs most commonly used to reduce the serum concentration of phosphorus (P). They are associated with gastrointestinal intolerance. The aim of our study was to compare these drugs in vivo and in vitro.

**Methods:** One tablet of SC 800mg, one of S 800mg and a tablet of LC 750mg were dissolved in solutions at pH2 corresponding to stomach-pH, following the USP dissolution IIpaddle method at a rotation speed of 50rev/min in 900ml of dissolution medium at a stable temperature of 37±0.01°C, maintained by a Haake cryostat. The dissolution profile obtained before and after addition of trehalose, a disaccharide used to stabilize pharmaceutical products for its effect on H-binding structures, was graphically reproduced using software TableCurve2D®. To calculate the amount of phosphoric acid stoichiometrically engaged by each single tablet, we followed the variation of pH of a phosphoric acid solution 4.00X10⁻⁹Mol. We also calculated the amount of CO2 produced from each tablet and evaluated gastric-pH in vivo using 24h esophago-gastric pH measurement with and without administration of PB and Proton pump inhibitor (PPi) in CKD patients and in a control group.

**Results:** The amount of CO2 produced by LC is 56ml, that of SC is 30ml; S does not produce CO2. The complete solubilization of a tablet of LC occurs in 60 min, while that of SC and S in 10 min. The dissolution of PB increases the pH of solution (p<0.0001), this action is linked to the ability of these drugs to bind protons. The addition of trehalose increases the density of medium, but not generate any significant variation in the profile of drugs solubility. Engaged by the amount of phosphoric acid there was a best action of SC (R undertakes 4.00X10⁻⁹mol/L, LC 3.99X10⁻⁹mol/L, S 3.95X10⁻⁹mol/L). The pHmeter shown that gastric-pH increases significantly after administration of the tablets, especially with SC (p<0.0001). The pH increases even more after administration of PPi.

**Conclusions:** The action of PB is linked to their ability to uptake protons, so it is preferable to take them after meal and especially after PPis; reducing the stomach acidity the protons detected are those of phosphoric acid. SC has a greater capacity to uptake phosphorus, S is the most tolerated because it doesn’t produce CO2, LC is the less soluble.
EPIDEMIOLOGY - CKD 5D II

**MP552**

**SHORT AND LONG-TERM OUTCOMES OF THE HEMODIALYSIS SELF MANAGEMENT INTERVENTION RANDOMIZED TRIAL (HED-SMART) - A PRACTICAL LOW INTENSITY INTERVENTION TO IMPROVE ADHERENCE AND CLINICAL MARKERS**

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**Introduction and Aims:** Adherence to treatment recommendations on diet, fluid and medication is important to maximize good clinical outcomes in Hemodialysis yet it remains suboptimal and not well-understood. This trial set out to examine the effect of the HED-SMART intervention, a four-session, group-delivered self-management intervention on treatment adherence indicators.

**Methods:** Eligible HD patients were randomized to either usual care (N= 133) or HED-SMART intervention (n=102). Measures of self-report adherence, self-management skills and biochemical markers were collected at baseline, immediately and at 3 and 9 months post-intervention. The intervention was facilitated by renal healthcare professionals and involved problem-solving and goal-setting for fluid control, diet and medication.

**Results:** A total of 235 participants were enrolled [mean age ± 53.46 (±10.41) years]. The study was completed by 74.8%. Significant differences between groups were found in change in interdialytic weight gains, potassium and phosphate levels during the intervention phase and the 3-month follow-up indicating improved dietary/fluid control and medication intake for the intervention participants (all p <0.01). The Improvements in weight gains were maintained by 9 months yet the change in interdialytic weight gains, potassium and phosphate levels at 9 months was small and not significant (p = 0.08). Significant differences between groups were found in secondary outcomes across all time points: self-reported adherence, self-management skills and self-efficacy. There were no adverse effects.

**Conclusions:** These analyses indicate the efficacy of the HED-SMART program with significant post-intervention improvements in both clinical markers and self-report adherence. These observed improvements, if supported and maintained at the longer follow-up (18 months), could significantly reduce ESRD-related complications in the longer term. Given the feasibility of this kind of program, it has strong potential for providing effective support to many hemodialysis patients in the future.

**MP553**

**LEFT VENTRICULAR MASS IS A POWERFUL RISK FACTOR FOR ALL-CAUSE AND CARDIOVASCULAR DEATH IN END STAGE KIDNEY DISEASE (ESKD) PATIENTS ON DIALYSIS BUT DOES NOT CONTRIBUTE TO PROGNOSIS: AN ANALYSIS IN TWO EUROPEAN COHORTS**

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**Introduction and Aims:** Left Ventricular Hypertrophy (LVH) is indisputably one of the strongest risk factors for death and CV events in end stage kidney (ESKD) patients. Causality apart, the concept that LVH is useful for CV risk stratification in ESKD has never been formally tested by state-of-art statistical analyses including risk discrimination (area under the ROC curve, AUC) and risk calibration and re-classification.

**Methods:** We re-analysed the prognostic power of LVMI for all-cause and CV death in two independent ESKD cohorts in Italy and in France, the Cardiovascular Risk Extended Evaluation cohort (CREED:age 60±15 years; mean FU duration: 55 months, n=254) and the Hospital Maleshes cohort (HM, Parities: 53±16 years, mean FU duration:33 months, n=270).

**Results:** Mortality rate was 16%100 persons-years (CV death:50%) in the CREED cohort and 19/100 person-years (CV death:68%) in the HM cohort. In both cohorts, LV Mass Index (LVMI) predicted all-cause [CREED, hazard ratio (HR)(2 g/m2.7): 1.05; HM, HR: 1.03] and CV death [HR: 1.06 and 1.05, respectively] (all P<0.001). In these cohorts, the AUCs of LVMI for all-cause death were 0.71±0.03 (CREED) and 0.67±0.03 (HM) and those for CV death 0.64±0.04 and 0.69±0.03 which were lower than those by age alone both for all-cause (CREED: 0.81±0.03; HM: 0.88±0.02) and CV mortality (CREED: 0.66±0.04; HM: 0.78±0.03). All predictive models were well calibrated, i.e. there was no significant difference between observed and predicted outcomes. In the CREED cohort a predictive model including Framingham risk factors, anti-hypertensive treatment, CV comorbidities, heart rate and two major ESKD-related risk factors (Hb and albumin) produced an AUC of 0.89±0.02 for all-cause death and 0.76±0.03 for CV death. The corresponding figures in the HM cohort were 0.92±0.02 and 0.87±0.02, respectively. LVMI did not materially affect the discrimination power for all-cause (CREED:0.89 vs. 0.89; HM: 0.93 vs. 0.92) and CV death (CREED:0.76 vs. 0.76; HM: 0.88 vs. 0.87). In an aggregate analysis of the two cohorts (n=524) the net reclassification index (NRI) by LVMI was low and not significant both for all-cause (NRI: 4.5%, P=0.11) and CV mortality (NRI: 3.4%, P=0.33). A re-classification analysis carried out by calculating the integrated discrimination improvement (IDI) provided similar results (all-cause mortality: IDI: P=0.89; CV death, IDI: P=0.88).

**Conclusions:** LVMI is a strong CV risk factor in the ESKD population. However, the prognostic power of this biomarker is by far lower than that by age alone or combined with standard,easily available, risk factors. While LVH remains a fundamental treatment target in ESKD, measurement of LVMI solely for risk stratification is unwarranted in these patients because it does not provide any additional information as compared to standard risk factors.

**MP554**

**PATIENT AND FACILITY-LEVEL VARIATION IN THE TIMING OF DIALYSIS INITIATION ACROSS CANADA: CANADIAN KIDNEY KNOWLEDGE TRANSLATION AND GENERATION NETWORK (CANN-NET)**

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1University of Manitoba Winnipeg Canada, 2University of Calgary Calgary Canada, 3University of Saskatchewan Saskatoon Canada, 4University of Toronto Toronto Canada

**Introduction and Aims:** The appropriate timing of dialysis initiation in outpatients with progressive chronic kidney disease remains controversial with concerns that initiation at a higher GFR is associated with an increase in mortality. The purpose of this study is to determine the variation in timing of dialysis initiation across dialysis facilities and geographic regions in Canada after accounting for patient level factors (case-mix).

**Methods:** Data on 33,263 dialysis patients, 63 dialysis facilities and 12 geographic regions from the Canadian Organ Replacement Registry (CORG) with an eGFR measure at dialysis initiation between Jan. 2001 and Dec. 2009 were included in the final analysis. eGFR was estimated by the MDRD equation. Multi-level models were used to evaluate the variation in timing of dialysis by eGFR at the patient-, facility- and geographic-level. Models were adjusted for patient and facility characteristics to determine the relative variability at each level.

**Results:** The mean eGFR and proportion initiated with an eGFR > 15 ml/min/m2 varied considerably across geographic regions and over the study period. For instance, in patients with >3months of predialysis care, the proportion initiating dialysis with an eGFR>10.5ml/min/m2 was 37.3% varying from 20.2% to 60.2% across geographic regions. In unadjusted models, variation of 2.6, 8.2 and 89.2% were attributable to geography, facility and patient-level characteristics. After adjustment for case-mix and facility-level quality indicators, 95.3, 4.5 and 0.2% of the variability was attributable to patient, facility and geographic-level. Models were well calibrated and re-classification was low.
facility and geography. The adjusted odds ratio for initiating dialysis with an eGFR > 10.5 was similar across all geographic regions except one suggesting that the noted variation across facilities and geographic regions was due to patient differences. This was consistent when eGFR was examined as a continuous variable, categorized as > 12.0 ml/min/m² or in an analysis limited to patients with > 3 months of pre-dialysis care.

Conclusions: We observed significant variation in timing of dialysis initiation across geographic regions, which were predominantly explained by patient-level variation. These data suggest similar practice patterns across Canada, with the predominant factor impacting dialysis initiation being patient characteristics.

**MP556 ASSOCIATIONS OF CHANGES IN QUALITY OF LIFE WITH MORTALITY AND HOSPITALIZATION: RESULTS FROM THE DOPPS**

Jeffrey Perl1, Angelo Karaboyas2, Francesca Tentori2, Hal Morgenstern2,3, Ananda Sen1, Hugh Rayner1, Raymond Vanholder2, Christian Comber1, Takeshi Hasegawa3, Donna Mapes4, Bruce Robinson2,3 and Ronald Pisoni2

1St. Michael’s Hospital, Univ of Toronto Toronto Canada, 2Arbor Research Collaborative for Health Ann Arbor United States, 3Univ of Michigan Ann Arbor United States, 4Birmingham Heartlands Hospital Birmingham United Kingdom, 5University Hospital Ghent Belgium, 6Centre Hospitalier Univ de Bordeaux Bordeaux France, 7Showa Univ Fujigaoka Hospital Yokohama Japan

**Introduction and Aims:** Cross-sectional measures of Health Related Quality of Life (HR-QOL) are associated with mortality and hospitalization among hemodialysis (HD) patients. Our aims were to describe within-patient changes in HR-QOL and estimate their effects on the rates of mortality and hospitalization.

**Methods:** 13,786 patients had ≥1 measurement of HR-QOL from the Dialysis Outcomes and Practice Patterns Study (DOPPS) annual patient questionnaire (PQ). Changes in physical (PCS) and mental (MCS) component summary scores of the KDQOL-36TM were defined as the score from the second PQ (PQ2) minus score from the first PQ (PQ1). Mean change from PQ1 to PQ2 was 12 months (IQR: 11, 14). Effects of change in HR-QOL (per 5 point decline) on both mortality and first hospitalization were estimated using Cox regression with time at risk (median: 11 months, IQR: 6, 18) beginning at PQ1, adjusting for potential confounders. In addition, effects of HR-QOL at PQ2 (3 categories) were estimated in separate Cox models by category of HR-QOL at PQ1.

**Results:** Mean ± SD age was 61±4 years; 59% were male, 32% diabetic, and mean albumin was 3.8±0.5 g/dl. Median PCS and MCS from PQ1 were 37.5 (IQR: 29.4, 46.2) and 46.4 (IQR: 37.2, 54.9); mean changes in PCS and MCS from PQ1 to PQ2 were -0.2 (IQR: -0.5, -0.4) and -0.1 (IQR: -0.6, -0.5). A decline in PCS and MCS from PQ1 to PQ2 was associated with all-cause mortality (PCS, HR=1.10 per 5 points, 95% CI: 1.07-1.13; MCS, HR=1.06 per 5 points, 1.04-1.08) and hospitalization (PCS, HR=1.02 per 5 points, 1.01-1.04; MCS, HR=1.02 per 5 points, 1.01-1.04). Change in HR-QOL was associated with all-cause mortality across levels of HR-QOL scores at PQ1 (Table).

**Conclusions:** Changes in HR-QOL in HD patients are common, and are associated with mortality and hospitalization. Monitoring changes in self-reported HR-QOL measures in HD patients may help to identify a subset of patients at high risk for adverse outcomes and allow for targeted interventions to improve HR-QOL and reduce these risks.
Introduction and Aims: We measured the involvement of in-center patients in their dialysis treatment and assessed cross-sectional associations with measures of health-related quality of life in the Dialysis Outcomes and Practice Patterns Study (DOPPS).

Methods: Data on self-care activities (listed in Table 1) were available in DOPPS phase 4 (2009-11). Descriptive analyses included 5657 patients in 8 countries with ≥2% of patients reporting ≥1 activity. 3242 of these patients reported the physical (PCS) and mental (MCS) component summary of the KDQoL-36 TM. Linear mixed models adjusted for many potential confounders, including country, estimated the effects of self-care activities on PCS and MCS.

Results: The % of patients who performed ≥1 self-care activity was 9% overall and highest in Australia/New Zealand and Sweden (16% each, Table 1). The activity most commonly performed was setting up the machine/dialyzer (7%). Facility % of patients who performed ≥1 self-care activity was 0% in 39% of facilities, with median 4% (IQR: 0%, 1%) and 95th percentile 36%. Patients performing ≥1 self-care activity were younger (51 vs 66 yrs), had longer vintage (6.2 vs 3.6 yrs), lower catheter use (23% vs 36%), higher albumin (3.9 vs 3.6 g/dL), higher creatinine (9.3 vs 7.5 mg/dL), longer session length, (256 vs 238 min), and fewer comorbidities than patients performing none of the 4 activities. For patients performing ≥1 self-care activity: crude mean PCS (39.2 vs 34.9) and MCS (47.7 vs 45.3) were higher, and after covariate adjustment, mean PCS was 1.6 points higher (95% CI: 0.3, 2.8) and mean MCS was 2.2 points higher (95% CI: 0.7, 3.7).

Conclusions: Greater patient involvement in the routine tasks of hemodialysis is associated with better physical and mental quality of life; however, methodological limitations limit causal inference. Marked variation in up-take of self-care is likely to represent facility preferences for empowering patients. The impact and safety of this approach requires prospective evaluation.

MP557

FUNCTIONAL DEPENDENCE FOR ACTIVITIES OF DAILY LIVING IN PREVALENT DIALYSIS PATIENTS IN THE DOPPS

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1Division of Nephrology Shanghai Pudong Hospital Shanghai China, 2Division of Nephrology Fudan University, Pudong Hospital Shanghai China

Introduction and Aims: We measured the involvement of in-center patients in their dialysis treatment and assessed cross-sectional associations with measures of health-related quality of life in the Dialysis Outcomes and Practice Patterns Study (DOPPS).

Methods: Data on self-care activities (listed in Table 1) were available in DOPPS phase 4 (2009-11). Descriptive analyses included 5657 patients in 8 countries with ≥2% of patients reporting ≥1 activity. 3242 of these patients reported the physical (PCS) and mental (MCS) component summary of the KDQoL-36 TM. Linear mixed models adjusted for many potential confounders, including country, estimated the effects of self-care activities on PCS and MCS.

Results: The % of patients who performed ≥1 self-care activity was 9% overall and highest in Australia/New Zealand and Sweden (16% each, Table 1). The activity most commonly performed was setting up the machine/dialyzer (7%). Facility % of patients who performed ≥1 self-care activity was 0% in 39% of facilities, with median 4% (IQR: 0%, 1%) and 95th percentile 36%. Patients performing ≥1 self-care activity were younger (51 vs 66 yrs), had longer vintage (6.2 vs 3.6 yrs), lower catheter use (23% vs 36%), higher albumin (3.9 vs 3.6 g/dL), higher creatinine (9.3 vs 7.5 mg/dL), longer session length, (256 vs 238 min), and fewer comorbidities than patients performing none of the 4 activities. For patients performing ≥1 self-care activity: crude mean PCS (39.2 vs 34.9) and MCS (47.7 vs 45.3) were higher, and after covariate adjustment, mean PCS was 1.6 points higher (95% CI: 0.3, 2.8) and mean MCS was 2.2 points higher (95% CI: 0.7, 3.7).

Conclusions: Greater patient involvement in the routine tasks of hemodialysis is associated with better physical and mental quality of life; however, methodological limitations limit causal inference. Marked variation in up-take of self-care is likely to represent facility preferences for empowering patients. The impact and safety of this approach requires prospective evaluation.

MP558

EFFECT OF PROLONGED WEEKLY HEMODIALYSIS ON SURVIVAL OF MAINTENANCE HEMODIALYSIS PATIENTS: META-ANALYSIS OF CONTROLLED STUDIES

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Introduction and Aims: Use of prolonged nocturnal or daytime hemodialysis (PHD, more than 12 h per week) is associated with improvement of some clinical parameters relative to conventional hemodialysis (CHD, 4 h sessions, thrice weekly), but the effect on survival remains unclear. The purpose of this meta-analysis is to determine whether PHD improves survival of patients undergoing maintenance HD.

Methods: Systematic review of observational studies by meta-analysis. Electronic searches in MEDLINE (PubMed, 1966 to 2012), EMBASE (1974 to 2012), www.clinicaltrials.gov, and the Cochrane Controlled Clinical Trials Register Database. All prospective or retrospective studies were considered eligible if they were prospective cohort studies or observational studies that compared CHD with PHD (more than 12 h of HD per week) due to mortality differences between HD sessions (independent of HD sessions) and the final outcome was all-cause death or mortality.

Results: 13 studies with a total of 85,722 participants (10,285 PHD patients, 75,437 CHD patients) met the inclusion criteria. Summary estimates indicated that PHD was associated with decreased risk of mortality (OR = 0.72, 95%CI: 0.64–0.81, p < 0.00001). Analysis of residual confounders of pooled results from six retrospective studies indicated that PHD patients were less likely to have low hemoglobin (11.7 vs. 11.2 g/dL, p < 0.01), younger (51.2 vs. 58.8 years, p < 0.01), less likely to have diabetes (27.1% vs. 40.8%, p < 0.01), and less likely to use a catheter (18.4% vs. 27.1%, p < 0.01), so these may have affected the outcome measure in these studies.

Conclusions: PHD is associated with improved survival relative to CHD, although residual confounders have affected this relationship in retrospective studies. Large, multi-center randomized, controlled trials are needed to confirm our results.

MP559

DETERMINANTS OF PRE-DIALYSIS SERUM SODIUM TRENDS AND VARIABILITY AND THEIR ASSOCIATIONS WITH SURVIVAL IN INCIDENT HEMODIALYSIS PATIENTS: RESULTS FROM THE MONITORING DIALYSIS OUTCOMES (MONDO) INITIATIVE

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1RRI NYC United States, 2FMC AP Hong Kong China, 3Maastricht University Medical Center Maastricht The Netherlands, 4FMC EMELA Bad Homburg Germany, 5FMC LA Bad Homburg Germany, 6FMC NA Waltham United States, 7MONDO Consortium NYC United States

Introduction and Aims: Stable pre-hemodialysis (HD) serum sodium (SNa) associates to reduced mortality in US HD patients (pts; Raimann, ERA EDTA 2012). We extend this analysis to other countries.

Methods: The global MONDO initiative encompasses pts who started HD between 2000 and 2010 (Uysvat, Blood Purif 2013). Individual pre-HD SNa average (avg), trend and variability as slope and standard deviation (SD), respectively, were calculated over Year 1. Pts were stratified in 3 avg SNa (<137, 137 to 141, >141 mEq/L). Groups and tertiles of SNa SD (<1.9, 1.9 to 2.9, >2.9 mEq/L) and SNa ≥slope (<0.1 to 0.1, >0.1 mEq/L/month). Multiple linear regression (MLR) adjusted for age, gender, race, diabetes, interdialytic weight gain as % of body weight (IDWG%); neutrophil-lymphocyte ratio, albumin, nPCR, presence of residual renal function (RRF), serum potassium (SK+), SNa+ and dialysate to SNa + gradient (GNa+) were employed to identify predictors of SNa SD and trends. Time to death in Year 2 was assessed by two Cox regression analyses, one each with SNa ≥slope and SNa ≥SD.
variability, adjusted for SNa+, age, gender, diabetes and IDWG%. Results: We studied 1077 HD pts [60±15 years, 5923 males, 4668 diabetics, IDWG% 3.8±1.4%]. Variability was positively related to diabetes, IDWG%, SK+ and GNa+, and inversely to albumin, nPCR, SNa+ and RRF. Trends related positively to age and nPCR. Survival analysis identified higher variability and unstable trends as significant predictors of death in some strata. Pts with SNa+<137 mEq/L showed the highest HRs without any discernible effect of SNa+ variability and trends (Table 1).

Conclusions: Our analysis in an international cohort of HD pts confirms previous findings that unstable SNa+ are associated with poor survival, particularly in pts with SNa+<137 mEq/L. This suggests that pts with unstable SNa+ may require close observation.

Introduction and Aims: Depression is highly prevalent in people with chronic kidney disease (CKD) and is linked to increased all-cause mortality, although the association with cardiovascular mortality remains uncertain and large prospective studies that sufficiently adjust for potential confounding variables are lacking. Our aim is to evaluate the association between depression and cardiovascular mortality when controlled for relevant clinical and demographic variables.

Methods: We conducted a multivariate prospective cohort study of 3868 adult outpatients receiving hemodialysis in 76 randomly selected dialysis centers in 9 countries within a collaborative dialysis network. Consecutive patients receiving hemodialysis between April and November 2010 were eligible. At baseline enrolment into the study, depression was assessed by the Beck Depression Inventory (BDI) II questionnaire. Participants with a BDI score of 14 or greater were considered to have depressive symptoms. The primary outcomes were total and cardiovascular mortality at 12 months. Cox regression models were used to analyze the association between depression and mortality adjusted for clinical and demographic variables.

Results: 2280 (62%) of enrolled patients provided complete data for the BDI questionnaire (mean age 64.7 (14.8) years; 60.8% of men). Of these, 1047 (46%) reported a BDI score consistent with depressive symptoms, which were associated with female gender, education, use of anxiolytic drugs, lower dialysis duration and lower albumin levels. During a mean follow-up of 11 ±2.5 months, 30 of 1047 participants with depressive symptoms and 36 of 1233 participants without depressive symptoms died from cardiovascular causes. Compared to participants with depressive symptoms experienced increased risks of all-cause (adjusted hazard ratio 1.51 [95% CI, 1.04-2.01]) but not cardiovascular-related mortality (HR, 0.64 [95% CI, 0.38-1.07]).

Conclusions: Depressive symptoms affect nearly one half of persons with end-stage kidney disease but are not associated with cardiovascular mortality in analyses controlled for clinical and demographic variables.
Conclusions: Fewer women were undergoing dialysis, and differed from men in many aspects of biology, especially serum creatinine, but also patient care. Our findings of regional variation in the survival advantage for women are only partly explained by similar observations in population studies. The impact of various levels of adjustments on gender-associated mortality is informative and serves to generate hypotheses regarding dialysis practices for women, e.g., with respect to catheter use and control of secondary hyperparathyroidism.

INNATE IMMUNITY AND CKD PROGRESSION
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1Clin. Epid. and Physiopath. of Renal Dis. and Hypertens. CNR-IBIM Reggio Calabria Italy, 2MAURO Work Group Reggio Calabria Italy

Introduction and Aims: Alterations in innate immunity play a role in renal damage in experimental models but the role of these alterations in the progression of CKD in humans is still poorly defined. Procalcitonin (PCT), is a biomarker of innate immunity produced by C-cells of the thyroid and by the adipose tissue.

Methods: We measured serum plasma PCT levels in a cohort of 670 patients with stage 3-5 CKD and tested the relationship between this biomarker and metrics of adiposity, proteinuria, GFR and progression to kidney failure over a 3 year follow-up. None of the patients had intercurrent infectious or acute inflammatory processes. PCT was measured by an ultrasensitive immunoluminometric assay. The GFR was estimated by a Cystatin-C based equation. The relationship between PCT and renal events was tested by multivariate Cox’s regression and interaction analysis.

Results: Procalcitonin exceeded the upper limit of the normal range (>0.064 ng/mL) in 492 patients (67 %) while the corresponding figure for high sensitivity CRP (>1 mg/L) was 170 (25 %). PCT was higher (P<0.001) in males and strongly associated with the GFR (r=-0.53) as well as diabetes (P=0.004) and a history of cardiovascular (CV) events (P=0.007). Furthermore PCT was inversely related with Hb (r=-0.16, P<0.001) and with serum albumin (r=-0.10, P=0.009) and directly associated with CRP (r=0.23, P=0.001) and with white blood cells count (r=0.12, P=0.002). Of note, PCT was higher (P<0.001) in patients with large waist hip ratio (IVth quartile) than in those normal or high normal WHR (1st to 3rd quartiles). During the follow up, PCT predicted the combined renal end-point (30% GFR loss, dialysis or transplantation) (HR for 1 ng/ml increase: 2.37, 95%CI:1.25-4.48, P=0.009) in a model adjusting for age, sex, diabetes, BP, smoking, cholesterol, background cardiovascular events and PCT interacted with baseline GFR in predicting renal outcomes. Indeed the risk of for the combined end-point was minimal in patients with low PCT and high GFR and maximal in those with low GFR and high PCT.

Conclusions: Plasma procalcitonin is a more sensitive biomarker of innate immunity than CRP in CKD patients and in part reflects excessive adiposity. High PCT in CKD patients predicts progression toward kidney failure. These results are compatible with the hypothesis that alterations in innate immunity play a role in the progression of CKD in humans.
Abstracts

MP565

PULSE WAVE VELOCITY IN END STAGE KIDNEY DISEASE PATIENTS IS A STRONG PREDICTOR OF DEATH AND CARDIOVASCULAR EVENTS BUT LARGELY FAILS TO IMPROVE RISK STRATIFICATION IN THIS POPULATION

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Introduction and Aims: Pulse wave velocity (PWV) is a highly reproducible indicator of arterial disease which is recommended for cardiovascular (CV) risk stratification by the European Society of Hypertension and the European Society of Cardiology. This biomarker is frequently altered in end stage kidney disease (ESKD) patients and the usefulness of PWV for risk stratification is taken for granted in this population. However, to date no study specifically investigated the prognostic value of PWV by state-of-art statistical methods including risk discrimination (Harrell’s C index), calibration and re-classification (net reclassification index NRI) neither in the general population or in the ESKD population.

Methods: We have therefore re-assessed the prognostic power of Aortic PWV in a cohort of ESKD patients on dialysis enrolled at Manhes Hospital of Paris (age: 53±16 yrs, mean follow-up duration: 33 months, n=270) and previously analysed with standard Cox regression analysis (Kidney Int. 2005;63:1852-60).

Results: PWV (mean 11.3±3.0 m/s) was above the upper limit of the normal range (cut-off: 12 m/s) in 30% ESKD patients. During follow-up, 135 patients died (CV death: 67%). In multivariate Cox regression models adjusting for Framingham risk factors and ESKD-related risk factors (Hb, albumin, phosphate), PWV was once again confirmed a strong predictor of all-cause [Hazard ratio (HR)(3rd vs 1st tertile): 3.3, 95% CI: 1.3-8.5] and CV death (HR: 5.7, 95% CI: 1.3-26.8) both P<0.001. The Harrell’s C index showed that this biomarker has a moderate discrimination power for all-cause and CV mortality (73% and 79%). However these figures did not differ from the discrimination power for the same outcomes provided by age alone (77% and 76%). A prediction rule was developed by multivariate logistic regression model. To clarify the clinical importance of PWV, we performed a risk reclassification analysis. Table 1 describes reclassification Index by PWV was not significant both for all-cause (NRI: 4.5%, P=0.14) and CV mortality (NRI: 7.3%, P=0.10). The association of PWV with 2-year mortality was explored using Cox regression with adjustment for demographic characteristics (age, sex, race), clinical conditions (n=13) and laboratory variables (n=3). The interaction term (eGFR*PWV) was significant in the full model. In stratified analyses, the association of PWV with mortality was assessed in quintile groups with eGFR 5-10 ml/min as the referent. Hazard ratios (HR) and 95% confidence intervals were determined and all analyses were conducted using SAS v.9.3 (Cary NC).

Conclusions: The relationship of eGFR with mortality is significantly influenced by PWV concentrations recorded prior to first dialysis. For levels of 27.5 mmol/l, the GFR-mortality relationship was U-shaped with mortality risks lowest for patients with eGFR 5-10 ml/min. In contrast, for levels >27.5 mmol/l, the GFR-mortality relationship was direct with the greatest risks for patients with the highest PWV concentrations. The HR and 95% CI are shown in Table below.

MP566

THE RELATIONSHIP BETWEEN GLOMERULAR FILTRATION RATE AND MORTALITY AT DIALYSIS INITIATION IS INFLUENCED BY BLOOD UREA NITROGEN CONCENTRATIONS

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Introduction and Aims: Recent studies have demonstrated an inverse relationship between timing of dialysis initiation and mortality in end-stage kidney disease with higher mortality risks for those who are initiated at higher estimated glomerular filtration (eGFR) values. It is unclear to what extent other laboratory variables influence this relationship. The aim of this study was to determine whether blood urea nitrogen (BUN) concentrations, measured at dialysis initiation, modified the association of eGFR with mortality among incident patients.

Methods: We compared mortality risks among early start (eGFR: 10-15, and >15 ml/min/1.73 m²) and late start patients (eGFR: <5 ml/min and 5-10) in 570, 903 incident patients who started dialysis between 1995-2005 in the US. To examine the influence of BUN concentrations on GFR- mortality relationships, we stratified by quintiles (Q1 < 21.8, Q2 21.8-27.5, Q3 27.5-33.2, Q4 33.2-40.7 and Q5+ 40.7 mmol/l). The association of eGFR with 2-year mortality was explored using Cox regression with adjustment for demographic characteristics (age, sex, race), clinical conditions (n=13) and laboratory variables (n=3). The interaction term (eGFR*BUN) was significant in the full model. In stratified analyses, the association of eGFR with mortality was assessed in quintile groups with eGFR 5-10 ml/min as the referent. Hazard ratios (HR) and 95% confidence intervals were determined and all analyses were conducted using SAS v.9.3 (Cary NC).

Conclusions: The relationship of eGFR with mortality is significantly influenced by blood concentrations of urea nitrogen. This new finding is likely to have important clinical and prognostic implications when determining optimal thresholds for dialysis initiation.

MP567

DEMOGRAPHICS AND OUTCOMES STUDY IN PATIENTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD) AND END STAGE RENAL FAILURE (ERF): A UK RENAL REGISTRY ANALYSIS ON BEHALF OF THE ADPKD STUDY GROUP

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Introduction and Aims: Despite ADPKD being the most common genetic cause of ERF, uncertainty remains over aspects of optimisation of routine clinical care. Aims: To describe ADPKD specific demographics, clinical characteristics and renal replacement treatment patterns in a population with ERF.

Methods: An incident adult population commencing RRT between 1/1/2000 and 2/10/2010 was included in this analysis. Simple cross tabulations of baseline demographics, co-morbidity and care related measures were performed. Results are stratified by Primary Renal Disease (PRD).

Results: Between 1/1/2000 and 2/10/2010 47,769 individuals commenced RRT. 3111 (7%) individuals had ADPKD as recorded on PRD, 34,595 (72%) individuals had another PRD other than ADPKD or diabetes, and 10,063 (21%) individuals had diabetes recorded as PRD. The median age of starting RRT was lowest in the ADPKD group (55 years (IQR 47-63) compared to 62 years (IQR 59-71) for those with diabetes and 65 years (IQR 49-75) years for those with all other causes of PRD. The median age of commencing RRT by PRD group has not changed over the last 10 years. There were less co-morbid conditions in those with ADPKD who were also seen earliest by renal

Variables

<table>
<thead>
<tr>
<th>Age &gt;75 years</th>
<th>Beta</th>
<th>OR (95% CI)</th>
<th>Points Assigned</th>
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<tr>
<td>Female</td>
<td>0.82</td>
<td>2.26 (1.51-3.40)</td>
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<tr>
<td>eGFR &lt; 10 ml/min</td>
<td>0.35</td>
<td>1.41 (1.03-1.94)</td>
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<tr>
<td>eGFR &gt; 15 ml/min</td>
<td>1.43</td>
<td>4.20 (1.76-10.01)</td>
<td>3</td>
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<tr>
<td>Cerebrovascular disease</td>
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<td>1.95 (1.29-2.96)</td>
<td>1</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>0.46</td>
<td>1.69 (1.05-2.40)</td>
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</tr>
<tr>
<td>eGFR &lt; 5 ml/min</td>
<td>1.03</td>
<td>2.79 (1.17-6.64)</td>
<td>2</td>
</tr>
</tbody>
</table>

b) Moderate activities little difficult very difficult 1.06 2.34 2.90 (1.86-4.52) 10.41 (5.77-18.78) 2.5 2.5

Clumping stairs little difficult very difficult 0.93 1.50 2.53 (1.50-4.26) 4.50 (2.48-8.20) 2.3 2.3

References:

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services. Patients with ADPKD were more likely to commence RRT with a renal transplant as first modality (11% in the ADPKD, compared with 5% in the non-ADPKD/non-diabetes group and 4% in the diabetes as PRD group). In those that start with dialysis the median time to transplant was the same irrespective of PRD.

Conclusions: Despite early engagement with renal services the median age of starting RRT remains lowest in individuals with ADPKD compared with other PRD’s. This could suggest that current management strategies are not effectively influencing the natural history of the disease. An ADPKD-specific national cohort and dataset is being developed as a resource for research to identify contributing factors to variation in and improvement of patient outcomes. International collaboration with other registries will be invaluable and we aim to focus on developing these networks further.

MP569
ADIPONECTIN IS A STRONG MODIFIER OF THE DEATH RISK BY RESISTIN AND LEPTIN IN END STAGE KIDNEY DISEASE PATIENTS
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Introduction and Aims: The plasma concentrations of the three major adipose tissue cytokines (adipokines) Adiponectin (ADPN), Leptin and Resistin were substantially raised in patients with End-Stage Kidney Disease (ESKD) but the relationship between these cytokines and major clinical outcomes in this population is highly controversial. The interactions among these adipokines for the prediction of all-cause and cardiovascular (CV) mortality has not been analysed.

Methods: We studied an incident-prevalent cohort of 231 hemodialysis patients (age: 60±15 years; 127 M and 104 F) monitored for 57 ± 44 months (range: 0.2 to 155 months) and, during this period, fatal cardiovascular events and death for other causes were accurately recorded. Plasma concentrations of ADPN and Resistin were measured by enzymatic immunoassays and plasma Leptin by radioimmunoassay.

Results: ADPN was inversely related to Leptin (r=0.38; p<0.001) and very weakly but not significant associated to Resistin (r=0.12; p=0.09). Leptin and Resistin were unrelated (p=0.24). During follow-up 165 patients died (96 for CV causes). On univariate analysis, patients in the first ADPN tertile had higher all-cause (p for trend=0.02) and CV death (p for trend=0.02) mortality than those in the other tertiles. Leptin and resistin failed to significantly predict all-cause and CV mortality (p<NS). Remarkably, ADPN modified the resistin-mortality link both on unadjusted analysis (p<0.001) and on multivariate-adjusted model with traditional, peculiar of ESKD and emerging risk factors (to 0.004). The risk excess for all-cause and CV mortality (p for effect modification 0.001 and 0.01, respectively) portended by a fixed increase in plasma ADPN (by 20 ng/mL) was indeed maximal in patients in the first ADPN tertile (all-cause death, HR: 0.71, 95% CI: 0.58-0.89; CV death, HR: 0.63, 95% CI: 0.51-0.79).

Conclusions: In ESKD, ADPN is a strong modifier of the link between Resistin and mortality with leptin. Some of these cytokines may not be as important as others in this clinical setting. Adipokines such as ADPN, Leptin and Resistin may be valuable biomarkers to better predict clinical outcomes in the dialysis population.

MP571
SURVIVAL AND DIALYSIS PRESCRIPTION IN VERY OLD PATIENTS ON DIALYSIS: DATA FROM SLOVENIAN RENAL REPLACEMENT THERAPY REGISTRY
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Introduction and Aims: The age of patients reaching end-stage renal disease and requiring renal replacement therapy (RRT) is increasing. The aim of our study was to analyze RRT survival and waiting times at a dedicated RRT center in Slovenia.

Methods: We evaluated patients from the Slovenian Renal Replacement Therapy Registry and included all incident (day 1) patients aged ≥ 70 years of age and who started RRT between Jan 1st, 2004 and Dec 31st, 2010. Patients were followed until Dec 31st, 2010. Survival was censored in case of recovery of renal function (4 cases); none of the patients was transplanted.

Results: In the observed period, 214 patients aged ≥ 80 years started RRT, which represented 13% of all incident (day 1) patients. Median age was 83 (inter-quartile range (IQR) 81-85, range 80-101) years, 48% were male, and 26% had diabetes. Most common comorbidities were hypertension (50%), cancer (34%), neuropsychiatric disorders (21%), and diabetic nephropathy (18%). At the end of their first year on RRT (or prior to death for patients not surviving the first year) the dialysis prescription was as follows: all patients were treated with hemodialysis, 10% were treated with convective methods, 29% were treated in single-needle mode; median weekly duration of dialysis was 12 (IQR 8-12) hours; 70% had 3 procedures, 29% had two and 1% had only one procedure weekly; vascular access was AV fistula in 48%, catheter in 45% and unknown in 7%. In the observed period 127 (59%) patients died, median survival was 21 months, 1-, 2- and 3-year survival rates were 68%, 45%, 36% and 18%, respectively. The cause of death was: cardio-vascular (45%), unknown (23%), infection (17%), other (9%), and malignancy (6%). Median expected survival for this group of patients using demographic data from national statistics would be 7.3 years.

Conclusions: Very old patients represent a significant portion of incident dialysis patients. Many are dialyzed only twice weekly or in single-needle mode and AV fistula is used as vascular access in half of patients. The survival of octogenarians on RRT, while being much shorter compared to healthy, age-matched population, is still good.

MP572
SATISFACTION PATIENTS OF DIFFERENT ASPECTS OF LONG-TERM HAEMODIALYSIS CARE: A MULTINATIONAL CROSS-SECTIONAL SURVEY OF PATIENTS
Suetonia Palmer1, Giorgia de Berrardis2, Jonathan C. Craig3, Fabio Pellegrini3, Marcella Rusop1, Allison Tong2, Marcello Torelli4, Jorgen Hegbrant5 and Giovanni F.M. Strippoli6
1University of Otago Christchurch New Zealand, 2School of Public Health, University of Sydney Sydney Australia, 3Consorzio Mario Negri Sud S. Maria Imbaro Italy, 4University of Alberta Edmonton Canada, 5Diaverum Medical-Scientific Office Lund Sweden

Introduction and Aims: Patients with end-stage kidney disease (ESKD) experience high rates of mortality, approaching 15-20% each year and have profoundly impaired quality of life. Better knowledge of how patients experience different facets of long-term dialysis could inform the design of targeted strategies to improve dialysis patients’ experience of illness and their quality of life. This study aims to assess patients’ satisfaction with different aspects of dialysis care.

Methods: This is a multinational cross-sectional survey using the 23-item Choices for Healthy Outcomes in Caring for End-Stage Renal Disease (CHOICE) questionnaire in 2145 long-term outpatient clinic-based haemodialysis patients in clinics in Europe (Hungary, Italy, Poland, and Portugal) and South America (Argentina). Patients’ ratings of these aspects of dialysis care ranged from 0 (very dissatisfied) to 10 (very satisfied). Patients were then asked to rate the importance of these aspects and report a global satisfaction score. Questions: Response rate differences by country; patients in Portugal were most likely to respond to the survey (97.4%), with decreasing response rates in Argentina.
(81.9%), Hungary (81.4%), Poland (74.4%), and Italy (73.6%). Fewer than half (46.5%) of haemodialysis patients rated their overall dialysis care as excellent. Within countries, global perceptions of care were uninfuenced by most patient characteristics except age and depressive symptoms; older patients were less critical of their care and those with depressive symptoms were less satisfied. Aspects of care patients most frequently ranked as excellent were attention to staff to cleanliness of the dialysis vascular access site (54%), caring of nurses (33%), responsiveness of staff to their pain or discomfort (51%), caring, helpfulness and concern of diatysis staff (50%), ease of reaching of staff by telephone (48%). The aspects of care least frequently ranked as excellent were information provided when patients chose a dialysis modality (23%), ease of seeing a social worker (28%), information provided about dialysis (34%), accuracy of information from nephrologist (for example, about prognosis or likelihood of a kidney transplant) (37%), and accuracy of nephrologist’s instructions (39%).

Conclusions: Patients are least satisfied with the amount and reliability of information they receive during care for end-stage kidney disease. Meeting patients’ expectations for information in line with the likelihood of kidney transplantation and patients’ options when choosing dialysis treatment, are likely to improve patient satisfaction of dialysis care.

### MP573 BRAIN Natriuretic Peptide as a Biomarker of Pulmonary Congestion in Stage 5 CKD on Dialysis

**Patrizia Pizzini**, Claudio Torino, Sebastiano Cutrupi, Belinda Spoto, Graziele D’Arigo, Rocco Tripepi, Giovanni Tripepi, Carmine Zoccali and Francesca Mallamaci

**Introduction and Aims:** High Brain natriuretic peptide (BNP) is a marker of left ventricular hypertrophy (LVH) and LV and LV diastolic dysfunction and ventricular overload and entails a high mortality risk in dialysis patients. Pulmonary congestion as assessed by the number of ultrasound B lines (US-B lines) is another emerging biomarker of death and cardiac events in the same population. We investigated the association between BNP and US-B lines and the interplay between these two risk factors in the high risk of mortality and death due to cardiovascular (CV) events in dialysis patients.

**Methods:** In a cohort of 136 dialysis patients (age: 63±14 yrs; M: 60%), we investigated the mutual associations among plasma BNP, LV mass (LVMI) and US-B lines and analysed the relationship between these biomarkers with a composite end point of death and/or fatal and non-fatal CV events. US-B lines were recorded over the whole lung area by using standard US probes by a novel technique well validated in dialysis patients (Mallamaci F, et al. JACC Img 2010:3:586).

**Results:** BNP (median 114 pg/ml; IQR: 46–307) and US-B lines (median 15 IQR: 9–31) were directly and signifi cantly correlated (r=0.42, P<0.001). This association was stronger than that between US-B lines and LVMI (r=0.27, P=0.002). In a multiple linear regression model, including age, gender, smoking, diatysis BP and CV comorbidities as well as BNP and LVMI, only BNP (β=0.30, P=0.002) maintained an independent relationship with US-B lines. In this model, LVMI failed to correlate with US-B lines (β=0.08, P=0.41) to become a significant correlate of this parameter (β=0.20, P=0.03) only after the exclusion of BNP from the model. The results of such a statistical modelling suggest that high BNP captures the explanatory power of LVMI for pulmonary congestion. During the follow-up period (median: 29 months; IQR: 14-36) 65 patients had the composite end point. In two separate multivariate Cox’s regression models both BNP (HR: 1.02, 95% CI 1.01-1.04, P<0.001) and US-B lines (HR: 1.05, 95% CI 1.02-1.08, P=0.003) were independently associated with the combined outcome while in a model including both risk factors only BNP maintained an independent relationship with the same outcome.

**Conclusions:** The strong, independent association between BNP and US-B lines in dialysis patients implies that this biomarker provides additional information on a pathway conducive to pulmonary oedema generated and/or potentiated by LV disorders and volume overload. This steady-state relationship accounts with prospective analysis showing that the predictive power for death and CV events of lung congestion largely overlaps with that of high BNP. Overall, these findings underscore the importance of targeting LV disorders and volume overload to curb the excessively high risk of death and CV complications in stage 5-D CKD patients.

### MP574 Number of Dialysis Sessions with High Ultrafiltration Rate are Associated with Poor Outcomes in an International Population of Hemodialysis Patients

**Gero von Gersdorff**, Len Usvyat, Mathias Schaller, Michelle Wong, Stephan Thijssen, Daniele Marcelli, Claudia Barth, Peter Kotanko and MONDO Consortium

**Introduction and Aims:** Ultrafiltration rate (UFR) > 10 ml/kg/h during haemodialysis (HD) has been associated with poorer outcomes (Sarnak KI 2008). Mechanisms proposed include arrhythmias secondary to cardiac stunning, hypertensive episodes and electrolyte disturbances. The number of dialysis sessions with high UFR may be associated with a cumulative risk for survival.

**Methods:** The MONitoring Dialysis Outcomes (MONDO) consortium consists of HD databases from Renal Research Institute (RRI) clinics in the US, Fresenius Medical Care (FMC) clinics in Europe (FMC Pacific (AP)), Latin America (LA), and Germany, Imperial College in UK, Hadassah Medical Center in Israel, and University of Maastricht, The Netherlands (Usvyat, Blood Purification 2013). Databases from RRI and KIH were queried to find all incident hemodialysis patients who had their first in-center treatment between 1/2000 and 12/2010 and who survived at least 12 months on HD. The fraction of sessions with UFR > 10 ml/kg/h (“high-UFR session; hiUFS”) was computed on a per patient basis in the first 6 months (“baseline”) and between months 7 and 12 on HD (“follow up”). Patients were then stratified into nine groups depending on the proportion of hiUFS during follow up.

**Results:** We studied 15,757 patients. Mean age was 64.9 years, 59.5% were male, 53.2% diabetic. Average UFR was 7.9 and 8.2 ml/kg/h during baseline and follow up, respectively. 40% had hiUFS < 5% and 40% had hiUFS > 20%. A higher proportion of hiUFS was associated with worse survival during follow up only moderately increased risk (Figure 1). By contrast, a decrease of hiUFS in the follow up period conferred a risk reduction.[figure]

**Conclusions:** Our international study indicates that performing > 20% of HD sessions, or about 3/month with UFR > 10 ml/kg/h is associated with poor survival in incident HD patients. This increased risk seems to be modifiable by subsequent reduction of hiUFS. These findings underscore the importance of balancing the interrelated parameters of treatment time, weight gain and UFR for every dialysis session. Further studies need to define more clearly the best strategies for reducing the risk associated with high UFR.

### MP575 SNOTRING IS A STRONG AMPLIFIER OF THE RISK BY HEART FAILURE FOR ALL CAUSE AND CARDIOVASCULAR MORTALITY IN CHRONIC KIDNEY DISEASE PATIENTS ON DIALYSIS (STAGE 5D-CKD)

**Claudia Torino**, Grazietta D’Arigo, Maurizio Postorino, Giovanni Tripepi, Francesca Mallamaci, Carmine Zoccali and on behalf of PROGREDE Work Group

**Introduction and Aims:** Self-reported snoring, an indicator of sleep disordered breathing (SDB), may associate with all-cause and cardiovascular (CV) mortality in the general population and in high risk conditions like heart failure (HF). SDB and HF are exceedingly frequent in the stage 5D-CKD population but the hypothesis that snoring may impact upon the relationship between HF and all-cause and CV mortality in these patients has never been tested. The issue is important because HF has been in part attributed to reversible pharyngeal edema secondary to volume expansion in HF patients (Chest 2007;132:440-6) and may therefore be a modifiable risk factor.

**Methods:** We investigated this problem in a cohort of 827 stage 5D-CKD patients, all of Caucasian descent. HF was assessed at baseline on the basis of clinical symptoms, radiological and echocardiographic examinations. At enrolment, participants provided self-reported information about snoring and were classified as non-snorers, moderate snorers and heavy snorers. Patients were followed up for a median time of 28 months (interquartile range: 21-35).

**Results:** One hundred and thirty-two patients (16%) were affected by HF at baseline. Overall, 194 patients (24%) were classified as heavy snorers, 308 (37%) as moderate snorers and 325 patients (39%) as non-snorers. During the follow-up period, 233 patients died of causes. Both on univariate (P=0.03) and multivariate (P=0.02) Cox regression analyses, HF significantly predicted the study outcomes whereas snoring did not (P=NS). However, snoring was a strong modifier of the risk of HF for all-cause and CV death. In fully adjusted Cox models (including age, gender, smoking, diabetes, systolic BP, anti-hypertensive treatment, CV comorbidities, albumin, CRP, phosphate, cholesterol, Hb and albumin), the hazard ratios (HR) associated to HF for the study outcomes were highest in heavy snorers [all-cause death: HR: 2.5 (95% CI: 1.5-4.2, P=0.001); CV death: HR: 3.1 (1.8-5.3), P=0.001], intermediate in moderate snorers [all-cause death: HR: 1.5 (1.2-2.1, P=0.01); CV death: HR: 1.6 (1.2-2.3, P=0.009) and lowest and not significant in non-snorers [all-cause death: HR: 0.9 (0.6-1.5); CV death: HR: 0.8 (CI: 0.5-1.5)].

**Conclusions:** Snoring is an effect modifier of the relationship between HF and all-cause and CV mortality independently of traditional and non-traditional risk factors in stage 5D-CKD patients. Clinical trials are needed to verify whether intensified surveillance and treatment (UF intensification) of HF snorers on dialysis may translate into better clinical outcomes in this very high risk population.

### WHAT DETERMINES WHETHER END-STAGE KIDNEY DISEASE PATIENTS COMMENCE ON THEIR CHOSEN TREATMENT MODALITY?

**Dimitrios Chanouzas**, Khai Ping Ng and Jyoti Baharani

**Introduction and Aims:** Despite the use of pre-dialysis programmes, there is often a discrepancy between initial pre-dialysis choice and actual treatment modality.
commenced. We aimed to examine the factors that determine whether end-stage kidney disease (ESKD) patients commence treatment on their chosen modality. **Methods:** This is a follow-up study of a previously published questionnaire study in 118 pre-dialysis patients. The questionnaire consisted of 20 items that patients were asked to rate based on their importance in influencing their modality decision. We followed up the study participants for 43 months to determine whether they indeed commenced treatment on their initial chosen modality. **Results:** 49% of patients reached ESKD. 94.3% (n=35) and 53.8% (n=13) of patients that chose haemodialysis (HD) and peritoneal dialysis (PD) respectively, commenced on their initial chosen modality. The remaining patients chose PD started on HD. This was not due to PD technique failure 90.0% (n=10) of patients that selected conservative management (CM) retained their choice. There was no association between age, gender or ethnicity and retention of choice. For HD choice, scoring the ‘distance to travel to hospital’ item highly was associated with commencement on HD (p=0.024). Among patients who had chosen PD, those who valued ‘modality fitting with lifestyle’ highly (p=0.008) were more functionally able (p=0.015) were more likely to commence on PD. Interestingly the ‘modality fitting with lifestyle’ factor was also found to be a crucial determinant of PD choice versus HD in our original study. There was a trend for patients with low educational attainment and patients who scored the item ‘importance of family in helping with decision’ highly, to commence on HD instead of their initial choice of PD, although the results did not reach statistical significance (p=0.092, p=0.060). **Conclusions:** Patients who initially chose PD but did not perceive the lifestyle benefits of PD as an important, or were less functionally able, were more likely to commence on HD. These findings are important in informing the design of more effective pre-dialysis programmes to increase the uptake of self-care modalities.

**MP577 THE IMPACT OF FIM SCORE IN THE SHORT TERM MORTALITY OF HEMODIALYSIS PATIENTS**

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**Introduction and Aims:** Decreased activity of daily living (ADL) has been associated with mortality in general population, in hemodialysis patients, decreased ADL seems to be more common than general population. Therefore, correlation between ADL and mortality in hemodialysis patients should be noted. However, these relations in hemodialysis patients are still unclear. We studied the level of ADL using functional independence measure (FIM) score, which is one of the major surrogate markers of ADL, and the association between FIM score and all-cause mortality in these patients. **Methods:** This prospective cohort study included 107 patients on maintenance hemodialysis (68 men and 39 women; mean age, 72.4 ± 9.9 years) in 2 years. The underlying diseases for hemodialysis were 54 diabetic nephropathy, 18 chronic glomerulonephritis, 10 nephrosclerosis, and 25 others. ADL was assessed using FIM score (total points, 126), which comprises 13 motor items (total points, 91) and 5 cognitive items (total points, 35). Each item is scored from 1 to 7 based on level of independence, where 1 represents total dependence and 7 indicates complete independence. A survival curve was drawn using Kaplan-Meier analysis and stratified into 4 groups using the interquartile range value of FIM score. The Cox proportional hazards analysis, adjusted for age, gender, albumin, and C-reactive protein, was used to calculate mortality hazard ratio (HR) and its 95% confidence interval (CI). **Results:** The mean total FIM score was 60.0 ± 24.7, and the scores for FIM motor and cognitive items were decreased in the study patients (34.4 ± 16.8 and 25.5 ± 10.5, respectively). Cumulative mortality rate was significantly higher in FIM 41 - 60 and ≤ 40 groups compared to the rate in the reference with FIM scores 85 ± 80. In addition, the HR for mortality significantly increased with FIM 41 - 60 and ≤ 40 groups.

**Conclusions:** The FIM score was decreased by half in hemodialysis patients, especially in motor items. FIM score was a novel predictive marker for 2-year mortality in these patients. Our findings suggest that comprehensive strategies which could increase ADL in hemodialysis patients are required.

**MP578 CLINICAL AND BIOLOGICAL VARIABLES ASSOCIATED WITH MORTALITY IN HEMODIALYSIS PATIENTS**

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**Introduction and Aims:** Global and cardiovascular mortality remains high in hemodialysis patients. Different hypotheses have been proposed to explain this over-mortality. We tested here potential clinical and biological variables which are associated with a higher mortality risk. **Methods:** Prevalent hemodialysis patients from three centers in Belgium (Liége) were recruited. Following clinical data were available: age, gender, BMI, dialysis vintage, status of hypertension and diabetes, smoking status, and history of cardiovascular (CV) disease. Among biological variables, we tested classical variables in serum like calcium, phosphorus, parathormone, 25-OH vitamin D, albumin and C-reactive protein (CRP). Several new biomarkers were also tested: bone-specific alkaline phosphate, C-terminal telopeptide of collagen type I (CTX), intact amino-terminal propeptide of type I procollagen, tartrate-resistant acid phosphatase 5b, osteoprotegerin, tropinin T, homocysteine, interleukin-6, TNFα, IGF-23, fetuin and desphospho-uncarboxylated matrix Gla-protein. Time of follow-up is expressed in months. Cox proportional hazards regression and logistic regression were performed to evaluate the possible effect of covariates. **Results:** The sample included 165 patients with the following clinical characteristics: median age was 74 y (63.80), median BMI was 26.7 kg/m2, median dialysis vintage 22 months (11.43), 44% were diabetic, 87% were hypertensive, 21% were smokers and 65% had history of CV disease. Median follow up time was 22.1±11.3 months. A total of 74/165 (44.8%) died with a mean follow up time of 13.1±9.1 months (median value was 11.3 [5.420.8]). Hazard ratios were calculated using Cox proportional hazards modeling with the following statistically significant covariates in the final model (HR and 95% HR confidence limits): history of CV disease (HR: 0.544 [0.31-0.95] for no history), age (HR: 1.054 [1.09-1.079]), phosphorus (HR: 1.232 [1.029-1.454]), tropinin T (HR: 253.283 [1.631-4325]) and CTX (HR: 1.599 [1.10-1.3]). When considering logistic regression to estimate mortality probability, age, phosphorus, tropinin T and CTX were still in the final model of prediction, but not history of CV disease. In this last analysis, concentration of 25-OH vitamin D was also significant. **Conclusions:** In this longitudinal study, we confirmed that age and phosphorus levels are closely associated with a higher risk of mortality. Among the “non-classical” variables, concentration of tropinin T is the most interesting one to assess the risk of mortality in our hemodialysis populations.

**MP579 IMPROVEMENT OF COGNITIVE FUNCTIONS AFTER A SINGLE DIALYSIS SESSION**

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**Introduction and Aims:** Cognitive function is impaired in CKD5D patients. The potential effect of a single dialysis function on cognitive function remains elusive. Aim of the study was to assess cognitive function using a wide test battery and avoiding excluding effects of circadian variations. **Methods:** Twentyfive (11 female) CKD5D patients (54 ±12 years, dialysis vintage 4.3 ±5.7 years) were enrolled. Cognitive testing was performed 1 h prior to dialysis as well as 24 h thereafter including assessment of memory, attention and concentration, executive functioning and psychomotor speed by using the following tests: Rivermead Behavior Memory Test (RBMT), Rey Complex Figure Test (RCFT), Trail Making Test A+B (TMT), Wechsler Memory Scale (WMS- R), Behavior Assessment of Dysexecutive Syndrome (BADS), Regensburger word fluency test (RWT) and test battery for attention (TAP).
Results: A single dialysis session lead to a significant improvement in logical and visual memory (RBMT [pre: 7.5 and 6 digits/ post: 8.5 and 8 digits] and RCF T [pre:32.5 digits/ post:48 digits]) psychomotor speed and concentration (TMT A), while task switching (TMT B) did not improve: 40% of patients were on psychotropic medication, but this factor did not affect outcomes.

Conclusions: Our data demonstrate improvements in memory functions, executive functions and psychomotor abilities after a single dialysis session, pointing to a reversible component of cognitive impairment in CKDSD.

Introduction and Aims: We hypothesize that the difference between the really attained and the prescribed end dialysis body weight (dBW), defined end-dialysis over-weight, (edOW; Kg) could impact survival of hemodialysis (HD) patients. Aim of this prospective observational study was to evaluate if edOW could influence survival in a cohort of prevalent HD patients, controlled for multiple dialysis and clinical risk factors and followed for 3 years.

Methods: 182 patients, 117 men, age 65±13 years, on regular HD treatment for at least 6 months (median 48; range 6-366 months) were followed from January 1st 2008 to December 31st 2010. Eighty four patients (46%) did not achieve dBW, their median edOW was 0.4 Kg (range 0.1-1.4 Kg). During follow-up 98 patients died, mainly for cardiovascular causes(69%). Multivariate Cox regression analysis was utilized to evaluate the effect on mortality of edOW, ultrafiltration rate (UFR), interdialytic weight gain (idWG), age, sex, dialytic vintage, cardiovascular disease (CVD), antihypertensive therapy, diabetes, duration of HD, body weight (dBW), body mass index (BMI), mean arterial pressure (MAP), Kt/V, protein catabolic rate (PCRn).

Results: At the Cox’s proportional hazard risk analysis (HR 1.04; CI 1.03-1.05; P <0.0001), idWG (HR 2.62; CI 2.06-3.34; p=0.01), UFR (HR 1.13; CI 1.09-1.16; p<0.01), PCRn (HR 0.02; CI 0.01-0.04; p<0.001) and edOW (HR 2.71; CI 1.95-3.75; p<0.02) were independently correlated to survival The relative receiver operating characteristic (ROC) curve identified a cut-off value of edOW in predicting death of 0.3 Kg. The same analysis was performed by examining edOW and cardiovascular mortality. A significant greater cardiovascular mortality was observed for patients with edOW ≥ 0.3 Kg (p< 0.009).

Conclusions: High edOW are independently associated with an increased long-term risk of all-cause and cardiovascular mortality in HD patients. Better survival was observed in patients with edOW < 0.3 Kg. For patients with higher edOW, longer or more frequent dialysis sessions should be considered in order to prevent the deleterious consequences of excessive body fluid expansion.
DEFINING THE SERUM SODIUM SET POINT TO IMPROVE FLUID STATUS IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Recent data suggest that tailoring dialysate sodium concentration to an individual patient’s serum sodium “set point” decreases the magnitude of interdialytic weight gain and improves blood pressure and volume control. Little information is available, however, to determine the number of same-patient serum sodium measurements needed to estimate a reliable homeostatic set point.

Methods: We conducted a retrospective analysis of all pre-dialysis serum sodium measurements taken from 10,413 randomly selected in-center hemodialysis patients, keeping dialysate sodium constant over a 6-month (m) period, January-June 2012. For each subject, we considered serum sodium as individual measurements and as 2m, 3m, 4m and 5m rolling window means. We used intra-class correlation coefficient (ICC) for each measure. Results: 10,413 patients contributed a total of 55,550 individual sodium measurements. Median (p25, p75) number of sodium measurements was 6 (4, 16) over the 6-month period. Mean sodium concentration for the cohort was 137.9 mEq/L. Intra-class correlation coefficient was incrementally higher for windows of longer duration. Incremental gains in intra-class correlation were comparatively less for window <3m in duration (Figure).

Conclusions: Predialysis serum sodium is reliably reproducible when evaluated over rolling windows as short as 2 to 3 months. Though longer intervals may yield incremental improvements in reproducibility, the clinical utility of the test would likely be offset by consequent delay in decision making. To tailor dialysate sodium to serum sodium in hemodialysis patients, clinicians and researchers should consider 2-or 3-month sampling windows to determine serum sodium set point.

RESULTS: Of 385 incident pts, 110 are younger than 60 ys and 10 with follow up less than 3 months. Of 265 elderly people 91 (35.7%) are jO, 121 (47.3%) cO and 43 (16.6%) vO. Cause of renal disease: diabetes is the first cause in jO, angiosclerosis in vO. ultrasound disease is relevant in cO glomerulopathies account for about 9-10% in all groups. Early referral: in all groups about 80% of pts refer to our Department during the preHD stage of the disease. 70% undergo arteriovenous fistula (AVF) creation on native vessels before starting HD. 11.6% in vO and 7.4% in cO do not receive AVF because of impracticable vessels (vs 1% in jO, p=0.03). Comorbidities: the prevalence of hypertensive status (50%), diabetes (40%), cardiac disease (35% in jO and cO, 50% in vO) and lower limb ulcerations (25%) are different. In vO arrhythmia is common (40% vs 17.5% in jO and 23% in cO, p=0.01) and neoplasia as well (not statistically significant). Therapy: Angiotensin Converting Enzyme Inhibitors or Angiotensin Receptor Blockers are assumed by 26.4% of jO and 10% of cO and vO (p=0.002); Vitamin K antagonists are assumed by 15.4% of jO, 19% cO and 9% vO. AVF is the first access in all groups for about 60-70% and the last access in jO, cO and vO respectively (p=0.003); in all groups the number of AVF creation per pt is 1.3±0.6 and 60% receive only one AVF. Catheters: in all groups the number of catheter per pts is 1.1±1.4; 40-45% and 25% need none or only one central venous catheter, respectively. The survival curves reveal lower but similar life expectancy for cO and vO in comparison to jO (median survival 34, 35 and 64 months respectively, p=0.001).

CONCLUSIONS: Our study demonstrates that, when old pts are referred early to the nephrologists, the vascular access presents a good outcome, since the native AVF is the main access and the catheter’s use is restricted to 10% in jO and 30% in vO. The prevalence of the comorbidities are high but similar with aging; the survival in vO is similar to cO and lower than in jO. The aging is the main determinant of death, that in cO and vO is becoming similar to non HD old people.

THE IMPORTANCE OF AGE IN DIALYSIS

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Introduction and Aims: The incidence and the prevalence of elderly people (age≥60 years, y) receiving hemodialysis (HD) is increasing in the western world. Elderly people represent an heterogeneous group of patients, burdened by several comorbidities. They could be divided in “young Old” (yO: 60-69 yrs), “common Old” (cO:70-79 yrs) and “very Old” (vO:≥80 yrs). The aim of our retrospective study is to evaluate the vascular access, the main therapies, the comorbidities and the mortality rate of elderly attending our Dialysis Centre during the last 13 years.

Methods: Subjects older than 60 years, starting HD from 01.01.2000 to 31.12.2012 were enrolled, divided in jO, cO and vO and compared each other. Patients (pts) with follow up less than 3 months were excluded.

Results: The average BMI rose from 23.5 kg/m2 in 1994 to 25.5 kg/m2 in 2011 (P=0.001) (Fig.1). This temporal evolution of average BMI was accompanied by a decline on the prevalence of severely underweight (BMI <18.5 kg/m2) and mild to moderate overweight (BMI 18.6-25 kg/m2) patients (Fig 2). Remarkably, both the prevalence of overweight (BMI 25.1-30 kg/m2: 26%→35%) , and frankly obese patients (BMI>30 kg/m2: 4%→14%) increased considerably (P<0.001) over the same time-frame. These secular trends were evident across various population strata including gender and age. The rising tide of overweight and obesity in this population was accompanied by a parallel increase in the prevalence of diabetic nephropathy as a diagnosis of ESKD (1994: 7%; 2011:11%). Similar analyses focusing exclusively in incident patients fully confirmed these trends and showed a substantial decline in the risk of underweight status (from 12% to just <3%) and a doubling in the risk of overweight and obesity.

Conclusions: Analysis of BMI in a Registry representative of the ERA-EDTA Registry shows a fast rise of the prevalence of overweight and obese patients in the dialysis population and a specular decline of patients in the underweight categories. These secular trends have obvious implications for the growth of the total ESKD population in the years to come.
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**MP586**

**OBSERVATIONAL STUDY OF THE PREVALENCE OF STAPHYLOCOCCUS AUREUS TOXIN GENE POSITIVITY IN DIFFERENT POPULATIONS INCLUDING A RENAL DIALYSIS UNIT IN GLASGOW, UK**

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**Introduction and Aims:** Staphylococcus aureus toxin genes have been held responsible for outbreaks of community acquired invasive disease. Prevalence of toxin gene colonisation varies in different geographical areas and populations. Up to 50% of haemodialysis patients and 10% of the general population are colonised with S. aureus. The prevalence of Panton Valentine Leucocidin (PVL), Toxic Shock Toxin (TST) and exfoliative toxins A and B (ETA and ETB) in these populations is unknown. We aim to assess the prevalence of PVL, TST, ETA and ETB toxin genes in 4 different patient groups.

**Methods:** Haemodialysis patients and healthy patients from an orthopaedic preoperative clinic were tested for S. aureus nasal colonisation. Isolates from skin infections from GP practices and hospital patients were tested for S. aureus nasal colonisation. 58 skin swabs positive for S. aureus were identified from the general microbiology laboratory and 64 blood cultures were S. aureus positive. There was no significant difference between the age of those colonised with S. aureus (mean 60.73 years) and those not colonised with S. aureus (59.68 years). There was no significant difference between the age of those colonised with S. aureus and those with no nasal or skin infection characterised by a positive skin or soft tissue swab or bacteremia (mean 61.1 years).

**Results:** The prevalence of S. aureus colonisation in HD patients and healthy patients from the orthopaedics preoperative clinic. Overall, virulence toxin gene prevalence was low. There were no isolates containing the PVL toxin gene.

**Conclusions:** Prevalence of S. aureus colonisation from this study was in keeping with previous research. Overall toxin gene prevalence in all populations was low. It was reassuring that there was no significant difference between the 4 groups although numbers are small. We suggest that although virulence toxin genes may cause more severe disease, they are not more likely to cause disease in a colonised patient. More observational research is required to determine virulence toxin gene prevalence in the general population.

**MP587**

**RENAI L PROGNOSIS AT ONE YEAR OF PATIENTS STILL ON DIALYSIS AFTER AN INTENSIVE CARE UNIT STAY**

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**Introduction and Aims:** Acute renal failure (ARF) in intensive care is common - from 35 to 65% and associated with excess mortality. In case of extra renal purificaction (ERP), hospital mortality can reach up to 60% of patients, surviving after an ICU stay. In case of persistent renal failure after the ICU stay, no data is available. This thesis offers describes this population and evaluates the vital and renal prognosis a year after the study with the associated risks factors.

**Methods:** Patients who have showed an ARF with an ERP were not weaned before the output of intensive care were included in this retrospective study realized in a French University Hospital between December 2005 and March 2011. Initially, survival without dialysis has been followed over a year thanks to the Cox model. A competitive risk model in sub distribution of Fine & Gray was also used to follow jointly the setting of chronic dialysis and the mortality.

**Results:** Among the 4132 ICU stays, 551 benefited from an ERP, 337 patients have survived whom 115 were still on dialysis after the output of intensive care. They were 77 men and 32 women, average age 63,5 years old (IQR: 55,73) with a severity score IGS II up to an average of 54,5 (IQR: 40,5;65,5). They received an injection of iodine, aminoglycosides or vancomycin in respectively 45,7%, 31% and 12,9% of the cases. The main etiologies of the ARF were the sepsis (23,3%), non-infectious shock (22,4%), functional (19,8%) or toxic (16,4%). Acute tubular necrosis (ATN) was admitted as the etiology of ARF for 102 patients (87,9%). Chronic dialysis-free survival at 1 year was 63,4% (95%CI= 54,9 to 72,3%). The cumulative risk of dialysis and death at 1 year was respectively 23,5% (95%CI=17-32%) and 12,1% (95%CI=7,4 to 19,7%). Independent factors associated with a lower survival without dialysis are: advanced age, a mechanism other than ATN, the administration of vancomycin during the ICU stay and lower renal function prior to 60ml/min/1.73m². In addition, the presence of statins in the treatment of substance is a protective factor with a HR=0,35 (95%CI= 0,17-0,71). The cumulative risk of chronic dialysis was significantly aggravated by a cause other than the ATN (SHR=3,5) and the use of aminoacidic solutions during the ICU stay (SHR=4,25 with 95%CI=1.36-13). It was reduced by a previous presence of greater clearance than 60ml/min earlier (SHR=0,03, 95%CI=0,004-0,27) and statins SHR=0,06 (95%CI=0,01 to 0,49). Statins did not alter significantly the cumulative risk of death (SHR=0,86 95%CI=0,68 to 2,43; p=0,09).

**Conclusions:** Two thirds of patients requiring ERP at the end of ICU stay are alive and not on dialysis at 1 year. The previous level of renal function, the age, the use of vancomycin and aminoglycosides during the stay and the presence of statins in the treatment of substance are determinant independent factors.

**MP588**

**MODELING TREATMENT TRAJECTORIES TO OPTIMIZE THE ORGANIZATION OF RENAL REPLACEMENT THERAPY AND PUBLIC HEALTH DECISION MAKING**

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**Introduction and Aims:** ERSD patients require thorough and balanced information about global long-term RRT strategies that combine various complementary modalities. Similarly, health-care planning requires anticipation of the necessary or available supply of these different modalities. ERSD registries provide numerous essential indicators about RRT, such as point prevalence rates. Nonetheless, these indicators are especially difficult to interpret when the underlying dynamic process is not well understood. To obtain a dynamic view of patient trajectories through RRT, we
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are developing a statistical tool to: 1/ illustrate the course of a cohort of incident ESRD patients over time through RR modalities, and 2/ simulate and quantify the impact of various expected changes or new strategies.

Methods: The model first estimated transition rates between 10 treatment modalities and between each of these modalities and death, in 6 separate groups stratified in three age groups (at ESRD onset), each with or without diabetes. In a second step a continuous-time deterministic structural model predicted the mean volume of each compartment at each time point for the 180 months after RRT began.

Results: The study used outcomes of 67,258 adult patients. As expected, the role of transplantation increased with age and with diabetes, a change mirrored by the increased role of in-center hemodialysis. In all groups, peritoneal dialysis accounted for only a small portion of the total time spent in RRT. To illustrate the possibility of simulating policy changes, a first scenario tested an increased use of non-assisted automated PD in patients aged 18-44 years without diabetes; a second scenario tested improving access to kidney transplants from cadaveric donors for patients 45-69 years with diabetes.

Conclusions: A model based on patient's treatment trajectories can usefully improve descriptions and understanding of the dynamic phenomenon of RRT. It should help nephrologists as well as the Ministry of Health and the health insurance funds to optimize the organization of renal care and public health decision-making. It may also be a tool to facilitate evidence-based public health decisions by evaluating the performance of the organization of dialysis care, before and after modification, under different useful configurations and over long periods of time. As many factors are related to treatment choice and in view of the lack of randomized clinical trials, simulations may be a way to promote translational research in public health and clinical medicine.

THE COMPARATIVE EVALUATION CONCERNING THE START OF DIALYSIS BETWEEN ELDERLY AND YOUNGER PATIENTS IN JAPAN

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Introduction and Aims: Elderly CKD patients start dialysis treatment in Japan. Median age at starting dialysis is more than 70 years-old and ageing tendency has not stopped yet. The elderly CKD patients have various senile complications and are anticipated to start dialysis treatment in earlier phase from uremic complications. We evaluated the clinical data at the beginning of dialysis concerning renal function and uremic conditions.

Methods: We evaluated 1829 stage 5 CKD patients who newly started dialysis from 2004 to 2008. Thirty one % of them were diabetic patients. They were divided into 3 groups; younger age group (YAG) <65 years-old (n=595), middle age group (MAG) from 65 to 75 years (n=487 years-old, and older age group (HAG) >75 years-old n=353. Clinical data including S-Cr, eGFR, Ccr, electrolytes and acid-base balance disorders were compared among three groups. ANOVA, Student t, chi-square tests were used as statistical methods.

Results: S-Cr was significantly lower in HAG group (p<0.001), while eGFR and Ccr were not significantly different among three groups. BMI, albumin, diastolic blood pressure, hematcrit and HCO3- did not showed significant differences between three groups. Over volume sings including edema and dyspnea on effort emerged at significantly higher rate in HAG group (p<0.005).

Conclusions: From the evaluation of renal function, commencing time of dialysis was even in three groups. S-Cr was not useful as a marker to determine the beginning of dialysis. The beginning of dialysis in HAG group was performed in milder electrolytes and acid-base balance disorders compared to younger groups. This might be induced from the higher rate of over volume sings such as edema and dyspnea.

THE EFFECT OF DIALYSIS DURATION ON MARGINAL DONOR TRANSPLANTATION DECISION IN DIALYSIS PATIENTS

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Introduction and Aims: Organ shortage is one of the most important problems in kidney transplantation (KT). For this reason, the expanded donor criteria have been developed in recent years. In this study, we aimed to compare the factors affecting the decision to accept marginal deceased kidney donation in dialysis patients with short or long dialysis durations.

Methods: 597 dialysis patients, according to the duration of dialysis were divided into two groups (Group 1: <40 months, n=145, Group 2: >40 months, n=452). Patients were asked about the acceptance of marginal associated donor and/or kidney properties with certain diseases or some of the features that differ from normal cadaveric kidneys. Hospital Anxiety and Depression Scale was performed. Patient’s donor kidney selectivity score (DKSS) was obtained by asking 32 questions that evaluate their consents for marginal kidney donation.

Results: Groups characteristics (gender, age, body weight, body mass index, systolic and diastolic blood pressure) were similar (p>0.05). While 69.3% of dialysis patients wanted to have KT, 30% of them registered on the waiting list. While 60 patients (10%) did not want to have KT, 299 of them (50.1%) wants to receive from live donors and 238 of them (39.9%) wants to receive from cadaveric donor. Ratios of patients that had live donor was 11.7%. DKSS to Group 1 is 37.8±23.6 and 31.9±3.23 in Group 2 (p<0.05). Patients in Group 2 were more selective for marginal donor KT. The acceptance of a donor kidney from close relatives, excessive fat or thin, alcoholic, the opposite sex, mentally ill or made illegal works was significantly higher in Group 1. DKSS and selectivity was significantly decreased as the duration of education was increased.

Conclusions: Increased waiting time negatively effects the decision of receiving kidney from marginal donor.

SURVIVAL OF PATIENTS ON HEMODIALYSIS THERAPY IN TURKEY: AN ANALYSIS OF 20,087 PATIENTS

Karri Serdergecti, Gultekin Suleymanlar, Mehmet Atiparmak, Nurhan Seyahi, Katty Jager, Sinan Trabulous and Ekrem Erek

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Introduction and Aims: Comparison of mortality across countries is an important tool to help us explore patient- and process-related factors that contribute to mortality differences reported in dialysis patients. However, data on dialysis survival on developing countries are largely missing. We aimed to analyze the survival and factors affecting survival in hemodialysis (HD) patients in Turkey.

Methods: Data from the patient-based database of the Turkish Society of Nephrology were used. Between 1995 and 2005, a total of 36654 patients were recorded in the database. At the end of data cleaning and elimination, 20087 HD patients were eligible for the study. The survival of HD was calculated according as “as-treated” method using Kaplan-Meier survival analysis. Cox regression analysis was used for determining the influences of the prognostic factors on survival.

Results: Demographic and clinical data of the patients were shown in Table 1. The survival at 1 year was 90.5%, at 5 years was 68.2%, and at 10 years was 54.2%. According to multivariate analysis, older age, male sex, diabetes mellitus, coronary heart disease, congestive heart failure, cerebrovascular disease, and malignancy were associated with decreased survival (Table 2). On the contrary hypertension was associated with a better survival.

Conclusions: Our analysis of data from over the 10-year period disclosed that the survival of HD patients in Turkey was comparable to other European countries.
Abstracts

Nephrology Dialysis Transplantation

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<table>
<thead>
<tr>
<th>Hazard Ratio (%95 confidence interval)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>1.038 (1.035–1.040)</td>
</tr>
<tr>
<td>Sex (Female)</td>
<td>0.887 (0.838–0.939)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.911 (0.861–0.963)</td>
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<tr>
<td>Diabetes Mellitus</td>
<td>1.504 (1.411–1.610)</td>
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<tr>
<td>Coronary heart disease</td>
<td>1.155 (1.063–1.255)</td>
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<tr>
<td>Congestive heart failure</td>
<td>1.485 (1.356–1.627)</td>
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<tr>
<td>Periferal vascular disease</td>
<td>0.981 (0.860–1.119)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>1.381 (1.193–1.593)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>2.100 (1.824–2.417)</td>
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Introduction and Aims: The benefits of regular physical activity (PA) are well known in general population. Patients with CKD are less active compared to general population. Pedometers have been validated for the quantification of PA, although these devices have not been widely used in the dialysis population. The objectives of this study were both measuring the level of PA in hemodialysis (HD) patients by the use of pedometers and determining the relation between PA with body composition and with biochemical parameters.

Methods: In a cross-sectional study we analyzed: PA with a questionnaire on 400 participants, body composition using bioelectrical impedance measurement and general biochemical parameters. For the measure of PA, patients were asked to use the pedometer during 6 days (2 HD days, 2 non-HD midweek days, 2 non-HD weekend days). The information of the activity carried out, was obtained from the memory of the device. It was necessary to have a minimum of 4 days measured for considering the value with validity. In addition to the number of steps taken, the device also provides the time of active walking (AW).

Results: 58 patients (mean age 64±12 years) with an median of 37 months (range 2-240) in HD. Thirty four participants (59%) were male, 18 (31%) were diabetic and 11 (19%) had history of isometric cardiopathy. Vascular and diabetic nephropathies were the most frequent causes of ESRD. In relation to PA, the average of steps taken per day was 3069±2632 steps. PA was lower in women (2103±1439 vs 3713±3402 steps; p=0.011). Likewise, the average number of steps taken in a HD day was lower compared to non-HD day (2276±2052 vs 3684±3292 steps). Also the number of steps taken in a non-HD weekend day was lower compared to a non-HD midweek day (3355±3352 vs 3798±3473 steps). Accordingly, nobody reached the objective of 10000 steps in a HD day and just the 9% (5) did in a non-HD day. In regard to the time of AW the mean was 30.57 minutes per day (22.2±0.5 vs 39.1±0.5 minutes between HD and non-HD day). No correlation between PA and Charlson Comorbidity Index was found. By linking the degree of PA with laboratory parameters, we found a positive association with urea (r=0.007), creatinine (r=0.001), total proteins (r=0.004), PTH levels (r=0.041) and an inverse association with CRP (r=0.007) and EPO resistance index (r=0.015). Concerning the relationship between PA and body composition, higher levels of PA were associated with increased lean mass (p=0.001) and a lower percentage of fat mass (p=0.001). In the same way, we found a strong positive correlation between the degree of PA with body cell mass (r<0.001) and phase angle (r=0.001).

Conclusions: Pedometers are useful for estimating PA in HD patients. Hemodialysis patients have a decreased level of PA. There is a strong correlation between PA with serum creatinine, body cell mass and lean body mass.

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Basal physical activity in hemodialysis patients: correlation with biochemical parameters and with body composition

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Conclusions: Pedometers are useful for estimating PA in HD patients. Hemodialysis patients have a decreased level of PA. There is a strong correlation between PA with serum creatinine, body cell mass and lean body mass.

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InCREASE OF RENAL REPLACEMENT THAREPY PATIENTS
WITH BODY COMPOSITION

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1Braun Avheim Hungary, 2CPL Dialysis Network Budapest Hungary, 3Central Laboratory of St Imre Teaching Hospital Budapest Hungary

Introduction and Aims: Disease registries have tremendous potential as tools for quality improvement and research. Chronic kidney diseases database in Estonia is an internet based system where data on patient (pts) status, treatment quality indicators and outcome are systematically gathered. Aim of the study was to examine renal replacement therapy (RRT) incidence and prevalence trends with regard to age and gender.

Methods: All pts on RRT between January 1, 2000 and December 31, 2012 were considered in the analysis. The information was obtained from the Chronic Kidney Disease Database.

Results: End-stage kidney disease affects more than 700 persons in Estonia, i.e., 552 per million population (pmp) among whom 41% are on dialysis and 59% are living with a functioning graft at the end of 2012. RRT incidence and prevalence pts increase was the highest during 2000-2008 even up to 19 percent of prevalence pts increase in 2001 but last 5 years increase was much lower and last two years we examined only small increase. Incidence rate has quite similar during the last four years (mean 65 pmp) compared with higher rate during previous years. The most common cause of kidney failure have been several years diabetes among incidence pts and among prevalence pts glomerulonephritis whereas diabetes holds the second place. We have noticed the higher acceptance of RRT among pts over 75 years and male predominance during all the study period.

Conclusions: Increase of RRT prevalent patients remain low already two years in the row and incidence tends to stabilize, except in persons aged 75 years or older and in those with diabetes in whom it continues to rise.
Conclusions: A 1% increment in RDW was associated with a 17% greater risk of mortality (hazard ratio [HR]: 1.17, 95% confidence interval [CI]: 1.1-1.24). Mortality HRs in the 2nd, 3rd and 4th quartile of RDW were 1.17 (0.87-1.56), 1.47 (1.10-1.95) and 1.83 (1.38-2.44), respectively, compared to the 1st quartile in the fully adjusted model. Our data suggests that RDW is a strong and independent predictor of mortality in dialysis patients.

MP595 INCIDENCE, PROGNOSIS AND RISK FACTORS FOR TRAUMATIC INJURY IN CHRONIC HEMIDIALYSIS PATIENTS

Ja-Ryong Koo1, Myung-Jin Choi2, Mi-Hyun Yoon2, Ji-Yean Park2, Eun-Young No2, Jung-Won Seo1, Young-Ki Lee2 and Jung-Woo Noh2
1Internal Medicine Hallym University Dongtan Sacred Heart Hospital Hwaseong Gyeonggi-Republic of Korea, 2Internal Medicine, Hallym University Chuncheon Sacred Heart Hospital, Kidney Research Institute Chuncheon Gangwon-Do Republic of Korea

Introduction and Aims: As the number of hemodialysis (HD) patients with multiple comorbidities continues to increase, more patients are at risk of traumatic injury during peri-dialytic period. However the incidence, prognosis and risk factors for traumatic injury in chronic HD patients have not been studied well.

Methods: 222 chronic HD patients (age 61.8±12.4 years, male 52.3%, diabetes 64.9%) were studied for a mean duration of 208±92 weeks starting from January 2007. Traumatic injury events requiring hospitalization were identified with review of medical records. Potential risk factors for traumatic injury were collected monthly until study end (July 2012), traumatic injury event, death, transplantation or transfer to another HD center.

Results: During the whole follow up periods, 49 traumatic injuries (38 falls, 8 traffic accidents, 3 falling object injuries) occurred (traumatic injury incidence: 5.5/100 person-year). Fifteen (30.6%) traumatic injury events occurred on Monday. Thirty-one patients (63.3%) were complicated by fracture and 9 patients (18.4%) were complicated by intracranial hemorrhage. The overall mortality rate during the follow up period was 34.7% (17/49) in the patients with traumatic injury and 20.8% (36/173) in the patients without traumatic injury. Kaplan-Meier survival curve (figure 1) showed significant difference in the cumulative mortality rate between two groups (log-rank P<0.05). In multivariate Cox analysis, independent risk factors for traumatic injury were pulse pressure (HR 1.67, 95% CI 1.21-2.30 for 10mmHg increase; p<0.002), intra-dialytic hypotension (HR 1.60, 95% CI 1.35-1.90 for every one event per 12 HD sessions; p<0.05) and increased high-sensitivity CRP level (HR 1.12, 95% CI 1.08-1.32 for every 10 mg/dL increase; p<0.001).

Conclusions: Traumatic injury is common in chronic HD patients and associated with high complication rate and mortality. Intra-dialytic hypotension with wide pulse pressure, malnutrition, inflammation and Monday seem to be major risk factors for the traumatic injury. The high risk population delineated by our study appears as a priority target for intervention support (including avoidance of intra-dialytic hypotension, nutritional support, control of inflammation and greater attention to weekend care) to reduce the incidence and complications of traumatic injury in chronic HD patients.
PROTEIN-ENERGY WASTING

MP596  RELATIONSHIP BETWEEN TRENDS IN NEUTROPHIL AND LYMPHOCYTE COUNTS AND MORTALITY IN INCIDENT HEMODIALYSIS PATIENTS

Rakesh Malhotra1, Len Useyva2, Jochen Ramann2, Stephan Thijssen2, Nathan Levine1 and Peter Kotanko2

1 UMDNJ, Newark, NJ, United States; 2 RPI, New York, NY, United States

Introduction and Aims: Elevated white blood cell (WBC) count associates with an increased mortality risk in hemodialysis (HD) patients. The prognostic value of trends (increase or decrease) of neutrophil and lymphocyte count is unclear. We aimed to analyze the relationship of changes in neutrophil and lymphocyte count and mortality in HD patients.

Methods: Incident HD patients treated in RRI clinics who had their first in-center treatment between 1/2000 and 12/2010 and survived a minimum of 12 months were included. Slopes of neutrophil and lymphocyte counts (as proportions of WBC) were computed for each patient using linear regression of all available values between months 4 and 12 from the start of treatment. Patients were stratified based on (a) the average rate of change in neutrophil % (declined:<7% points/yr; stable: 7% to 7% points/yr; increased: >7 points/yr) and (b) the average rate of change in lymphocyte % (declined: <5.5% points/yr; stable: 5.5% to 5.5% points/yr; increased: >5.5 points/yr); which resulted in 9 groups. Survival was then analyzed in months 13 to 18 following HD initiation using a Cox hazards model adjusted for age, gender, race, ethnicity, diabetes, access type, BMI, albumin, systolic blood pressure, body temp, nPCR, eKt/V, interdialytic weight gain, urea distribution volume, and slope of neutrophils and lymphocytes.

Results: A total of 2809 patients were studied. The median (IQR) age at the start of HD was 62.9 (51.7-72.7) yrs, 55.1% were male, 44.7% were white and 46.5% of patients were black. The Cox Hazards model showed that simultaneous increases in neutrophil and lymphocyte counts (HR=12.3; 95% CI=1.3-131.5, P=0.03) or decrease of neutrophil and lymphocyte counts (HR=4.7; 95% CI=0.6-38.4, P=0.14) were associated with an increased risk of mortality as compared to reference group (stable neutrophil and stable lymphocyte). Declines in lymphocyte count and increases in neutrophil count were at increased death risk (HR=1.8; 95% CI=1.2-2.6, P=0.003) whereas increase in lymphocyte count with stable or decrease neutrophil count exert a protective effect on survival (HR=0.3; 95% CI=0.07-1.13, P=0.07 & HR=0.8; 95% CI = 0.5-1.3, respectively).

Conclusions: Our results shows survival advantage for patients with stable neutrophil and lymphocyte counts. HD patients with high neutrophil count and low lymphocyte count are associated with increased mortality risk. This relationship may be partially explained by the presence of protein-energy malnutrition and acute inflammation. Further studies are required to understand the roles of neutrophil and lymphocyte counts, their temporal trends and the prognostic significance of these trends.

Introduction and Aims: The central nervous system is in part a regulator of innate immunity via the cholinergic anti-inflammatory pathway (CAP) which transmits signals in the vagus nerve that suppresses proinflammatory cytokine production by an α7 nicotinic acetylcholine receptor (α7nAChR) mechanism. In case of injury, inflammation or infection the effervesent vagus nerve transmits an acetylcholine (ACh)-mediated signal to these receptors present on immune cells and thereby inhibits inflammation in the periphery. Dialysis patients have autonomic dysfunction with increased sympathetic and suppressed parasympathetic activity (vagus nerve function). In CKD patients elevated levels of inflammatory markers such as CRP, TNF, IL-6 are associated with poor outcome. Aim: to investigate deficiencies in CAP in CKD patients with hemodialysis and peritoneal dialysis treatment.

Methods: Twenty patients; twelve patients in chronic HD (7 male, 5 female; age range 26-84), eight patients in chronic PD (5 male, 3 female; age 47-84) and 8 healthy controls (5 male, 3 female; age 31-52) were analyzed for CRP, TNF, IL-1, IL-6 and IL-10 at baseline. Whole blood samples were stimulated ex vivo with two concentrations of LPS (10 and 100 ng/mL) to induce an inflammatory reaction. TNF, IL-1, IL-6 and IL-10 were measured at these concentrations and again in the presence of 45 and 90 umol/L GTS-21, a cholinergic analogue with ACh-like effect.

Results: TNF and CRP were significantly increased at baseline in both HD- and PD patients compared with controls. After LPS stimulation TNF was increased in patients and controls but there was a robust decrease in both groups after addition of GTS-21 (see figure and scale). The IL-1 and IL-6 pattern were similar but the GTS-21 effect was not as pronounced. Interestingly IL-10 increased with GTS-21 in a dose-dependent manner in both patient groups but significantly only in PD patients.

Conclusions: We have shown that immune cells in dialysis patients are able to react in a functional way ex vivo through endotoxin exposure and cholinergic stimulation suggesting a functional CAP. These findings imply that it may be possible to pharmacologically target the α7nAChR control of cytokine release in these patients. This may open new possibilities to treat patients with CKD 5 with underlying inflammation and thereby improve both morbidity and mortality. As there were no differences between HD- and PD-patients the data suggests that it is CKD 5 status that is important rather than dialysis modality for cytokine expression in this model.

MP597  CHOLINERGIC ANTI-INFLAMMATORY PATHWAY ACTIVITY IN HEMO- AND PERITONEAL DIALYSIS PATIENTS

Marialistta Minco1, Giennaro Argentino1, Lucia Grumetto1, Loreana Postiglione1, Bruno Memoli1 and Eleonora Riccio1

1 Nephrology, Federico II, University, Naples, Italy, 2 Pharmaceutical and Toxicological Chemistry, Federico II University, Naples, Italy, 3 Cellular and Molecular Biology and Pathology, Federico II University, Naples, Italy

Introduction and Aims: HFR is a double chamber hemodialfiltration with reinforcement of ultrafiltrate (UF) regenerated through a resin cartridge. The resin component of the cartridge is able to adsorb several medium-high molecular weight solutes and, probably, pro-inflammatory cytokines. Aim of this study was to evaluate if a single HFR session was able to significantly reduce the pro-inflammatory activity of the ultrafiltrate by adsorbing both Interleukin-6 (IL-6) and p-cresol, a protein bound solute.

Methods: We selected 8 inflamed chronic HD patients, which underwent a single 240 minutes HFR session. We studied the change in both IL-6 and p-cresol circulating levels, by comparing pre- and post-HFR serum concentrations. In addition, we collected UF samples, pre- and post-cartridge at the start (after 15 minutes) and at the end (after 225 min), respectively, where we evaluated IL-6 and p-cresol concentrations. Finally, to evaluate the overall change in the inflammatory activity of the UF, we also included Peripheral Blood Mononuclear Cells (PBMC) from a healthy donor. With UF aliquots (20%) collected pre-cartridge (at 15 min) and post-cartridge (at 225 min) of the HFR session and compared both IL-6 gene expression and production under basal condition (no UF addition) with those obtained after these 2 different stimulations.

Results: IL-6 serum levels slightly decreased after the treatment, without significant differences between pre- and post-HFR samples. On the contrary, p-cresol serum levels decreased significantly after the HFR single session (p<0.02). Both IL-6 and p-cresol...
UF concentrations decreased significantly after the passage through the cartridge, either at the start or at the end of HFR session (p<0.05). IL-6 gene expression was significantly higher in PBMC from healthy subjects incubated with 20% UF collected pre-cartridge at 15 min than in both unstimulated (p<0.02) and PBMC cultured with 20% UF collected post-cartridge at 225 min (p<0.01). Similarly, IL-6 production by PBMC from healthy subjects resulted higher with UF pre-cartridge than both with UF post-cartridge (p<0.05) and no UF stimulation (p<0.01).

Conclusions: Our preliminary results suggest that HFR is a promising method that might reduce the burden of pro-inflammatory mediators circulating in HD patients. Moreover, a single session of HFR is also able to significantly reduce p-cresol serum levels. So, a role of HFR in limiting the cardiovascular risk of dialysis patients in is conceivable.

METHYLGLYOXAL (MG) LEVELS ARE MARKEDLY HIGHER IN DIABETIC HEMODIALYSIS (HD) PATIENTS THAN NON-DIABETIC HD PATIENTS, WHICH MAY CONTRIBUTE TO INCREASED MORBIDITY AND MORTALITY IN DIABETICS

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1Medicine/Geriatrics, Mount Sinai School of Medicine, New York, NY, United States

Introduction and Aims: The increased morbidity and mortality in diabetic hemodialysis (HD) patients, compared to other HD patients, may be related to higher OS and other CVD risk factors. MG, a very reactive advanced glycation endproduct (AGE), increases OS and CVD risk factors in early CKD. Sevelamer carbonate (SC) was recently shown to bind diet-induced AGEs in the GI tract, thereby reducing circulating and cellular pro-inflammatory risk factors for CVD, including OS and MG in Type 2 Diabetics with CKD Stage 2-4.

Methods: To determine if MG levels could a contributor to increased mortality in diabetic/HD patients, compared to non-diabetic/HD patients, we examined sera for MG from a randomized, double-blind, placebo-controlled 4-arm study of diabetic/HD and non-diabetic/HD patients, given SC at 2, 4, 4.8 or 7.2 g/d for 3 wks.

Results: Baseline serum MG levels were 50% higher in diabetic/HD than in non-diabetic/HD patients. There was a dose-dependent decrease in MG (p<0.01) in diabetic/HD, but not in non-diabetic/HD patients, in whom MG was reduced only at 7.2g/d. There was a dose-dependent decrease of serum phosphate, plasma total and LDL-cholesterol levels in all HD patients (p<0.01).

Conclusions: Sevelamer rapidly and effectively lowers serum MG levels in diabetic/HD patients. Since AGEs, such as MG, induce OS and MG in Type 2 Diabetics with CKD Stage 2-4, SC may prove effective in reducing morbidity and mortality in diabetic/HD patients. Longer trials are needed to confirm these findings.

SURPRISING GOOD ANTIOXIDANT STATUS IN PATIENTS WITH BALKAN ENDEMIC NEPHROPATHY ON HEMODIALYSIS UNDERGOING VITAMIN C THERAPY-A PILOT STUDY

Mircea Modica1, Mihaiela Margineanu2, Gheorghe Gluhovschi2, Corina Vernic4, Silvia Velicov2, Liviu Petrea2, Emil Buzuc2, Cristina Gluhovschi2, Cristian Balgradean4 and Adriana Kaycsa4
1Nephrology, University of Medicine and Pharmacy Timisoara Romania, Timisoara, Romania, 2Nephrology, Emergency County Clinical Hospital Timisoara Romania, Timisoara, Romania, 3Renamed Dialysis Center, Drobeta Turnu Severin, Romania, 4Medical Informatics and Biostatistics, University of Medicine and Pharmacy Timisoara Romania, Timisoara, Romania, 5Biochemistry University of Medicine and Pharmacy Timisoara Romania Timisoara Romania

Introduction and Aims: End Stage Renal Disease (ESRD) represents a microinflammatory state accompanied by oxidative stress and an imbalance between pro- and antioxidants. Vitamin C is a highly effective antioxidant, acting to lessen oxidative stress. The aim of our study was to assess the Antioxidant Capacity of Water soluble substances (ACW) and the Antioxidant Capacity of Liposoluble substances (ACL) in patients with Balkan Endemic Nephropathy (BEN) on hemodialysis undergoing vitamin C therapy as compared to healthy controls.

Methods: Twenty-one patients with BEN on hemodialysis (HD), mean age: 63.33±5.42 years, 6 M and 5 F, were enrolled into the study. Mean duration since BEN diagnosis was: 4.92±3.4 years. Eleven apparently healthy subjects, mean age: 63.73±5.21 years, 6 M and 5 F, served as controls. The photochemiluminescence assay was used to measure the antioxidant activity of plasma samples. The results are presented in equivalent concentration units of vitamin C for water soluble antioxidants and in equivalent concentration units of Trolox (synthetic vitamin E) for lipid soluble antioxidants. Both concentrations are expressed in μmol/L. Statistical analysis (non-parametric Wilcoxon test) was performed using NCSS.

Results: Mean vitamin C concentrations (μmol/L) were significantly lower in HD patients than in controls: 198.05±196.63 μmols/l; p=0.01, whereas the Antioxidant Capacity of Liposoluble substances (ACL) in patients with BEN was 33.9±22.99 μmol/L, non-significantly different as compared to controls: 27.38±6.21 μmol/L p=0.02.

Conclusions: We conclude that vitamin C therapy in patients with BEN on HD...
significantly increases the Antioxidant Capacity of Water soluble substances (ACW) as compared to controls and could be used to counter oxidative stress in patients with ESRD.

**Introduction and Aims:** Patients with chronic kidney disease present selenium (Se) plasma deficiency. Se is an essential element with important biological functions and its best known biological role is attributed to its presence in antioxidant enzyme, glutathione peroxidase (GSH-Px). The Se content of foods depends on soil and some authors have suggested that Amazon soil has high concentrations of Se when compared to other regions in Brazil. The objective of this work was to compare the Se status of patients in hemodialysis from the Amazon with the Southeast region in Brazil.

**Methods:** Thirty-eight patients from Southeast region (22 men and 16 women, 15% were diabetic, 53.5 ± 26.4 yrs) were compared to forty patients from de Amazon region (28 men and 12 women, 22.5 % diabetic, 63.5 ± 11.9 yrs). Se in plasma was determined through atomic absorption spectrophotometry with hydride generation (HITACHI®, Z 5080). Statistical analyses were performed using SPSS 17.0.

**Results:** The Se plasma levels of the HD patients from Southeast region were significantly lower (17.5 ± 11.9 μg/L) when compared to the patients from Amazon region (37 ± 15.8 μg/L) (p < 0.001). However, both patient groups presented Se plasma levels (normal values - 60-120 μg/L).

**Conclusions:** We concluded that patients from Amazon region present higher plasma Se levels when compared to the patients from Southeast of Brazil and, this difference can be explained by high concentrations of Se in the soil in Amazon region. However, independently of the region, both groups present Se deficiency. Thus, more attention should be pay to the Se status in HD patients.

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**UNINTENTIONAL BODY WEIGHT CHANGES AND THE RISK OF HOSPITALIZATION AND DEATH IN EUROPEAN HAEMODIALYSIS PATIENTS: RESULTS FROM COSMOS**

Juan Jesús Carrero1, Ivan Cabezas-Rodríguez1,2, Carmine Zoccali3,4, Abdul Qureshi1, Markus Ketteler1, José Gorri2, Boleslav Rutkovský3, Vladimir Teplian2, Reinhard Kramar2, Draško Pavlović2, David Goldsmith4, Mila Benedikt1, José Fernandez-Martín1,2, Jorge Cañantia-Andres1,2 and On behalf of COSMOS²

**Introduction and Aims:** A high body mass index (BMI) is associated with lower mortality in CKD5 patients. Short-term weight gains and losses have been related to reduced and increased mortality risk, respectively. It is unknown if it associates with the rate of hospitalizations. The implications of weight gain/loss may, however, be different for obese individuals than for non-obese counterparts.

**Methods:** COSMOS is an observational study including 6797 European hemodialysis patients, with prospective data collection every 6 months for 3 years. Time-dependent Cox proportional hazard regressions assessed the impact of BMI and weight changes on mortality. The risk of hospitalizations in 1-year incidence rate ratios (IRR) was estimated by Poisson regressions. Analyses were performed after patient stratification according to their starting BMI.

**Results:** A total of 1643 deaths and and 9731 hospitalizations occurred in 6296 patients with complete data. At study entry, 42% of patients had normal BMI (BMI 20-25 kg/m²), 11% were underweight, 31% overweight, and 16% obese (≥30 kg/m²). Whereas underweight patients were at increased mortality risk (2.08 [1.75-2.48]) overweight (0.70 [0.59-0.83]) and obese patients (0.61 [0.48-0.78]) showed opposite trends. Similar results were observed for hospitalization rates. Weight loss or gain exhibited an association with higher rates of mortality or survival, respectively. After stratification by BMI categories, a null impact on mortality prediction was noted for obese patients losing (1.28 [0.76-2.16]) or gaining weight (0.98 [0.58-1.66]). In the remaining BMI categories, especially in underweight patients, weight losses and gains greatly affected the outcome. Across BMI strata, weight gains did not associate with the risk of hospitalization. Weight losses associated with a higher hospitalization risk in all BMI categories, especially in underweight patients (IRR 2.85 [2.33-3.47]).

**Conclusions:** Rapid unintentional weight changes impacted both, hospitalization and mortality risk. Weight losses have a strong negative effect on the risk of hospitalization, especially in underweight patients. Weight changes have important implications in the mortality risk of non-obese hemodialysis patients, in contrast with the lack of...
association in obese individuals gaining or losing weight. Study supported by Amgen and Fundación Renal Igino Alvarez de Toledo.

**MP606**

**CITRATE-BASED DIALYSIS BUFFERS ARE MORE BIOCOMPATIBLE IN COMPARE TO STANDARD BICARBONATE BUFFERS AND COULD PREVENT THE PROGRESSION OF DIALYSIS VASCULOPATHY**

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**Introduction and Aims:** Bioincompatibility plays a key role in the pathogenesis of dialysis related vascularopathy responsible for the high mortality in CKD hemodialyzed patients. Beside membranes, acetate-based dialysis buffers seem to be one of the main actors in the pathogenesis of vasculopathy. Acetate, even in the low concentrations present in bicarbonate buffer, by stimulating inducible nitric oxide synthetase, alter the intracellular redox state responsible for endothelial cells biological activity resulting in apoptosis and inflammation related to activation of stress sensitive pathways, including NF-kB and others. For these reason new available dialysis buffers have been proposed, among those the citrate based dialysis buffers. Citrate by itself is provided with antioxidant as well as antioxidants properties. Aim of this study was to compare the effects of acetate- or citrate-based dialysis buffers on some biologic parameters, such as NF-kB activation and total antioxidant capacity (TAC), in human endothelial cells in culture.

**Methods:** Human endothelial cells were incubated using transwell devices, with the following dialysis buffers: acetate 38 mmol/Lt; acetate 4 mmol/Lt, bicarbonate 34+ acetate 4 mmol/Lt/citrate 1 mmol/Lt, acetate 38 mmol/Lt/citrate 1 mmol/Lt, acetate 4 mmol/Lt/citrate 1 mmol/Lt/bicarbonate 34+ acetate 4 mmol/Lt/citrate 1 mmol/Lt. LPS 10 μmol/ml was used as positive control. Cells were incubated at 37°C in humidified athmosphere for 1 and 4 hours. TAC levels were measured in the supernatants. Cell lysates were used for studying NF-kB nuclear translocation using western blot analysis.

**Results:** Results are expressed in the table as fold increase (FI) or decrease (FD) vs values obtained in basal unconditioned cells after 1 hour incubation.Supersimply results were obtained after 4 hours conditioning of human endothelial cells with different dialysis buffers. ° p<0.01 vs basal condition, & p<0.05 acetate + citrate vs acetate alone.

**Conclusions:** Our results allow us to conclude that citrate-based dialysis buffers are more bioincompatible than acetate-based ones and bicarbonate dialysis buffers containing low concentrations of acetate. Citrate per se exerts an antioxidative activity. The new citrate-based dialysis buffers is potentially useful to limit the bioincompatible reactions involved into the pathogenesis of long-term dialysis vasculopathy.

**MP607**

**ONE YEAR MORTALITY OF HIGH BMI PATIENTS ON HEMODIALYSIS CORRELATES WITH DIFFERENT FACTORS THAN ONE YEAR MORTALITY IN NORMAL AND LOWER BMI ONES**

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**Introduction and Aims:** It is known that survival on dialysis is better in patients with higher BMI. Less is known about the causes of this improved survival. The paper addresses this issue.

**Methods:** 600 patients(mean age 54.5+/–13.5 years, 332 men,268 women) from 7 HD centers from Romania have been followed up for 1 year. Patients were on hemodialysis, for an average of 4+/–3.7 years. Data concerning dialysis quality, anemia, mineral and bone disorders, serum albumin, CRP, BML, hepatitis, have been analyzed. Cardiovascular disease, diabetes mellitus, DM, therapy and one year mortality rate have been analysed. Data have been processed using SPSS 16 data analysis system.

**Results:** DM was present in 15.68% of the cases and the mean BMI was 25.5kg/m². According to BMI the patients have been divided into 3 groups:1- underweight (BMI<18.5 kg/m²),N=48/8 % of the cases),2-normal(BMI 18.5 - 25 kg/m²),N=283 (44.9%) and 3- overweight and obese(BMI > 25 kg/m²),N=269(44.8%). When comparing underweight patients with the normal group(1 with 2)we observed that in group 1 were significantly younger (47.5 vs. 52.8 years - p<0.023), though mean time on dialysis therapy did not differ. Hemodialysis adequacy was similar in both groups. Mean hemoglobin and ferritin levels did not significantly differ but mean TSAT value was significantly lower in group 1 (25.5% vs. 32.3 %p<0.047).The mean Ca, PO4, ITPH and alkaline phosphatase values of underweight HD patients did not differ from the normal ones, but the mean 25OH D levels were significantly lower (17.9 vs. 23.1 ±0.18).The one year mortality rate of group 1 was significantly higher than the one year mortality in group 2 (20.8% vs. 14.4%) and was correlated only with the prevalence of Hepatitis B virus infection. Patients in group 3(overweight) were older (56.5 ±5.8 years p<0.0008), had lower mean sKt/V (1.33 vs. 1.47 ±0.00001), lower mean TSAT values (28.6 vs. 32.3% p<0.045). Higher mean serum albumin levels (4.34 vs. 4.18 ±0.018) when compared to group 2. One year mortality rate was significantly lower when compared with group 2 (8.17 vs. 14.4%) and mortality was positively correlated with age (p<0.023), alkaline phosphatase levels (p<0.001), coronary artery disease (p=0.024), DM (p<0.030) and negatively with blood flow (Qb) (p<0.03). Conclusion: Our study shows that one-year mortality is influenced by other factors in high BMI patients as compared to lower BMI ones, but even if obese patients have a better outcome, cardiovascular disease and diabetes are still significantly correlated with mortality.

**MP608**

**ASSOCIATION OF CHANGES IN LEAN AND FAT TISSUE MASS AND PATIENT CLINICAL AND LABORATORY PARAMETERS**

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**Introduction and Aims:** Protein-energy malnutrition has been shown to be a major risk factor for hemodialysis (HD) patient mortality. We aim to evaluate associations of lean and fat tissue mass and their changes with clinical / laboratory parameters.

**Methods:** The MONitoring Dialysis Outcomes (MONDO) consortium data (Usvyat, Blood Purification 2013) from FMC clinics in Europe were used for this analysis. Only patients in whom >=2 routine measurements of Lean/Fat Tissue Mass using Fresenius Medical Care BCM were performed within 365 days. Lean Tissue Index (LTI) was computed as ratio of Lean Tissue Mass to body surface area and Fat Tissue Index (FTI) was computed as a ratio of Fat Tissue Mass to body surface area. Changes in all variables were computed over 365 days using simple linear regression. Correlations were assessed using Spearman’s correlation coefficient.

**Results:** We studied 527 HD patients. The median (IQR) LTI and FTM at baseline were 34.9 kg (28.8-42.4) and 25.6 kg (18.7-33.3). Starting FTI was positively and significantly associated with age (p<0.018). The group 1 was significantly higher than the group 2 and 3. The one year mortality was significantly higher in group 1 (20.8% vs. 14.4%) and was correlated only with the prevalence of Hepatitis B virus infection. Patients in group 3 were older (p<0.023), had lower mean sKt/V (1.33 vs. 1.47 ±0.00001), lower mean TSAT values (28.6 vs. 32.3% p<0.045). Higher mean serum albumin levels (4.34 vs. 4.18 ±0.018) when compared to group 2. One year mortality rate was significantly lower when compared with group 2 (8.17 vs. 14.4%) and mortality was positively correlated with age (p<0.023), alkaline phosphatase levels (p<0.001), coronary artery disease (p=0.024), DM (p<0.030) and negatively with blood flow (Qb) (p<0.03).

**Conclusions:** Our study shows that one-year mortality is influenced by other factors in high BMI patients as compared to lower BMI ones, but even if obese patients have a better outcome, cardiovascular disease and diabetes are still significantly correlated with mortality.
and pre-dialysis systolic blood pressure. LTI was negatively and significantly correlated with age, CRP, nPCR, cholesterol, and LDL cholesterol (figure 1a). Increases in LTI were associated with increases in cholesterol and triglycerides. Increases in LTI were associated with declines in triglycerides (figure 1b).

Conclusions: Baseline as well as changes in fat and lean tissue mass are associated with changes in multiple other clinical and laboratory parameters. Multivariate models are needed to understand factors most strongly associated with body composition; survival analysis to understand whether fat and tissue mass are independently associated with survival are also needed.

**MP609**

PROCALCITONIN AS AN EARLY PREDICTOR OF ACUTE INFECTION IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Hemodialysis patients have a greater risk of infection than general population. This present study evaluates serum procalcitonin levels as an early predictor of infection in patients on hemodialysis.

Methods: A historical cohorts study was performed of 211 prevalent hemodialysis patients (median age 73 years (range 60-80), 58% males, 32% diabetes mellitus) covering the period 2005-2012. Regarding vascular access, 55% of the patients had an autologous fistulae, 31% a polytetrafluoroethylene graft and 14% a permanent catheter. All patients received 4 hour in three session per week of high-flux hemodialysis (25.6% online hemodiafiltration). Serum samples were thawed and patients were followed-up for 25.5 months. Demographic and laboratory data (including inflammatory markers such as C-reactive protein [CRP], procalcitonin and albumin) were recorded at baseline. During follow-up, all infections were documented and analyzed.

Results: During follow-up, 112 patients (53.3%) suffered acute infection (25% vascular access infection, 25% respiratory, 22% skin, 12% gastrointestinal, 6% urinary, 8% others). CRP showed a positive correlation with procalcitonin (ρ = 0.482, p < 0.0001) and a negative correlation with serum albumin (ρ = -0.256, p = 0.002). No association was found between procalcitonin and albumin. Procalcitonin was found to be the only independent predictive factor for infection at the first month in the uni and multivariate analysis, after adjustment for the rest of the inflammatory parameters, sex and age. The receiver operating characteristic (ROC) values were 0.636 (95% CI 0.469-0.802, p = 0.126) and 0.506 (95% CI 0.315-0.696, p = 0.946) for procalcitonin and CRP, respectively. However, CRP was the best predictor of infection over global follow-up (p = 0.003), after adjusting for all the studied factors. Linear regression analysis adjusted for a history of heart disease, renal graft carrier, gender, age and cardiovascular risk factors, identified time on dialysis (B 0.007 [0.002-0.012] p = 0.007) and vascular access other than autologous fistulae (B 0.134 [0.154-1.914] p = 0.22) as the only independent predictors of CRP elevation.

Conclusions: Procalcitonin is an early predictor of infection in the first 30 days in hemodialysis patients. Periodically monitored procalcitonin levels in patients at high risk of infection can give us the possibility of detecting subclinical infections, including asymptomatic vascular access infections, in order to initiate an early treatment.

**MP610**

OVERHYDRATION BY BIOIMPEDANCE SPECTROSPECTRO (BCM) IS RELATED TO INFLAMMATION AND MALNUTRITION

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Introduction and Aims: Fluid overload is an important cardiovascular risk factor by itself and its effect on blood pressure. Furthermore, fluid overload involves an inflammatory condition and also influences on the morbimortality of patients on haemodialysis. Fluid overload can be easily measured by BCM (Body Composition Monitor, Fresenius Medical Care) helping us to control the hydration status of our patients. Demonstrate the association between hydration/nutrition parameters by BCM with clinical and analytical indicators related to morbimortality in dialysis.

Methods: We included 1,316 patients with monthly BCM. Excluded hospitalized during the monitoring period and amputations on unpolar pacemakers. We followed our patients during 3 months after their first BCM and we recorded: renal disease etiology, comorbidities, age, hemodialysis vintage, blood pressure; BCM parameters; analysis and treatment. The analysis was performed with the SPSS computer program, version 21; p<0.05 was considered to indicate statistically significant. We set two groups based on their relative dehydration: greater than 15% versus lower or equal to 15% (table 1). There were 921 patients (69.08%) with a ROH lower or equal to 15% in front to 395 patients (30.92%) with ROH higher 15%.

Results: Patients with a baseline ROH higher than 15% showed higher CRP, ERI and consumption of ESA, lower haemoglobin level; higher systolic blood pressure and higher consumption of antihypertensives. As well as lower seric albumin, and lean/fat tissue index (p<0.05 for all). Groups are not really different looking at age, ferritin and ISAT (p>0.05). It seems that ferritin does not follow a clear pattern related to overhydration; it probably depends on the presence of confounding factors.

Conclusions: Overhydration is correlated with an increase of ERI and CRP, likewise lower albumin, and lean and fat tissue index. Moreover, there is a clear connection between higher consumption of ESA together with hyperhydration. Hypervolemia described as relative overhydration higher 15% is related to a higher blood pressure and a higher consumption of hypotensive drugs. The correlation between parameters of biopendence spectroscopy and markers of inflammation and malnutrition indicates that overhydration is the optimal strategy for reducing cardiovascular events in haemodialysis patients.
EICOSAPENTAENOIC ACID DECREASES ADVANCED GLYcation END PRODUCTS RESULTing IN THE PREVENTION OF AUTONomous DYsCOnomy IN JAPANESE NON-DiABETIC HAEmodialysis PATIENTS

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Introduction and Aims: Advanced glycation end products (AGEs) are well known to accumulate in the autonomic system inducing its dysfunction in diabetic haemodialysis (HD) patients. Serum levels of AGEs were reported to elevate even in non-diabetic HD patients. On the other hand, many reports have documented beneficial effects of dietary intake of eicosapentaenoic acid (EPA), a major omega-3 fatty acid, on improving the autonomic dysfunction. The aim of the present study was to investigate the effects of EPA on AGEs and autonomic dysfunction in Japanese non-diabetic HD patients.

Methods: We recruited 41 stable Japanese non-diabetic HD patients (18 men and 23 women, 57.5±14.3 years) who had taken ordinary diet for chronic renal failure. Patients with coronary heart disease, malignancy or significant malnutrition, or those with regularly taking a fish oil supplement were excluded. We measured serum levels of AGE expressed as weight percentage of total lipids (%), pentosidine as a parameter of AGEs, glycoalbumin (GA) and glycated hemoglobin (HbA1c) after overnight fasting. The patients were divided into two groups based on the median of serum EPA: high EPA and low EPA groups.

Results: Serum levels of AGE was significantly lower, and HF was significantly higher in the high EPA group than in the low EPA group (P<0.05, respectively). There were no significant correlations between GA and HbA1c after overnight fasting. Our data indicate that the modern means of RRT eliminate amino acids to an extent that has not been met by our nutritional support standards. Especially the removal of glutamine, important for immune function and cell regeneration might have detrimental effects on the recovery of critically ill patients.

Conclusions: No data are available that indicate the modern means of RRT eliminate amino acids to an extent that has not been met by our nutritional support standards. Especially the removal of glutamine is important for immune function and cell regeneration which might have detrimental effects on the recovery of critically ill patients.

EFFECTS OF THE INTRADIALYTIC PARENTERAL NUTRITION ON THE AMINOACID POOL: A KINETIC STUDY

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Introduction and Aims: Malnutrition in dialysis patients could be offset by means of intradialytic parenteral nutrition (IDPN), provided it proves itself to be capable of improving the aminoacid (AA) pool, notwithstanding the possibility of dialysis clearance.

Methods: We conducted a short-term kinetic study in 10 malnourished patients, on thrice-weekly low-flux HD, 240 mins/session (Bologna Malpighi and Trento Hospitals, Italy). After an HD session without IDPN (baseline), the patients received an IDPN solution with 20 AAs (all-in-one bag, Nutrispecialid, B Braun- Aventum, Italy: 625 ml, AA 35.9 gr, 740 kcal) over a one-month period. After HD at baseline, after 2 and 4 weeks, pre- and post-HD plasma and dialysate AA concentrations were measured. Dialysate samples were collected with the spilling technique. The AA mass balance was then calculated.

Results: Even with a low-flux dialyzer (alpha-polysulphone) and with no IDPN infusion, an AA loss in the dialysate did occur, increasing with the IDPN infusion (3.9±0.3 g/session with no IDPN versus 7.7±0.5 g with IDPN, p=0.00043), up to almost 26% of the infused AA mass. Nevertheless, the AA mass balance proved positive to the patients (+21.6±6.95 g of AA/session). After a one-month period with IDPN, the pre-dialysis concentration of all the infused AA had indeed increased as compared with the baseline, with a mean overall increase of 36.8%. We did not report any severe glucose imbalances.

Conclusions: Our data are available that indicate the modern means of RRT eliminate amino acids to an extent that has not been met by our nutritional support standards. Especially the removal of glutamine is important for immune function and cell regeneration which might have detrimental effects on the recovery of critically ill patients.

LONG TERM MAINTENANCE OF ORAL NUTRITIONAL SUPPLEMENTATION IMPROVES NUTRITIONAL PARAMETERS AND DECREASES MORTALITY IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Protein-energy wasting (PEW) is common in patients with chronic kidney disease (CKD) and is one of the major factors adversely affecting their prognosis. Clinical guidelines and reviews support the use of enteral nutrition in patients with renal failure. The aim of this study was to evaluate short (6 months) and long term (18 months) effects of ONS in maintenance hemodialysis (MHD) patients with malnutrition.

Methods: Patients with serum albumin concentration <4 g/dl and SGA B group were included in the study. Patients who accepted to use the ONS (Nutrena®, Abbott Nutrition) were defined as the study group the individuals who refused to use the ONS served as the control group. All patients’ clinical, laboratory data, anthropometric measurements (DW, body mass index (BMI), intradialytic weight gain (IDWG), the triceps skin-fold thickness (TSFT)), were analysed. For bioelectrical analysis (BIA), a Body Composition Analyzer (Tanita BC-420MA) was used. All patients were followed up at least 18 months and according to the duration of using ONS divided in three groups: Group 1 (n=29) patients who refused using ONS for 18 months, patients in Group 2 (n: 11) used ONS for 6 months then gave up and Group 3 (n:18) patients used ONS for at least one year.

Results: According to initial assessment, there were no significant between three groups in demographic and clinical characteristics. In 6 months evaluation, albumin levels, BW, BMI, TSFT and BIA (fat free mass and muscle mass) values significantly increased in group 2 and 3 and significantly declined in Group 1 (p<0.001 for all). The 6, months serum albumin level levels were 3.50 ± 0.31, 3.67 ± 0.22, and 3.71 ± 0.24 g/dl (p < 0.04 in group 1.2 and 3 respectively). After cessation of nutritional support there was a significant deterioration of albumin levels in group 2 but antropometric measurements remained stable while albumin levels remained as the highest in group 3 (p<0.01). Mortality rates were 31% in Group 1, 54% in Group 2 and 0% in Group 3 (p<0.001). A logistic regression analysis revealed that albumin levels <3.7 g/dl was main predictor of mortality in 18 months of follow up period (p<0.012).

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Conclusions: Our findings indicate that consuming ONS improves albumin and nutritional measures in MHD patients. We also suggest regular, constant and long-term use of ONS to decrease high mortality risk in malnourished patients.

Introduction and Aims: Pentosidine (PEN) is one of advanced glycation end products (AGEs) and widely known as a marker of oxidative stress (Kidney Int. 1998). PEN levels are high in patients with renal dysfunction including diabetic nephropathy. Especially in hemodialysis patients PEN is also reported to be useful in predicting cardiac disease and carpal tunnel syndrome, therefore the evaluation of PEN is considered beneficial also in this population. No report exists with regard to the relationship between anemia and PEN. In this study, we studied the relationship among anemia, PEN, and mortality in hemodialysis patients.

Methods: We conducted an observational study of 100 patients, who underwent hemodialysis at our clinic in December, 2011. Routine laboratory data and plasma PEN levels were obtained. In addition, we calculated the erythropoiesis-stimulating agent (ESA) index (ESAI) to evaluate ESA resistance. We conducted a univariate analysis with ESAI as a dependent variable. Thereafter, we performed multivariate analysis to examine the independent association between PEN and ESAI. After dividing patients into 2 groups by the median value of PEN or ESAI, the survival rate was compared between the groups by the Log-rank method. Finally, hazard ratio was estimated by cox proportional hazards model.

Results: The median value of PEN was 0.30 μg/ml [range: 0.090-0.893], obviously higher than that in healthy subjects. PEN was significantly associated with higher ESAI (r=0.327), higher ferritin, lower Hb and lower Kt/V, while having no significant association with age, hemodialysis vintage, Alb, or CRP. In addition, in a multivariate analysis, PEN was found to be a positive determinant of ESAI independent of factors reported to be associated with ESAI resistance. Eleven patients out of 100 died during the observation period of 1 year. The life time was significantly longer in the low PEN group (p<0.05 log-rank), with a hazard ratio of 4.39 (95% CI 1.10-29.09). The results were identical when using ESAI as a stratifying factor (figure).

Conclusions: Given that PEN is a marker of oxidative stress, our data suggest that oxidative stress plays some role in the pathogenesis of ESA resistance. Moreover, PEN is a equivalent value as a risk stratifier to ESAI in predicting mortality in hemodialysis patients.

Introduction and Aims: Recent studies are continuously revealing oxidative stress related cellular responses such as gene expressions or signal transductions, while interactions between reactive oxygen or nitrogen species themselves are less clear, because of their high reactivity. In the current study, we investigated multiple free radical dynamics of hemodialysis (HD) patients using a novel electron paramagnetic resonance (EPR) technique.

Methods: Multiple free radical dynamics, namely hydroxyl radical, superoxide radical, alkoxyl radical, alkyperoxyl radical, alkyl radical, and singlet oxygen, were investigated measuring the scavenging activities of these reactive oxygen species (ROS) using a newly developed EPR spin-trapping reagent 5-(2,2-dimethyl-1,3-propoxycyclophosphoryl)-5-methyl-1-pyrroline N-oxide (CYPMO). Nitric oxide (NO) metabolites and inflammatory cytokines were also measured. These methods were applied to a cohort of HD patients (n=15) and a healthy control subjects (n=16).

Results: Superoxide scavenging activities of HD patients significantly increased compared to that of the healthy controls (18.2±2.9 and 12.5±3.2 SOD equivalent Unit/ mL, mean±SE, respectively), whereas no significant differences were observed among the other ROS. In the healthy control group, superoxide scavenging activity showed strong positive correlation with serum NOX concentration (r=0.814) and moderate positive correlation with those of alkoxyl and hydroxyl radicals (r=0.690 and 0.626, respectively), while these relations were disappeared in the HD group. In HD patients, scavenging activity of hydroxyl radical were negatively correlated with that of singlet oxygen, whereas this relationship was not observed in the control group. No correlations between measured ROS and TNF-α, IL-6, adiponectin and hs-CRP were observed.

Conclusions: These results indicate that NO act as a compartment of radical scavenging system in healthy subjects while this role is eliminated in HD patients. Despite the increased superoxide scavenging activity, ROS/NO balance deteriorates in HD patients. Also, radical chain reaction systems including singlet oxygen, hydroxyl and alkoxyl radical, are altered in HD patients.
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**MP618**

**ORAL ESSENTIAL AMINO ACID SUPPLEMENTATION IN MAINTENANCE HEMODIALYSIS PATIENTS**

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**Introduction and Aims:** The nutritional status in maintenance hemodialysis (MHD) patients is a predictor of prognosis. Malnutrition is associated with cardiac co-morbidity, inflammation and poor survival in this population. Serum albumin is a well-known marker of nutrition in MHD patients. The aim of this study was to evaluate the six months’ nutritional effect of essential amino acid (EAA) supplementation on MHD patients.

**Methods:** Patients with serum albumin concentration <4 g/dl were included in the study. Patients whose serum albumin level <3.5 g/dl were defined as the study group (EAA Group) and was given EAA supplementation for 6 months. Control group (CON group) did not take any EAA supplementation. All patients’ clinical, laboratory data, biochemical impedance (BIE) measurements (BIA) were analysed. For biochemical impedance (BIE), a Body Composition Analyzer (Tanita BC-420MA) was used. Short Form Health Survey (SF-36), was administered to all patients at the initiation and at the 6 months’ evaluation.

**Results:** Eighty two eligible patients participated in the study, 36 in the EAA group and 46 in the CON group. No significant difference was found between two groups in demographical and clinical characteristics. As shown in [Figure 1], although at baseline, serum albumin level of the EAA group was significantly lower than the CON group (p<0.001), at the end of the study, EAA group’s serum albumin level was significantly increased; whereas in the control group serum albumin level did not differ from baseline values (p > 0.680). At baseline and the end of the study, BIE parameters and SF-36 score were similar between two groups.

**Conclusions:** This study shows that oral EAA supplementation may represent a valid alternative to achieve the target albumin levels and may also allow for an improvement in nutritional status for MHD patients.

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**MP619**

**THE ASSOCIATION BETWEEN INFLAMATION, OXIDATIVE STRESS AND CADMIUM LEVELS IN DIALYSIS PATIENTS**

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**Introduction and Aims:** It is speculated that serum cadmium levels are increased in hemodialysis (HD) population due to the exposure of large volumes of water which has been linked to inflammation, malnutrition and endothelial dysfunction. The aim of this study was to investigate the association between serum cadmium levels, inflammation and oxidative stress in end stage renal disease patients under two types of dialysis including peritoneal dialysis and hemodialysis.

**Methods:** Thirty two HD, 30 peritoneal dialysis (PD) and 23 healthy controls were included. Patients who have diabetes mellitus, malignancy, active inflammatory disease or any infection and smokers were excluded. Serum levels of cadmium, IL-6, hs-CRP, MDA and AOPP were measured in all subjects.

**Results:** No difference was found between three groups regarding to age and body mass index. Serum HDL cholesterol levels were significantly lower in both dialysis population compared to the healthy controls, whereas no difference was observed about total and LDL cholesterol levels between groups. Serum cadmium concentrations were similar in all three groups. The serum levels of IL-6, hs-CRP and AOPP were significantly higher in dialysis population compared to the controls (p<0.001). However, no significant difference was found between PD and HD groups. Serum MDA level was significantly higher in PD patients compared to the HD and control subjects (p<0.001). Although, HD patients tend to have higher MDA levels than control group, it did not reach statistically significance. In each dialysis population spearman analyses showed no significant correlation between cadmium levels with inflammatory and oxidative stress parameters.

**Conclusions:** This is the first study which analyse the association between serum cadmium levels, inflammation and oxidative stress in dialysis population by including both HD and PD modalities. Our results suggest that cadmium concentration has no trigger effect on inflammation and oxidative stress in both dialysis population.

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**MP620**

**NUTRITIONAL EVALUATION OF ONLINE HDF PATIENTS: RELATIONSHIP BETWEEN CLINICAL, ANTHROPOMETRIC, BIOCHEMICAL AND BODY COMPOSITION IN IDENTIFYING PROTEIN ENERGY LOSS (PEW) AND PREFERENTIAL NUTRITIONAL INTERVENTION**

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**Introduction and Aims:** There is no simple and objective method available for assessing nutritional status and identifying malnutrition in chronic kidney disease. Objective: Combination of some of the currently tools (clinical, biochemical, anthropometric and body composition monitoring by bioelectrical impedance (BCM), malnutrition-inflammation score (MIS)) to assess the nutritional status of our patients in online hemodiafiltration (HDF), determine the prevalence of preferential protein energy waste (PEW) and identify those patients at most risk of malnutrition and requiring preferential nutritional intervention.

**Methods:** Cross-sectional study of 91 patients (86 men) in on line HDF for 43 ± 47 months and 60 ± 14 years old. We determined nutritional status by clinical evaluation anthropometric (biceps and triceps skinfold thickness, abdominal perimeter, MCA (muscle circumference arm), blood tests (Albumin Prealbumin Transferin, Total Cholesterol, Total Protein, Creatinine, PCR), and BCM Fresenius®. Patients were assessed with the MIS score. We used the definition of PEW with BCM, based on BCM FTI < p10, and we performed a cross sectional study of 91 patients in online HDF.

**Results:** Average Charlson index was 5 ± 2, Kt/Ve 2.94 ± 0.82, Diabetes Mellitus 36.5%. The average dry weight was 65.9 ± 12.9 kg with an estimated BMI of 24 ± 4.1, being 20.2 ± 2.5 (OR = 0.68 and p = 0.001) in the PEW group. 73.3% of the patients with albumin < 37 g/l (OR = 7.7 and p = 0.001) and 93.3% with prealbumin < 30 mg/dl (OR = 18.24 and p = 0.006) had a PEW. Mean MCA in the PEW group 19.7 ± 2.2 cm (OR = 0.41 and p <0.001). Regarding BCM FTI < p10 was significantly lower in the PEW group (OR = 0.8 and p = 0.003), while no differences were detected in LTI difference nor phase angle. Patients classified with/without PEW and compared with a patient classification in adequate or inadequate nutritional status according to BCM and with data obtained with the MIS score.

**Conclusions:** We observed that

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**NUTRITIONAL INTERVENTION PROTEIN ENERGY LOSS (PEW) AND PREFERENTIAL NUTRITIONAL INTERVENTION**

Average Charlson index was 5 ± 2, Kt/Ve 2.94 ± 0.82, Diabetes Mellitus 36.5%. The average dry weight was 65.9 ± 12.9 kg with an estimated BMI of 24 ± 4.1, being 20.2 ± 2.5 (OR = 0.68 and p = 0.001) in the PEW group. 73.3% of the patients with albumin < 37 g/l (OR = 7.7 and p = 0.001) and 93.3% with prealbumin < 30 mg/dl (OR = 18.24 and p = 0.006) had a PEW. Mean MCA in the PEW group 19.7 ± 2.2 cm (OR = 0.41 and p <0.001). Regarding BCM FTI < p10 was significantly lower in the PEW group (OR = 0.8 and p = 0.003), while no differences were detected in LTI difference nor phase angle. Patients classified with/without PEW and compared with a patient classification in adequate or inadequate nutritional status according to BCM and with data obtained with the MIS score.
combining these three elements, 12.1% of our patients requiring preferential nutritional intervention.

Conclusions: Currently, there exists no simple and objective method for the determination of nutritional status and for the assessment of nutritional risk. Combining BCM, nutrition scores and biochemical, and anthropometric parameters to calculate PEW allows a global nutritional assessment to prioritize nutritional intervention.

ONODERA’S PROGNOSTIC NUTRITIONAL INDEX AS A RISK FACTOR FOR MORTALITY IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Nutritional risk is one of the strongest predictors of morbidity and mortality in maintenance HD patients. However, a standard method for the assessment of the nutritional status in HD patients does not exist. The Onodera’s Prognostic Nutritional Index (OPNI) is composed of serum albumin and total lymphocyte count within the equation. A simpler tool may involve common measures and can be applied rapidly in a large number of patients. Validation of OPNI has been applied for patients with end-stage liver disease, active tuberculosis, and gastrointestinal malignancy.

Methods: We examined the OPNI scores of 140 maintenance hemodialysis patients (59.8 ± 12.9 years, 64 males and 76 females) and conducted follow-up of these patients for 120 months. The OPNI will be calculated based on the serum albumin and total lymphocyte count, using the following equation: OPNI = 10 × serum albumin (g/dL) + 0.005 × total lymphocyte count (/mL). Predictors of all-cause death were examined using life table and Cox proportional analyses.

Results: The average OPNI was 43.8 ± 6.5, and was negatively correlated with age. 18 patients died during the 120-month follow-up period. OPNI presented normal distribution. Life table analysis revealed that patients with an OPNI < 40 (n = 31) had a significantly lower survival rate, compared to those with OPNI ≥ 40 (n = 109) (Wilcoxon test, P = 0.044). Multivariate Cox proportional hazards analyses demonstrated that OPNI was a significant predictor of mortality [hazard ratio (HR) 6.491, 95% confidence interval (CI) 1.985–21.233, P = 0.002], after adjustment for age, gender, presence of diabetes and body weight.

Conclusions: These results suggest that OPNI is a significant predictor of mortality in Korean hemodialysis patients. The simple OPNI method is a clinically useful marker for the assessment of nutritional status in Korean hemodialysis patients.

DIFFERENCES IN ALBUMIN LEVELS AMONG DIFFERENT ETHNICITIES

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Introduction and Aims: Malnutrition is common in patients with end stage renal failure undergoing dialysis and often goes unobserved. It is well established that a low serum albumin can be a marker of malnutrition in these patients and is associated with poorer outcomes, particularly excess hospitalization and mortality. The aim of this study is to evaluate difference in albumin levels between different ethnicities resident in 2 multiethnic countries.

Methods: As part of the monthly routine data were collected from patients on HD on age, gender, nationality, presence or absence of diabetes, dialysis dose and serum albumin (according to BCP in UK, BCG in UAE) for the month of August. Albumin levels were considered low if they were < 35 g/L in UAE or < 30 g/L in UK. The data were analyzed by Chi Squared, Bonferroni and ANOVA where appropriate and logistic regression undertaken using the variables, gender, age and the presence of diabetes. P<0.05 was taken as statistically significant.

Results: 586 HD patients treated in the UAE and 2234 in UK were considered. Demographics, presence of diabetes, k/V and albumin levels in August 2012 are shown below. Of the UAE nationals 19.3% had a low albumin compared to 13.5% in UAE residents of other nationalities, 13.1% in UK Caucasians and 10.2% in UK residents of other ethnicities. In respect to Caucasian British, logistic regression (figure)
suggested that the odds ratio of low albumin for UAE nationals was 1.58 (95% CI 1.104 – 2.274; p=0.013), for UAE non-nationals was 1.03 (95% CI 0.74-1.44; p=NS) and for UK residents of other ethnicities was 0.75 (95% CI 0.55-1.03; p=0.07). When the age, gender, presence of diabetes are included in the logistic regression the OR of a low albumin among the different ethnicities became not statistically different from the reference. The inclusion of dialysis dose in the model did not affect the results. **Conclusions:** Difference in albumin levels among different ethnicities are mainly related to difference in age, the proportion of females and diabetics.

**Abstracts**

**THE FEATURES OF ENDOXEMIA IN PATIENTS WITH CKD 5D AGAINST CHRONIC INFLAMMATION AND VIRAL HEPATITIS C BACKGROUND**

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**Introduction and Aims:** The patients with end-stage renal feature (ESRF) on hemodialysis (HD) are characterized by high morbidity on chronic hepatitis C (CHC). By-turn, CHC infection negatively affects both on system conditions of patients with CKD 5D or on dialysis efficiency, and on patient’s quality of life as whole. Study objectives: characterizing of endotoxemia among the patients on hemodialysis infected by hepatitis C virus. **Methods:** Toxicokinetic analysis of endotoxic parameters with determination of molecule sizes and toxin particles (<10 nm, 10-200 nm, and >200 nm), damaging activity potentials (toxicity), prevalent accumulation sites in bloodstream on different plasma fractions (albumin, globulin, cell membranes, in free circulation), and its involvement in forming of toxin-inducing autoimmune and cytotoxic reactions was executed among 43 patients with CKD 5D (25 with CHC in replication stage, basic group; 18 without CHC, comparing group). Autoleucocytes of patients was used as biological target for damaging activity assessment of endotoxins with different toxicometric characteristics. **Results:** In patients of basic and control groups was noted the substantial increase of indexes of cytotoxic (55.3±3.10% and 54.25±0.05%, respectively; p<0.05) and autoimmunity (56.70±3.83% and 51.89±2.28%, respectively; p=0.05) activity of endotoxins in plasma whole blood. In determined the high cytotoxic activity (CA) level of toxin-carrying plasma fractions and free-circulation endotxin fraction, representing the serious stage of endotoxemia, characterized by uniform distribution of endotoxins in all plasma fractions of patients from basic and comparative groups (p<0.05). In patients with CHC was noted the lower level of CA globulin-associated (41.60±3.95%) and albumin-associated (47.59±2.97%) endotoxins with molecule sizes less than 10 nm (p<0.05). The level of CA endotoxins with particle sizes 10-200 HM (p=0.05) was higher as compared with patients of control group. Toxic-induced autoimmune activity (AA) of all toxin-carrying fractions was raised and conformed to moderate or serious grade of endotoxemia manifestations. In patients with CKD 5D and CHC the level of AA free-circulating endotoxins was 57.40±1.96% and was significantly (p<0.05) higher as in control group (46.56±3.13%). Maximal level AA was noted for free-circulating endotoxins with particle sizes 10-200 nm. **Conclusions:** Clinical and laboratorial manifestations of endotoxemia in patients with CKD 5D and CHC have some distinctive features as compared with patients with CKD 5D, but without CHC. Toxicometric parameters of endotoxemia during CKD 5D and CHC was characterized with lower level of cytotoxic activity globulin-associated endotoxins with molecule sizes less than 10 HM (p<0.05), and higher level of autoimmune activity globulin-associated endotoxins with particle sizes 10-200 nm or molecule sizes less than 10 nm (p<0.05).

**BIOMARKERS TO APPRAISE PROTEIN-ENERGY WASTING AND ASSOCIATION OF INFLAMMATION IN MAINTENANCE HEMODIALYSIS PATIENTS**

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**Introduction and Aims:** Protein-energy wasting (PEW) contribute significantly to the increased cardiovascular mortality among dialysis patients. However, there is no isolated marker capable of assessing the nutritional status of hemodialysis patients. We investigated several parameters to appraise PEW and association of inflammation in maintenance hemodialysis patients. **Methods:** Sixty patients were enrolled in this cross-sectional study. The nutritional status of the patients was divided three groups according to subjective global assessment (SGA): 1) Severe malnutrition (SGA 1 to 3), 2) Mild to moderate malnutrition (SGA 4 to 5), 3) Well nutrition (SGA 6 to 7). We also simultaneously checked inflammatory markers, nutritional markers, and performed an anthropometric results. **Results:** Of all patients, sixteen patients (26.7%) were malnourished. PEW-positive patients had a difference in body mass index, % usual body weight, % standard body weight, geriatric nutritional risk index, skinfolds, fat mass, air circumference, cardiovascular disease, albumin, high sensitivity C-reactive protein (hsCRP), transferrin, ferritin, hemoglobin, hematocrit compared with PEW-negative patients. hsCRP levels were significantly higher in the malnourished group than that of well-malnourished group. Compared with patients without PEW, the presence of PEW was associated with incrementally higher cardiovascular disease (p<0.05). **Conclusions:** Serum hsCRP is a strong predictor of malnutrition and inflammation in hemodialysis population. The sensitivity can be increased by associating serum albumin with other nutritional and anthropometry markers to correctly evaluate the nutritional status of hemodialysis patients. Also, SGA is a simple and inexpensive method in clinical practice for detection in the patients with PEW.
Introduction and Aims: It is possible to observe improvement in the general state of patients receiving maintenancehemodialysis, including decreased joint symptoms, decreased pruritus, and better appetite, by using a high-efficiency, high-flux dialysis membrane. We aimed to determine the effects of the use of a high-flux dialysis membrane on improvement in the nutritional status of dialysis patients.

Methods: Two months before the replacement with a high-efficiency, high-flux dialysis membrane and one, three, six, and twelve months after the replacement, the subjective global assessment (SGA), biochemical markers, and a Body Composition Analyzer (Inbody-720, Biospace Co., Korea) were used to assess the nutritional status and determine hemodialysis adequacy, along with a biochemical test, in 25 stable patients receiving dialysis three times a week.

Results: The patient group in this study consisted of 10 men and 15 women, the average age of which was 61.2 ± 15.8 (18-81) years. They had received dialysis for 11.5 ± 4.2 (3-182) months, and their renal diseases included 9 cases of diabetes, 7 cases of chronic glomerulonephritis, and 5 cases of hypertension. Of all the patients, 3 got better results from SGA, 12 the same results, and 10 worse results, in the follow-up period. There was no significant increase or decrease after the replacement with a high-flux dialysis membrane in Hb, Hct, serum albumin, total cholesterol, LDL cholesterol, HDL cholesterol, BUN, or normalized protein catabolic rate (nPCR). While there was also no improvement in body weight, fat mass, muscle mass, lean fat, visceral fat, or the degree of edema measured by the body composition analyzer after the replacement, basal metabolism was improved from 1179.2 ± 143.5 kcal before the replacement to 1246.8 ± 145.4, 1241.1 ± 138.3, and 1201.0 ± 317.0 kcal one, three, twelve months after the replacement, respectively, on the average (p < 0.001, p = 0.001, p = 0.033), thus, the improvement was greatest one month after the replacement and, then, decreased over time.

Conclusions: In conclusion, the use of a high-efficiency, high-flux dialysis membrane generally failed to improve the nutritional status of patients receiving maintenance hemodialysis. However, the indirect index of basal metabolism increased at its early stage. More efforts should be made to help dialysis patients have better nutritional status.

Methods: Twenty-nine patients (55±5±3 (mean±SEM) years old, 13/16 females/males) were tested before and after 16 weeks of resistance training thrice weekly. The training comprised leg press, knee extension, and knee flexion. Effects on neuromuscular function and muscle strength were tested using surface electromyography (EMG) in the vastus lateralis muscle during dynamic knee extension in an one repetition maximum test. Electromyography was also recorded during a 20 seconds isometric knee extension with 50% of the one repetition maximum load. In addition, dynamic muscle strength was tested in a leg press one repetition maximum test. Knee extension RFD was tested using the Good Strength dynamometer chair. Muscle fibre sizes were analysed in muscle biopsies from the vastus lateralis muscle.

Results: Knee extension and leg press muscle strength increased 46% and 134%, respectively (p < 0.01). Mean EMG amplitude covering 0–300 ms in dynamic muscle contractions increased during 200–300 ms from 182.84 ± 33.91 to 315.37 ± 65.77 μV (p < 0.01), whilst EMG frequency was unchanged. The mean amplitude during 0–1000 ms increased from 321.81 ± 32.97 to 483.04 ± 53.99 μV (p < 0.05). The EMG signal during the 20 second isometric contraction remained unchanged. Left leg RFD increased after training from 1244 ± 134 to 1722 ± 185 Newton per second (p < 0.05), right leg RFD from 1472 ± 134 to 1788 ± 176 Newton per second (p < 0.05). The right and left knee extension RFD was significantly associated with type 2 muscle fibre size at baseline (r = 0.430, respectively) and during the intervention (r = 0.647 and r = 0.526, respectively).

Conclusions: Resistance training was associated with increased muscle strength and improved neuromuscular function in patients undergoing dialysis. The improved neuromuscular function may be due to improved synchronisation in activated motor units and the data are important in the interpretation of the increased muscle strength. The neuromuscular improvement in the early phase of the muscle contraction was shown in parallel with increased RFD, which may have important clinical implications for daily physical function.

Introduction and Aims: Patients with end stage renal diseases (ESRD) suffer from sleep disturbances. Subjective sleep complaints have been reported in up to 80% of patients with ESRD. Although the increased prevalence of sleep disorders in patients with ESRD is well established, no study, to our knowledge, has investigated the relationship between sleep disorders and nutritional characteristics in patients receiving hemodialysis (HD). The aim of this study was to investigate the associations between feeding habits, nutritional parameters and quality of sleep in HD patients.

Methods: A nested case-control study was designed. Eighty four patients fulfilling the inclusion criteria were enrolled. All the patients were receiving HD for three times a week. Serum fasting blood glucose, urea, creatinine, serum albumin, prealbumin, potassium, phosphorus, total cholesterol, Very Low Density Lipoprotein (VLDL), Low Density Lipoprotein (LDL), High Density Lipoprotein (HDL), triglyceride, homoglobin, total protein, uric acid, sodium, calcium, total lymphocyte count, serum iron, Cretinin and total iron storage capacity values were measured in predialysis blood samples in all patients. The questionnaire developed by the researchers included 17 questions about socio-demographic features including gender, age, marital status, education, financial status, employment, health insurance, the number of people in the household and whether the house/flat was rented or not, time to start treatment, duration, frequency and duration of HD, primary renal disease, fluid intake between two dialyses, smoking and the number of cigarettes smoked and taking medicine. The Pittsburgh Sleep Quality Index (PSQI) was used to evaluate the quality of sleep. Anthropometric findings (body mass index, circumference of the upper middle arm and skin thickness on the triceps), biochemical findings and Arizona Food Frequency Questionnaire (AFFQ) were used to evaluate nutritional status. All data were collected by the researchers at face to face interviews.

Results: The quality of sleep was poor in 51.2% of the patients. These patients were older than the patients with the good quality of sleep (4.04±1.30 vs. 37.4±1.18, p<0.01). The patients with the good quality of sleep consumed significantly more meat-offal-cheese-egg (p<0.01) and fruit (p<0.05). The patients with the poor quality of sleep had significantly lower albumin (p=0.01), pre-albumin (p=0.02) and total lymphocyte counts (p=0.02). The patients having gastrointestinal complaints (especially stomachache and flatulence) had the poor quality of sleep. The patients having gastrointestinal complaints (especially stomachache and flatulence) had the poor quality of sleep. The patients with the poor quality of sleep have a lower albumin (p<0.05), pre-albumin (p<0.05) and total lymphocyte counts (p<0.05). The patients with the poor quality of sleep have a lower albumin (p<0.05), pre-albumin (p<0.05) and total lymphocyte counts (p<0.05). The patients with the poor quality of sleep have a lower albumin (p<0.05), pre-albumin (p<0.05) and total lymphocyte counts (p<0.05).
TRANSPANTATION - CLINICAL STUDIES II

**MP629** SCREENING FOR INHERITED AND ACQUIRED THROMBOPHILIA PRIOR TO RENAL TRANSPLANTATION

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Introduction and Aims: Renal allograft recipients with thrombophilia are at higher risk for early allograft loss, microvascular occlusion and acute rejection with major consequences for allograft survival. The aim of the present study was to evaluate the prevalence of prothrombotic risk factors in patients awaiting renal transplantation and its contribution to patient and transplant outcomes.

Methods: All patients with a history of a thromboembolic event, early or recurrent vascular access thrombosis, family history of thrombosis, or multiple miscarriages underwent laboratory screening for thrombophilia.

Results: Since the introduction of the screening for hypercoagulable risk factors, 156 candidates for renal transplantation underwent laboratory evaluation. Eighty-eight patients (56%) exhibited at least one prothrombotic laboratory parameter, besides of isolated hyperhomocysteinemia, which confirmed a thrombophilic state. Lupus anticoagulant, antiphospholipid and beta-2-glycoprotein was present in 30%, 18% and 13%, and antithrombin III, protein C and protein S deficiencies in 11%, 8% and 10%, respectively. Factor V Leiden mutation was present in only one patient and prothrombin gene G20210 mutation was not found. Among the 156 patients, 30 underwent renal transplantation and were followed for a median of 199 days (range, 9 – 418). All patients were on triple immunosuppressive regimen comprising mycophenolate, tacrolimus and prednisone. Thrombophilia was identified in 16 (53%). Seventeen (57%) received perioperative anticoagulation with unfractionated heparin (9 patients with thrombophilia and 8 without laboratory confirmed thrombophilia). Five (30%) of these patients developed perihepatic hematomas. Three patients with thrombophilia developed thrombotic complications (2 upper limbs deep-vein thrombosis and 1 allograft artery thrombosis) and 1 patient without thrombophilia developed allograft vein thrombosis, p=0.35. Nine patients developed acute rejection (5 in the group with thrombophilia and 4 in the group without thrombophilia, p=0.87). Mean glomerular filtration rate was similar between thrombophilic and non-thrombophilic patients in the last follow-up (54.27 ± 47.52 mL/min/1.73m², p=0.35). One graft loss and 1 patient death were observed in each group.

Conclusions: Prothrombotic risk factors, especially antiphospholipid antibodies, are highly prevalent in patients awaiting renal transplantation with a clinical or familial history suggestive of thrombophilia, including early and recurrent vascular access failure. Despite pre-transplant screening and perioperative treatment and/or monitoring, thrombotic and bleeding complications are still frequent and severe.

**MP630** THE PREVALENCE OF ANTIPHOSPHOLIPID ANTIBODIES IN RENAL RECIPIENTS AND CHRONIC KIDNEY DISEASE

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Introduction and Aims: The prevalence of antiphospholipid antibodies (APLA) and thrombotic events in CKD are higher than in general population. The aim of the study was to assess APLA in CKD pts as a marker of thrombosis.

Methods: We analysed 3 groups: 37 renal recipients (Ktx) with stable renal function (mean age 40.3±12.6), 36 pts with CKD stage II-IV (mean age 39.4±12.5), 33 haemodialysed (HD) pts (mean age 50.6±16.7). Tested parameters included lupus anticoagulant (LA), anticardiolipin antibodies (ACLI), anti-B2-Glucoprotein I antibodies (anti-B2-GPI), anti-Phospholipid antibodies (anti-PPT) in IgM/G/IgG isotype. According to previous history of thrombosis we identified pts with strong thrombosis in the past called T(+) subgroup, whilst pts with no additional thrombotic risk factor were included to T(-) subgroup. APLA were tested twice: at the beginning of the study and 6 months later. Activity of protein C and S, factor VIII, ADAMTS-13 and anti-ADAMTS-13 were investigated in order to exclude other causes of thrombosis.

Each group: ktx, CKD and HD was analyzed separately. Mean observation time in months was 12±5.7 (ktx), 11.9±3.9 (CKKD), 10.9±3.2 (HD). Endpoint of the study was appearing of thrombosis during follow-up in APLA+/− pts. Statistical analysis was performed using Wilcoxon test, Chi-square, Fisher exact test.

Results: The prevalence of APLA in tested groups was higher in than in general population: in ktx, CKD and HD was 16.22%, 22.23%, 45.16%, respectively. We found no significant differences in APLA between T(−) vs T(+) in ktx and HD, in CKD differences between T(−) vs T(+) were detected in ACL IgG (p=0.018) and anti-B2-GPI IgG (p=0.0033). During follow-up, in ktx occurred one endpoint - graft thrombosis in T(+) pts with APLA, in CKD – 2 thrombosis (stroke, one in T(+) pts with APLA), in HD – pulmonary embolism in T(+) pts with no APLA. The most frequently observed antibodies were in ktx: anti-B2-GPI IgM (16.22%) and ACL IgG (13.88%), in CKD: LA (22.3%), anti-B2-GPI IgM (12.5%), in HD: LA (45.16%) and ACL IgM (20%). In HD correlations were found between ACL IgM and anti-B2-GPI IgM (p=0.0028), ACL IgG and anti-B2-GPI IgG (p=0.0377), anti-PT IgM and anti-PT IgG (p=0.0007); in ktx correlations were observed between anti-B2-GPI IgM and proteinuria (p=0.0441), serum creatinine concentration (Scr) and anti-B2-GPI IgG (p=0.0191), anti-B2-GPI IgM and ACL IgM (p=0.0328), ACL IgG and ACL IgG (p=0.0252), but identified correlations were weak (r<0.3). In ktx and CKD renal function remained stable, no significant differences in Scr between T(+) and T(−) were detected.

Conclusions: The prevalence of APLA in CKD, HD, ktx is higher than in general population. Endpoint of the study was achieved in 2 cases, so based on that we cannot clearly determined the role of APLA as a marker of thrombosis in tested groups. Screening for APLA in all CKD pts seems to be unnecessary.

**MP631** OPTIMISATION OF AZATHIOPRINE DOSES IN RENAL TRANSPLANTATION - A PRACTICAL AND REALISTIC OPPORTUNITY

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Introduction and Aims: Immunosuppression for renal transplantation (RTx) has shifted from azathioprine (AZA) to mycophenolate mofetil (MMF)-containing regimens with improved five-year patient and graft survival rates. However, data to support this strategy did not include AZA optimisation by measurement of thiopurine-S-methyltransferase (TPMT) activity, or AZA metabolites, thioguanine nucleotides (TGN) and methyl-mercaptopurine (MMP). Our aim was to assess TPMT activity and AZA metabolites in RTx recipients. We hypothesized that these biomarkers would identify patients at risk of AZA toxicity, under-dosing and non-adherence.

Methods: RTx blood samples were collected from 93 AZA long-term RTx patients and tested for TPMT activity and AZA metabolite profiles. TPMT activity, TGN and MMP levels were correlated with mean white cell counts (WBC), lymphocyte counts, alanine transaminase (ALT), haemoglobin (Hb) and mean cell volume (MCV) concentrations, and with clinical outcomes.

Results: The distribution of TPMT within our cohort mirrored that seen within the general population. Patients with normal TPMT activity (n=81) and intermediate TPMT activity (n=7) had been prescribed similar doses of AZA (1.094mg/kg and 1.015mg/kg respectively), but had predictably significantly different levels of TGN (209.9pmol/8x10⁸RBC and 546.0pmol/8x10⁸RBC respectively; p=0.0001). The dose of AZA correlated with both TGN (n=0.332, p=0.002) and MMP (r=0.468, p=0.0001) in those with normal TPMT activity. 58/93 patients had potentially sub-therapeutic TGN levels ≤240pmol/8x10⁸RBC, without impacting on GFR decline. However, this group did contain fewer patients who had developed skin cancer, in comparison to those with TGN levels ≥240pmol/8x10⁸RBC (p=0.046; OR=2.91, 95% CI 0.99-8.56). 14/93 patients had TGN and MMP levels of 0, suggesting non-adherence. 1/2 had a progressive decline in renal function.

Conclusions: The majority of patients in our cohort had a TGN level less than the range considered therapeutic in a number of chronic inflammatory conditions (240-400pmol/8x10⁸RBC). Increased macrocytosis seen in patients on higher doses of AZA may be an index of marrow toxicity, and may suggest that dose reduction is warranted. Prospective studies are needed to determine the ideal therapeutic range of AZA metabolites in RTx, since switching AZA to MMF without optimising the dose of AZA is potentially a missed opportunity.

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Introduction and Aims: The deceased donor kidney transplant to non heart-beating donor may have a higher rate of venous thrombosis (VT). The aim of this study is to analyze whether resistance index (RI) high (>0.8), measured by Doppler ultrasound can be a predictor of VT. We also analyzed whether early anticoagulation may decrease graft loss associated with VT.

Methods: We analyzed 227 patients with renal transplant non heart-beating donor made since 2005-2012. In November 2009 began prophylactic anticoagulation if RI were elevated. Patients were divided in group I (no anticoagulation historical group) and group II (anticoagulated by RI).

Results: The Table compares the Group I to Group II. In univariate analysis cold ischemia time, body mass index of the donor, antitacrolimus globaline and high RI were factors that were associated with VT of the graft. In multivariate analysis thymoglobulin treatment was a factor associate with VT (p 0.03, HR 5.2 IC 1.1-23.8). We analyzed the subgroup of 89 patients with high RI, 34 patients were anticoagulated, and none had a VT compared with 55 patients who received no anticoagulation, of which 7 had vasculat thrombosis (0% vs. 14.5%, p<0.05).

Conclusions: This study suggests that in renal transplant from non heart beating donor when RI is higher than 0.8, anticoagulation may decrease the rate of VT. In these transplants, a careful choice of donor and reduced cold ischemia time are related with better result.

**MP634**

## ASSOCIATION OF GENETIC POLYMORPHISMS OF MATRIX METALLOPROTEINASES WITH NEW-ONSET DIABETES AFTER TRANSPLANTATION IN RENAL TRANSPLANTATION

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**Introduction and Aims:** New-Onset Diabetes After Transplantation (NODAT) is a serious metabolic complication that may follow renal transplantation. Excess fat deposition requires space, creating adipocyte (hypertrophy and hyperplasia) and extracellular matrix (ECM) remodelling. This process is regulated by several factors, including several adipocyte-derived Matrix metalloproteinases (MMPs) and the adipokine cathepsin, which degrades fibronectin, a key ECM protein. Excess fat, also deposited in visceral organs, generates chronic low-grade inflammation that eventually triggers insulin resistance and the associated diabetes mellitus. Therefore, we examined the association between NODAT and 11 single nucleotide polymorphisms (SNPs) located within the 3 genes of Matrix metalloproteinases (MMPs) which might be related with NODAT.

**Methods:** A total of 369 renal transplant recipients were included without a history of diabetes. We analyzed the association between NODAT development and a panel of 11 SNPs within 3 genes (MMP1, MMP2, MMP3) of MMPs.

**Results:** In terms of allele frequencies, rs243849 (MMP2) was significantly higher in patients with NODAT. Two SNPs among 11 (18.1%) were significantly associated with NODAT development after adjusting for age, sex, and tacrolimus usage. They include MMP2 (rs1132896) and MMP2 (rs243849). In multiple logistic regression analysis, these 2 SNPs were significantly associated with the development of NODAT in the codominant and recessive or, codominant and dominant models, respectively.

**Conclusions:** The data suggest that excess fat deposition and ECM remodelling might play a role in the pathogenesis of NODAT in renal transplantation recipients. In particular, significant variations of MMP2 might confer susceptibility to NODAT in patients who receive renal transplants.
percentage of LVH, based on both LVM indexes (66.7 ± 4.84%, p=0.02 for LVM/BSA and 86.6 ± 7.4%, p=0.06 for LVM/height1 vs 2, respectively). The OR for LVH in patients with patent fistula was 2.13 (1.11-4.69), p=0.03, and 2.18 (0.94-5.05), p=0.06, respectively. IEF was associated with MACE. Mean cystatin C concentration in the fistula group was 2.13mg/dl (SD 0.63) with a mean eGFR of 37.34ml/min (SD 15.37) and 1.54mg/dl (SD 0.91) and 53.75ml/min (SD 19.8) in patients without MACE, respectively. Mean creatinine levels and eGFR for the MACE group were 1.69mg/dl (SD 0.69) and 44.9ml/min (SD 18.87) and 1.48mg/dl (SD 0.69) and 50.1ml/min (SD 19.42) in the non-MACE group (n.s.). Cystatin C levels were associated with a high IRR (1.75) for MACE. IR for MACE increased by 75% for each mg/dl serum cystatin C increase (IRR 1.75 95%CI 1.14-2.69, p=0.009). A decrease of eGFR<60 ml/min was significantly associated with risk of MACE. The incidence increased per mg/dl eGFR loss by 4.7% (IRR 0.953; 95%CI 0.93-0.98, p<0.001). No significant association with MACE could be demonstrated for serum creatinine levels (n.s.) and creatinine-based eGFR.

Conclusions: We showed a significant correlation between serum cystatin C and the incidence of MACE. Since creatinine was not predictive these results suggest a prognostic role of cystatin C independent of glomerular filtration rate.

**Cost-effectiveness in Italy of kidney transplantation from donors after circulatory death**

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Introduction and aims: The global increase of end-stage renal failure (ESRF) is progressively eroding health care budgets at regional level all over the world. Italy expenditure for ESRD patients has been calculated between € 31,472 and € 36,234 per year. It is about 1.8% of total Italian health care budget and such increase of morbidity and mortality (MDM) patients (MDM) has caused a significant growth of HD waiting lists for renal transplantation. In order to enlarge kidney donations, in 2007 the “Fondazione IRCCS Pollicino San Matteo (Pavia, Italy)” designed and actually is carrying on, the “Programma Alba i.e. the Italian proposal for organ donation After Circulatory Death (DCD).” The present study was designed to calculate detailed costs for HD, renal transplantation analysed according to all sources of kidney donation with particular regard to DCD.

Methods: The Markov model based on Italian population of the Italian Region Lombardia was used. Sources have been the “Italian National Institute for Statistics” (ISTAT) and the “Lombard Registry of Dialysis and Transplantation”. Results: Italian Hospital costs for one DCD patient is € 169,818 for the first year, in the base case of two kidney extra transplants, and € 92,286 in a modeled future scenario of ten extra transplants per year. DBD expenditure is € 54,455 for patient the first year decreasing to € 11,531 the second and € 9,781 the subsequent years. Figures for live donation are € 49,306 the first transplantation year, € 10,532 and € 8,744 for second and subsequent years. HD costs are € 37,881 per patient/year.

Conclusions: Our data show that increasing transplantation rate is less expensive and more effective when compared to current ESRF treatment patterns. In particular intensifying DCD transplants, as currently applied in several European countries, should progressively improve current insufficient organ supply reducing local health care expenditure.

**Impact of cystatin C on MACE after kidney transplantation**

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Introduction and aims: Cystatin C is a well established marker of kidney function. There is evidence that cystatin C concentrations are also associated with mortality. The present analysis evaluates the associations of cystatin C with major adverse cardiac events (MACE), end stage renal disease (ESRD) and all-cause mortality in a well defined kidney transplant patient cohort.

Methods: We determined serum concentrations of cystatin C and creatinine from patients who underwent kidney transplantation between February 2000 and May 2011 in our transplant centre. MACE (i.e. non-ST-elevating and ST-elevating myocardial infarction, need for coronary artery bypass graft operation and autopsy results), all cause mortality, ESRD and biopsy proven graft rejections were recorded. We performed a regression analysis using the generalized estimating equation model (GEE, Poisson) with adjustment for age, sex and graft rejections. Risk estimation is expressed as incident rate ratio (IRR) and incident rate (IR in %). eGFR was calculated with the MDRD formula for creatinine and for cystatin C as eGFR=76.7*CysC1.19 (AKD 2008:51:395), respectively.

Results: We investigated 265 patients, thereof 56.7% male, with a mean age at transplantation of 49.2 years (SD 12.3) and mean observation time of 4.27 years (min.

0.05 max. 11.99). Within 1131 patient years, 33 MACE were observed, resembling an incidence of 29/1000 patient years (95%CI 21-41). Mean age at MACE was 60.32 years (95%CI 56-64.4) and differed significantly from the mean age of 54.7 years (95%CI 53.63, p=0.016) in patients independent of patent fistula to the presence of LVH and higher LVM.

Conclusions: In a largest study to date, we show that long-lasting patent arteriovenous fistula after kidney transplantation plays the important role in the increased prevalence of left ventricular hypertrophy in kidney transplant recipients.

**Conversion from calcineurin inhibitors to everolimus resulted in decrease of serum TGF-beta and urinary NGAL in renal transplant recipients**

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Introduction and aims: Calcineurin inhibitor (CNI) treatment has been implicated for chronic allograft dysfunction in renal transplant recipients. We aimed to investigate the effects of switch from CNI to Everolimus treatment on serum/urinary markers of fibrosis (TGF-beta), inflammation and MACE. Methods: In this prospective-randomized study, 30 renal transplant recipients on CNI treatment were enrolled. Fifteen patients were converted to Everolimus and remaining 15 patients were continued on CNI treatment as control group. Age, gender, dialysis vintage, baseline serum creatinine and eGFR-MDRD levels were similar between the two groups. Biomarkers of fibrosis (serum and urine TGF-beta), inflammation (hs-CRP, urinary MCP-1) and also tubular injury (serum NGAL) were measured in baseline and 3th month after conversion to Everolimus in both groups.
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Comparision of Kidney Paired Donation Transplantations With Living Related Donor Kidney Transplantation

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Introduction and Aims: Kidney Paired Donation (KPD) is a rapidly growing modality for facilitating living related donor renal transplantation (LRDRTx) for patients who are incompatible with their healthy, willing and living donors. Data scarcity on outcome of KPD vs LRDRTx prompted us to review our experience.

Methods: This was a single center study of 224 patients on regular follow-up, who underwent LRDRTx from January 2010 to June 2012 at our institute. The aim of this study was to compare graft survival, patient survival and rejection rates of KPD (group 1, n=34) with those of LRDRTx (group 2, n= 290). All recipients received immunosuppression with a steroid, mycophenolate mofetil/azathioprine, and a calcineurin inhibitor and thymoglobulin induction in high risk patients. Kaplan-Meier curves were used for survival analysis. In group 1, mean recipient age was 35.5±11.3 years, and 29 were men and mean donor age was 44.1±8.17 years, 10 were men. In group 2, mean recipient age was 29.1±10 years, and 155 were men. Mean donor age was 47.5±9.66 years, 74 were men. Mean HLA matching in group 1 and 2 was 1 vs 3.2 (p<0.05).

Results: One, two- year patient survival showed no significant difference between the 2 groups (97.1%, 97.1% vs 96.2%, 94.8%, p=0.01). Graft survival also showed no significant difference (97.1%, 97.1% vs 97.6%, 96.7%, p=0.73). Acute rejection incidence were also similar (8.7%, 9.9%, p=0.62).

Conclusions: Our results showed similar graft survival, patient survival and rejection rates of KPD vs LRDRTx over 2 years post-transplantation, encouraging use of this approach.

Clinical Significance of Asymptomatic Bacteriuria During First Year After Renal Transplantation

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Introduction and Aims: Urinary tract infections (UTIs) are the most common infections in renal transplant recipients and are considered a potential risk factor for poor graft outcomes. Asymptomatic bacteriuria (AB) is the most prevalent form of UTIs, however its clinical impact has not been thoroughly evaluated and so far there are no established guidelines for screening and treatment of AB in renal transplant population. Therefore the aim of the study was to evaluate incidence, microbiology and risk factors for AB and to identify patients who would benefit most from the treatment of asymptomatic bacteriuria.

Methods: We performed a retrospective cohort study reviewing medical records of 209 renal transplant recipients, including 59.3% of male gender, with mean age of 46±14 years. We analyzed urine cultures performed within first 12 months after RTx with reference to clinical data.

Results: We studied urine cultures and clinical data from 209 renal transplant recipients, including 59.3% of male gender, with mean age of 46±14 years. We observed 170 AB episodes in 83 patients and this accounted for 53% of all diagnosed UTIs in n=111 patients. More than half of AB episodes were diagnosed during the first month post-transplant and the most frequently isolated uropathogen was Enterococcus faecium (36.8%, n=32).Beginning from the second month the bacterium most frequently found in urine cultures was Escherichia coli (54.2%, n=45). Female gender, use of induction, comorbidity measured by Charlson Comorbidity Index, history of acute rejection and CMV infection were risk factors for developing AB in univariate analysis and were similar to risk factors for developing any kind of UTI. 46 out of 83 patients with AB also developed symptomatic UTI. AB in multivariate analysis was an independent risk factor for symptomatic UTIs (both lower and upper UTIs) and in patients with AB also developed symptomatic UTIs. AB in multivariate analysis was an independent risk factor for symptomatic UTIs.

Conclusion: Conclusion: AB in a single center is the most frequent form of UTIs. AB in renal transplant population is a potential risk factor for infection and other complications. Treatment of AB might explain possible beneficial effects of Everolimus on graft survival.

Severity of Coronal Disease, Cardiac Events and Mortality in Patients Evaluated for Renal Transplantation

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Introduction and Aims: The best strategy for investigation and treatment of coronary artery disease (CAD) in renal transplant (Tx) candidates is controversial. The aim of this study was to evaluate the relationship between CAD extension and management, transplantation status and both the peri-operative and mid-to-long term outcome of CKD stage 5D patients (pts) undergoing evaluation for kidney transplantation, in a single centre registry.

Methods: Between June 1996 and January 2009, 167 pts (mean age 53.9±8.6 y.o.) considered to be at high risk for CAD performed coronary angiography (CAG) as a part of renal Tx evaluation. The cohort was divided in three groups according to CAD extent (defined as >50% stenosis of at least one major epicardial vessel): group 1 (n=74) had no significant stenosis, group 2 (n=49) had one vessel disease and group 3 (n=44) had two/three vessel or left main disease.

Results: Fifty-eight pts were transplanted during the observation period (37.7±23 months after CAT for the entire cohort; 89.8%±1 year); 35 in group 1, 11 in group 2 and 12 in group 3. Increasing CAD severity was independently associated with a 34% decrease in the likelihood of receiving a graft (HR 0.62; 95% CI 0.43-0.91; p=0.013). Despite overall event-free survival was higher in Tx recipients, CV events and mortality consistently increased with increasing severity of CAD in both transplanted and non-transplanted pts. Performance of percutaneous coronary intervention (PCI) was not associated with lower event rates and all 5 peri-Tx myocardial infarctions (MI) occurred in group 3 pts. After correction for baseline characteristics and for the probability of receiving a graft, both CAD extension (HR 2.6; 95% CI 1.5-4.6) and Tx-status (HR 0.28; 95% CI 0.13-0.61) were the only independent predictors of death/MI.

Conclusions: CAD extent is a powerful predictor of event-free survival in renal Tx recipients/candidates. Despite a high incidence of acute coronary syndromes in severe CAD pts that received a renal graft, total mortality seems to be in an acceptable range. We did not detect any significant difference in the outcome related to the pre-Tx revascularization status, event stratification according to study defined CAD extent.

The Association of Acute Kidney Rejection and Nitric Oxide Level - Could it be a Non-Invasive Marker of Choice?

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Introduction and Aims: Acute renal allograft rejection (AR) continues to have a negative effect on the graft survival despite a better understanding of the molecular basis of renal allograft rejection. Nitric oxide (NO) has important biological functions in cell defense and injury and some evidence exists that it may act as an immunomodulator in allograft transplantation (TX). The aim of our study was to analyze the relationship between NO with histological parameters in biopsy-proven allograft rejection and other reasons of allograft dysfunction, as well as to evaluate the clinical impact of NO measurement as a non-invasive marker for early diagnosis of AR.

Methods: Forty-five consecutive recipients receiving their first living-related kidney grafts (mean age 35.7±10.4 years, 26 females) were prospectively recruited. Serum NO levels were measured at: 20 min after graft reperfusion (NO1), on days: 1(NO2), 5(NO3) and 14(NO4), and at 1th(NO5) and 6th (NO6) month after Tx. Protocol allograft biopsies (Bx) were performed at 1st and at 6th months after Txs, and regular biopsies upon clinical indication. Renal function tests were done as per our unit protocol.

5.55 ± 1.39 mg/dL (p=0.01), serum TGF-β2 (8727 ± 11222 vs 194 ± 1415 pg/mL, p=0.03) and urinary NGAL (0.26 ± 0.40 vs 0.12 ± 0.07 ng/mL, p=0.05) were found to be significantly decreased. In contrast, serum total cholesterol and LDL-cholesterol levels increased (213 ± 46 vs 235±64, p=0.02 and 125±32 vs 143 ±36 mg/dL, p=0.03, respectively). Serum NGAL, hs-CRP, urinary MCP-1, albumin excretion rate did not change after conversion.

Conclusions: Conversion from CNL to everolimus resulted in significant decrease of serum TGF-β2 and significant increase of NGAL. Recurrent AB episodes, may be considered either a risk factor or a marker of increased susceptibility to symptomatic infections. It seems that patients with history of recurrent UTIs before RTx and exposed to greater immunosuppression due to use of induction and episodes of acute rejection are at risk of developing serious symptomatic infections and therefore could benefit most from systematic screening and proper prophylaxis including treatment of AB.
Results: Thirty-eight of the paired protocol Bx (42.2%) showed histological features of subclinical acute rejection (SAR) and 52 (57.8%) Bx had no histological signs of AR. Significantly higher NO levels: (NO5) and (NO6) were found in Bx showing SAR as compared with negative Bx (208) for NC. Five patients in NC group were radiologically diagnosed LC. Six patients in NC group had liver failure at death, but the other was Child class A. Eight patients in NC group died median 13.5 months after KT (range 1-161 months).

Conclusions: Our study represents one of the largest series of pts with MGUS pre or post-KT to date. The finding that only 2 out of 42 MGUS patients progressed to developed a myeloma. From November 1998 to February 2012, a total of 851 adults underwent KT. An hematological evaluation was performed in all pts with a monoclonal gammapathy to rule out myeloma and lymphoproliferative disease. Pts with MGUS who received a KT were compared with pts on dialysis with MGUS.

Results: From November 1998 to February 2012, a total of 851 adults underwent KT. 1) 16 pts were found to have a MGUS before transplant. Median follow-up was 7.8 years (range 2.2-18.95), median follow up pre-transplant 3.7 years (range 0.19 – 10.2). Median age at the MGUS diagnosis was 61.3 years (range 42-72). The distribution of MGUS chain isotypes was as follows: IgG (12/16), IgM 2/16, IgA 2/16. Bone marrow biopsy and aspirate were performed in 13/16 pts (81.2%). During a median post-transplant following-up of 4.1 yrs, 1 pt developed a myeloma. 2) 16 pts with MGUS who received transplant were compared to pts with MGUS on dialysis at the time of the study. During a median following-up of 3.18 yr. No one developed a myeloma. 3) 26 pts developed a MGUS after kidney transplant, median follow-up was 4.84 years. Median age at the diagnosis was 52.7 years. The distribution of MGUS chain isotypes was as follows: IgG 21/26 pts (80.8%), IgA 4/26 pts (15.4%), IgM 1/26 pts (3.8%). Bone marrow biopsy and aspirate were performed in 15/26 pts. During a follow up of 4.84 years 1 pt developed a myeloma.

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Methods: This is a retrospective study. We evaluated all kidney transplanted pts between November 1998 – February 2012. We included all pts found to have MGUS at the time of transplant. The follow up was stopped at August 31, 2012. An hematological evaluation was performed in all pts with a monoclonal gammapathy to rule out myeloma and lymphoproliferative disease. Pts with MGUS who received a KT were compared with pts on dialysis with MGUS.

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ERYTHROPOIETIN TREATMENT MODULATES SERUM KLOTHO LEVELS IN KIDNEY TRANSPLANT RECIPIENTS

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Introduction and Aims: Klotho protein exists in two forms: a transmembrane protein acting as co-receptor of FGF23; and a circulating soluble secreted protein with pleiotropic activities. Data on soluble Klotho (Kl) in Chronic Kidney Disease (CKD) are contradictory and even less is known about its expression after renal transplantation (TX). Few studies evaluated the pharmacological modulation of Kl. In vivo experimental studies demonstrated that the observed Kl reduction caused by renal damage can be mitigated by erythropoietin (EPO) treatment. The aim of this study was to determine Kl serum levels in a population of TX recipients and to evaluate whether EPO treatment can modulate these levels.

Methods: 75 TX recipients who had received their transplants at least 6 months previously were enrolled in the study. Serum and 24-h urine samples were collected at enrollment. We discontinued the use of EPO for 5 weeks in all transplant patients with stable Hb level. Whole blood was collected before and after the EPO interruption to measure changes in Kl serum levels. By ELISA assay, we measured Kl concentrations in culture media of tubular proximal cells HK-2 cells treated with Cyclosporin (CaA) and EPO.

Results: Serum Kl levels in TX patients were 0.68 ng/ml, ranging from 0.06 to 3.91 ng/ml. No significant differences were found with CKD patients (0.6, IQR 0.48-1.12), while healthy controls showed significantly lower median Kl levels (0.37, 0.27-0.52). In TX patients serum Kl was significantly inversely associated with eGFR (r = -0.378, p < 0.001) independently from age and gender. Klotho was positively associated with serum phosphate (r = 0.374, p < 0.001) and negatively with daily phosphaturia (r = -0.354, p = 0.003), serum FGF23 (r = -0.307, p = 0.007) and serum HGB (r = -0.311, p = 0.006). After adjusting for age, gender and eGFR only FGF23 remained significantly associated with Kl. In the 11 patients in treatment with EPO at the baseline, after a 30 days wash-out period, serum Kl significantly decreased (1.17 vs 0.76 ng/ml). As expected we observed also a significant reduction in HGB and EPO levels, while other parameters were comparable to basal values. Finally, ELISA assay revealed that Kl was only detectable in culture media obtained from cells treated for 24 hours with CaA and CaA+EPO.

Conclusions: In the present study we find that soluble Klotho levels in TX are significantly increased respect to healthy controls and similar respect to CKD patients. To our knowledge this is the first report on serum Kl levels in TX. In the past we demonstrated, for the first time, a link between EPO treatment and Kl levels in a cohort of TX and in HK2 cells, suggesting that EPO could exert its beneficial effect also through the modulation of soluble Klotho.

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PREGNANCY AFTER KIDNEY TRANSPLANT REPORT OF THE STUDY GROUPS KIDNEY TRANSPLANT AND KIDNEY/PREGNANCY OF THE ITALIAN SOCIETY OF NEPHROLOGY

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Introduction and Aims: We evaluate the gestations of transplant patients analyzing outcomes and complications.

Methods: outcome of 101 pregnancies in 89 renal transplant recipients. variables: Type of nephrology age when dialysis started, at transplantation, at pregnancy, time between dialysis and transplantation, and between transplantation and baby birth. Immunosuppressive therapy type of delivery baby weight, Appgr score and mother baby follow up.

Results: In 9 pts diagnosed: chronic pyelonephritis, 1 post partum cortical necrosis ,11 Ila GN, Sclerotic nephropathy ,35 unknown nephropathy ,1 ADPKD, 1, 5 Nephrotic syndrome, 26 Glomerulonephritis, 2 cistic Kidney disease, 1 Nephrometosis, 1 Tubulo intestinal Nephropathy, 2 Obstructive Nephropathy, 1 Alport syndrome, 1 Renal displasia. The patients' age at start of hemodialysis 28.05±2.35 years, the patients' age at transplantation: 30.25±2.32 years, the patients' age at pregnancy 33.9±3.1 years, the interval between the start of hemodialysis and transplantation 16±23.3 months, the time between transplantation and child birth 4.45±3.15 years. Immunosuppressive therapy: Prednisone, Azathioprine and CyA in 39, Prednison e Tacrolimus in 1, Prensone e CyA in 16, Aza e Prednison in 3, Prednison, Aza, CyA, Pm 1, Aza, Prednison, Fk in 5, CyA 2, 5 FK 5, Azal e CyA 7. The renal function normal before (creatinine 1.10±0.15 mg/dL), during (0.9±0.10 mg/dL) and after pregnancy (1.09±0.125 mg/dL). Mode of delivery: Caesarean section in 99% cases, 1% vaginal delivery. Mothers' complications: Non Nephrotic Proteinuria 6, Urinary Tract Infection 4, Preclampsia 4, Internal Placenta Detachment 1, Spontaneous Abortion 26, High Blood Pressure 14, acute rejection 3. During the mother's follow up there was no acute rejection episode. Currently all patients show good renal function (creatininina 1.09±0.25 mg/dL) Observed 35 term births, 60 preterm births with 26 cases of child weight at birth lower than expected by the gestational age. Mean gestational age 35.4±15 weeks, the birth weight was 2350±890 grams, Appgr score between 4/8 and 6/9.5 babies were admitted to the neonatal intensive care unit.Fetal complications: IUGR 2, Acute Distress Respiratory Syndrome 2, Klinefelter Syndrome 1. Breastfeeding was admitted to the neonatal intensive care unit. Fetal complications: IUGR 2, Acute Distress Respiratory Syndrome 2, Klinefelter Syndrome 1. Breastfeeding was admitted to the neonatal intensive care unit.

Conclusions: The majority of pregnancies have a good outcome with increased irrepaircmia reduced gestational age and low birth weights and patients therefore to be referred to highly specialized centres where nephrologists obstetricians providing surveillance and treat.
progressive interstitial fibrosis and tubular atrophy. Although graft biopsy provides the definitive diagnosis and indicates the degree of fibrosis, it is an invasive procedure and not free of risks. Urinary procollagen is associated with degree of renal fibrosis detected by biopsies performed on patients with chronic kidney disease and renal transplant protocol biopsies. The aim of this study is to find out the predictive role of urinary procollagen in determining the amount of fibrosis in renal transplant recipients with a pre-biopsy clinical diagnosis of chronic allograft injury.

Methods: Adult renal transplant recipients that underwent graft biopsy with a probable diagnosis of chronic allograft injury in Hacettepe University Medical Faculty in a 12 month period were included in this study. Renal fibrosis was quantified by using Bannf classification (grade 0-10; grade 1-10 to 25%, grade 2-25% to 50% and grade 3: >50%). Urine samples were collected from all patients on the same day with biopsy to determine procollagen levels. Procollagen/creatinine ratio was used in analyses to eliminate the effect of urine volume. The relation between fibrosis score and urinary procollagen/creatinine ratios were lower in the grade 0 group and highest in the grade 3 group. Urine procollagen/creatinine ratio was significantly correlated with degree of fibrosis (r=0.251, p=0.04).

Conclusions: Urine procollagen measurements can be a reliable predictor of degree of renal interstitial fibrosis in renal transplant recipients that underwent renal biopsy with a pre-biopsy diagnosis of chronic allograft injury.

**MP649**

### CLINICAL EPIDEMIOLOGY OF RESISTANT HYPERTENSION IN RENAL TRANSPLANT PATIENTS

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**Introduction and Aims:** Adequate treatment of hypertension is considered as an absolute priority by current KDIGO renal transplantation guidelines. However, only scattered information exists on treatment-resistant hypertension (RH) in these pts and the prevalence of RH in this population has never been assessed according to rigorous criteria nor face to face compared with that in well matched CKD populations.

**Methods:** We investigated an unselected series of 219 renal transplant pts (67% M; age 47±12 yrs; 11% diabetics; eGFR 55, IQR 40-66 ml/min) with a follow up intensity adhering to recommendations by the Am Soc of Transplantation (JASN 11:S1–S86, 2000) and in a series of 46 pts with CKD stage 2-5 (CKD-A) matched to transplant pts for age, and diabetes status. Both transplant pts and CKD-A pts systematically underwent ABPM studies. In these groups we applied the stringent criterion for RH by NICE (Mean daytime BP>135/85 mmHg despite treatment with 3 drugs).

**Results:** Seventy patients (45 male, 25 female; mean age 36.5±10.1 years) were included in the biopsy specimen analyses of 64 patients were adequate for fibrosis assessment. Mean urinary procollagen/creatinine ratios of the patients in each group according to BANNF classification score were presented in table. Mean urinary procollagen/creatinine ratios were lower in the grade 0 group and highest in the grade 3 group. Urine procollagen/creatinine ratio was significantly correlated with degree of fibrosis (r=0.251, p=0.04).

**Conclusions:** Urine procollagen measurements can be a reliable predictor of degree of renal interstitial fibrosis in renal transplant recipients that underwent renal biopsy with a pre-biopsy diagnosis of chronic allograft injury.
(cyclosporine-CsA and tacrolimus-Tac) on adipocytokine levels in KT recipients. Methods: 59 recipients that use CNI after KT were included in the study. Patients were divided into two groups as Tac (n=43) and CsA users (n=16). Demographic properties, blood pressures, antihypertensive treatment, anthropometric measurements and glucose-lipid profiles and adipocytokine levels were measured. Results: Age, gender distribution, donor type, transplantation period, history and family history of smoking, HT, DM, CAD, obesity were similar. While number of diabetic patients were higher in CsA group (25% vs. 6%, p<0.05), dialysis duration prior to KT were longer in Tac group (51.1±6.9 vs. 27.0±5.9 month, p<0.05). No significant differences were found in BMI, blood pressures, waist-hip, wrist, mid arm and triceps circles, suprailiac and suprascapular fold thickness and body fat ratios. Neck circle was higher in CsA group (38.3±0.5 vs. 40.5±0.9 cm, p<0.05). Kidney functions, glucose, fibrinogen, homocystein, lipid and apolipoprotein profiles of the groups were comparable. No differences were observed in serum adipocytokine levels. Conclusions: As a result, we did not observe any differences among the effect of CNIs on adipocytokine levels. Neck circle is another indicator of visceral obesity that has been more strongly associated with insulin resistance than waist circle. Further adequately designed prospective studies are needed to determine the relationship between CNIs and neck circle.

**EPIDEMIOLOGY AND CLINICAL CHARACTERISTICS OF LOWER RESPIRATORY TRACT INFECTIONS AMONG KIDNEY TRANSPLANT RECIPIENTS**

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Introduction and Aims: Infections, especially pneumonia, continue to be an important cause of disability and death in renal transplant recipients. An appropriate empirical treatment of post transplant pulmonary infections requires knowledge of the spectrum of the microorganisms involved in causing these infections. We investigated the epidemiology and outcome of pulmonary infections in transplant patients over a 24-year period. Methods: This is a retrospective study of kidney transplant recipients who were transplanted at our center between December 1988 and April 2011. Subjects were included if they developed radiological features suggestive of pulmonary infection, with one or more of the following respiratory manifestations: cough with or without expectoration, dyspnea, pleuric chest pain and reduced partial pressure of oxygen in arterial blood. Results: We reviewed the clinical records of 406 consecutive kidney transplant recipients, of whom 248 (61%) was male. Approximately 37.4% (152) of the cohort received a deceased donor kidney. Eighty-two recipients had 111 episodes of pneumonia throughout the study period, an incidence of 8/100 patient years. The mean interval from transplantation to the onset of pneumonia was 22.2±32.7 months. Fifty-six percent of the pneumonias were community acquired. Twenty-eight patients (25.2%) died due to pneumonia. Bacterial infections were the most common cause (30.6%), especially Haemophilus influenzae, Stenotrophomonas maltophilia and Pseudomonas aeruginosa. Among 38%, there was no positive microbiologic isolation. Of the total number of episodes, fungal infections, especially Aspergillus fumigatus, represented 22.5% and viral 9%. Diagnosis was achieved in 35 episodes by only physical examination and chest radiography. Bronchoscopy was performed in 23 episodes, giving a final overall diagnostic yield of 12 patients (52.2%). The most common presenting symptom was fever with or followed by cough (n=81) or sputum (n=51). At least one complication developed in 40 (%36) pneumonia episodes during treatment of pneumonia. Hematologic complications developed in 22 episodes, renal complications in 14 episodes and hepatotoxicity in 7 episodes. Nosocomial pneumonias accounted for 71.4% of pneumonia episodes resulting in mortality (p<0.001). Pneumonia occurring time was significantly earlier in nosocomial pneumonia than in community acquired (15 and 27.9 month, respectively). Nosocomial pneumonia episodes had higher procalcitonin, urea and LDH values and lower hemoglobin and albumin values. Conclusions: In our cohort, bacterial pneumonia was the most common cause, but it is necessary to rule out other pathogens that affect immunosuppressed hosts. Fungal infections were significantly more frequent in the interval of 1-6 month after transplantation. Early diagnosis of pneumonia in renal transplant recipients reduces morbidity and mortality.

**BEHAVIOUR OF DONOR-SPECIFIC ANTIBODIES IN KIDNEY TRANSPLANTATION: POSTTRANSPLANT DQ HLA CLASS II DSA HAVE THE STRONGEST IMPACT**

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Introduction and Aims: The impact of donor-specific antibodies (DSA) after kidney transplantation (KT) on graft survival is becoming clearer, but which DSA have the greatest impact or how they behave after KT is still imprecise.
Methods: In this study we focused on KT recipients with grafts functioning more than 3 months. 440 KT performed between 1979-2012 with a negative CDC crossmatch were included in a prospective observational study between 1/2008-12/2012. Anti-HLA antibodies were tested using Luminex Lx2000 Lifescreen and LSA Class I and II assays (Gen-probe, Stanford, CT). Cut-off for a positive reaction was set in MFI raw value=1000.

Results: During the 4 years of follow-up, 33 patients lost their grafts, 21 died and 5 were lost to follow-up. We found: - PreKT DSA in 43/289 (14.9%) patients: 5 HLA-I, 36 HLA-II, 7 HLA-III. Graft survival was not significantly different preKT DSA-positive patients. AllrprKT DSA-I and 50% DSA-II disappeared postKT. - First postKT tests showed DSA in 26/247 (6.7%), median 54 months post KT. 3 HLA-I and 23 HLA-II (immunodominance: 16 DQ,3 DRB1,1DRB3,1DRB4,2 DRB5). Graft survival was lower in DSA-positive patients (p<0.001 uncorrected, p=0.002 censored, median follow-up 32 months). Graft loss occurred in 58% DSA-positive KT performed- 5 years before, 37.5% transplanted 1-5 years before and 0% DSA+ patients< 1 year after KT. Interestingly, 50% DQ DSA>7000MFI lost their grafts. - Second monitoring showed DSA in 41/288 (10.6%), median 59 months post KT and 32 after first post-KT tests: 3 HLA-I, 35 HLA-II, 3 HLA-III. Immunodominant DSA were again 58% DQ. At least 18 were de novo DSA, 19 preformed and 5 unknown. There were not significant differences between de novo and preformed DSA groups except for less retransplants, lower PRA and longer postTR follow-up (103.8±78 vs 83.29 months, p=0.003), but similar DSA specificity and MFI level (11792±153 vs 8964±6921).

Conclusions: PreKT DSA not associated to early graft loss disappeared after KT under conventional immunosuppression, as well as 50% of DSA-II. Posttransplant DSA significantly impact graft survival, especially high MFI DQA DSA or DSA in long-term transplant patients. Around half posttransplant DSA are de novo but are similar to preformed DSA in MFI or specificity.

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MP668 OUTCOME OF KIDNEY TRANSPLANTATION IN HEPATITIS C INFECTED PATIENTS: A SINGLE CENTRE STUDY

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Introduction and Aims: Hepatitis C Virus infection is not uncommon in patients of CKD on Haemodialysis. The incidence of HCV infection in our haemodialysis population is 10%. It has been documented that Transplantation (Kidney) gives a survival benefit than dialysis to even to HCV infected patients. It also significantly improves the quality of life. Ours is a large dialysis and transplant unit. We do around 3500 sitting of dialysis per month and 200 kidney Transplantation in a year.

Methods: We retrospectively analysed the HCV infected patients who received Renal Transplantation from January 2007 to December 2011. Over a period of five years 25 Transplants out of 642 Transplants (with live kidney donors) had HCV infection pre Transplant. All these patients had HCV RNA PCR quantitative and Genotype study pre Transplant. 16 of these patients received Peg Interferon varying from one to three months pre transplantation. The rest did not receive interferon for either economic or medical reason. Cirrhosis of Liver was excluded in all patients.

Results: Two of the patient received ATG on induction because of previous crossmatch positivity. The rest of the patients received Cyclosporine, Prednisolone and Mycophenolate on induction. Though in four of them Cyclosporine was converted to Tacrolimus for rejection. The acute rejection rate was 20%, which was more than the other transplant recipients (8%) in our centre. Two of the acute rejection patients needed ATG treatment. And one needed Plasmapheresis and IVIG therapy because of TGT for severe antibody mediated rejection. The One year patient survival was 92%, comparable to the other transplant recipients (97%). Both the deaths were due to severe Pneumonia. The One year death censored Kidney survival has been 100%. The incidence of NODAT has been less (12%), less than the non HCV infected patients (15%) possibly because of non use of Tacrolimus in this group. Besides mildly deranged Liver function in four patients, none had any significant liver disease in one to six years of observation.

Conclusions: We conclude that the kidney survival and patient survival in HCV infected patients is nearly similar to HCV negative patients after living donor kidney transplantation. In short term observation they donot suffer from any other ailments after transplantation.

MP659 OUTCOMES OF LIVING UNRELATED ABO BLOOD TYPE INCOMPATIBLE KIDNEY TRANSPLANTS

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Introduction and Aims: Due to the severe shortage of deceased-donor kidneys in Japan, ABO incompatible (ABoI) living donor kidney transplantation (LKT) has been performed since the late 1980s. Recently, ABO LKT has been performed in patients with various backgrounds such as unrelated combinations. We compared the results of ABOI unrelated LKT with those of ABO related LKT.

Methods: Thirty-four consecutive ABOi LKT recipients were included. Patients were divided into two groups: G1 (unrelated donors, n=23), G2 (related donors, n=11). Mean recipient/donor age was 57.1±7.5/56.7±8.2 yrs in G1 and 39.8±14.5/57.9±11.1 yrs in G2. Mean duration of dialysis was 54.0±58.2 months in G1 and 24.6±24.2 months in G2, respectively. We compared the difference in the patient and graft survivals, and complications, such as acute rejection, cytomegalovirus antigenemia, and surgical complications between the groups. All patients received desensitization with plasmapheresis until pre-transplant ABO IgG titers became <16. Seven patients of G1 and 5 patients of G2 received rituximab before transplantation and others underwent spleenectomy at the time of transplantation.

Results: The patient/graft (death censored) survivals were 100%/100% at 1 year and 91%/100% at 3 years in G1, 100%/100% at 1 year and 91%/100% at 3 years in G2. Acute rejection occurred in 5 (22%) of G1 and 3 (27%) of G2. The incidence of cytomegalovirus antigenemia was 70% in G1 and 73% in G2. Surgical complications occurred in 4 (17%) of G1 and 3 (27%) of G2. The serum creatinine levels at 1 and 3 years were 0.9±0.3 and 0.9±0.2 mg/dl in G1, 1.2±0.3 and 1.0±0.2 mg/dl in G2.

Conclusions: The patient and graft survivals, graft function and complications after LKT were the same in both groups. Unrelated donor kidneys had no negative impacts on the outcomes of ABOI LKT.

MP660 SAFETY OF LOW THYMoglobulin DOSES IN RENAL TRANSPLANT

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Introduction and Aims: Transplantation of kidneys from old donors is followed by an increase of delayed graft function (DGF) and acute rejection. In these circumstances, induction treatment with antithymocyte globulin or with interleukin-2 receptors blockers could delay the introduction of calcineurin inhibitors with effective prevention of rejection episodes. However, treatment with antithymocyte globulin has been associated with an increase in the development of infections and neoplasia. AIMS We analyzed the efficacy and safety of induction treatment of two low doses of thymoglobulin comparing to two doses of basiliximab.

Methods: We compared a group of 47 patients, treated with thymoglobulin, with 61 patients treated with basiliximab. The patients presented a minimum follow-up of two years. All of them received tacrolimus as calcineurin inhibitor. Thymoglobulin group received two doses of 1.25 mg/kg on alternate days, and basiliximab group two doses of 20mg.

Results: Despite a higher donor and recipient age in Thymoglobulin group, no differences were observed in relation with incidence of DGF (p=0.938). Only 1 rejection (2.3%) was diagnosed in thymoglobulin group, but 12 patients (20 %) were diagnosed in basiliximab group (p=0.008), and three of them needed rescue treatment with thymoglobulin. We did not find any differences in the incidence of CMV disease (p=0.59), admission due to infections (p=0.428), urinary tract infection (p=0.278) and neoplasia (p=0.709). There was not any case of lymphoproliferative disease in both groups. We did not observe any differences in graft (p=0.74) and patient (p=0.71) survival.

Conclusions: In our series, low thymoglobulin doses are not associated with a higher risk of infection and neoplasia compared to basiliximab treatment in long term follow-up. Similar survival was observed, in spite of higher donor and recipient age in thymoglobulin group.
did not meet the NICE guidelines.

Conclusions: Renal Transplant patient should be assessed for risk of NODAT and risk factors should be addressed. Patients at risk of NODAT would benefit from strategies including exercise programme pre and post transplantation, tailoring immunosuppressive therapy (early steroid withdrawal and rationalized Tacrolimus usage) and a multidisciplinary approach with close liaison with the diabetic team.

National guidelines specific for NODAT may be helpful.

**MP662 POST-TRANSPLANT ANAEMIA AS AN INDEPENDENT PREDICTOR OF MORTALITY. A 10-YEARS FOLLOW-UP STUDY**

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Introduction and Aims: Findings on the association between anaemia and mortality in post-transplant patients are scarce. This study therefore explored whether post-transplant anaemia (PTA) shortly after kidney transplantation (KT) predicts mortality at up to 10 years follow-up.

Methods: We performed a prospective observation cohort study of 318 patients (58% of male; average age 47.9±12.2 years) between the 3rd and 12th month after successful KT. Demographic and clinical data were retrieved from medical records. Estimated glomerular filtration rate (eGFR) wascalculated using the CKD-EPI formula. PTA was divided into 3 categories according to the haemoglobin (Hb) level: 1) severe PTA (Hb<10 g/dl), 2) mild PTA (Hb 10-11.9 g/dl) and 3) no PTA (Hb≥12 g/dl). The observation period was up to 10 years follow-up. Cox regression was used to identify whether different categories of PTA predicted mortality in KT recipients.

Results: Older age (HR=1.1, p<0.001), male gender (HR=2.2, p<0.05), worse eGFR (HR=1.0, p<0.01) and severe PTA (HR=10.0, p<0.001) contributed significantly to this model on mortality. The risk of death in patients with severe PTA starts to rise at 3 years after KT.

Conclusions: Severe PTA compared to no and mild PTA in the first year post-transplantation indicated a 10-fold higher risk of mortality during 10 years follow-up. PTA should be closely monitored in patients post kidney transplantation and patients with PTA should undergo clinical investigation and treatment (e.g. Erythropoiesis Stimulating Agents, iron therapy, etc.) to reduce their high risk of mortality.

**MP663 FIRST 50 BLOOD TYPE ABO INCOMPATIBLE KIDNEY TRANSPLANTATIONS, SINGLE CENTER EXPERIENCE**

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Introduction and Aims: Blood type O patients are at a disadvantage for matching with a compatible blood type kidney donor in donor exchange programs compared to blood type A or B patients. In recent years protocols have been developed that allow for transplantation of ABO blood type incompatible (ABOi) kidneys without the need for plenectomy. These less invasive protocols aim to desensitize the patient pre-transplantation and have greatly improved graft survival. This study describes the single center experience in the Netherlands of ABOi kidney transplantation.

Methods: Four weeks pretransplantation patients received a single dose rituximab and started triple immune suppression (ciclosporin, mycophenolate mofetil, prednisolone), two weeks later. Immunosuppression (IA) through columns with either synthetic A or B antibodies was performed in the week before transplantation. The frequency of IA depended on the height of the anti donor blood type antibody titers at the start of the protocol and the objective was to lower the titer to <1.8 the day before transplantation. Fifty patients received a ABO kidney transplant in a period from 2006 to 2012. We matched 100 blood type ABO compatible controls for age of donor and recipient during the same period.

Results: In the ABOi group a very high percentage (86%) of the patients had bloodtype O, compared to only 39% in the control group. The donors had bloodtype O in 60% of the controls. This illustrates the donation of O donors (60-39=21%) in every ABOi program, this is why O recipients can fall behind on the waiting list. Within the first week, 11 antibody mediated humoral rejection were noted of which 3 were mixed reactions humoral and cellular mediated rejection. Also 9 cellular mediated rejection occurred, mostly within the first week after transplantation.

During the first year two grafts were lost due to rejection. One year graft survival and renal allograft function of the ABOi grafts were similar to 100 matched ABO compatible renal grafts, 96% vs 99%. During our 5 year follow up period graft survival was 96% in the ABOi vs 97% in the control group. Adverse infections events specifically related to the ABOi protocol were not observed.

Conclusions: The currently used ABOi protocol shows good short and long-term results despite a relatively high frequency of humoral rejection. It facilitates an optimal use of the available living kidney donors and the bloodtype O patient especially from this program.

**MP664 DEVELOPMENT OF A DEDICATED CARE PATHWAY FOR MANAGEMENT OF THE FAILING TRANSPLANT**

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Introduction and Aims: Patients with failing transplants represent a unique group as a result of immunological, non-immunological and psychological factors which all impact on patient subsequent co-morbidity. In 2005 we reported the outcomes of our failed transplants over a 10-year period (Renal Association, UK). The majority were starting renal replacement with an average eGFR of 7mls/min/1.73m2 (less than Renal association (RA) guidelines for the non-transplant population). A number were poorly adjusted psychologically and had significant co-morbidity. We proposed it essential to have a well-defined pathway for patients with failing transplants, intercalated into existing care pathways for patients with end-stage renal failure (ESRF).

Methods: Between the years 2008 and 2012, a total of 27 patients with transplant patients reached end stage. Patients found to have grafts with progressive irreversible worsening renal function were cohorted as low clearance patients in a dedicated clinic for intensified management. Patients were flagged and all team members were made aware. A multidisciplinary approach: targeted medical/nursing/psychological/dietary input were made available early on, in one visit where required a “one-stop-shop”.

General practitioners were also integrated early on to support transition and to ensure hepatitis B vaccination were administered and appropriate.

Results: T: patient age ranged: 13-71 years, male: female ratio (70.4%: 29.6%). 70.3% Caucasians, 7.4% Black, 74.8% Asians and 11.1% others. The aetiology of primary renal disease was variable and not necessarily related to the cause of the failing transplant. Transplant age ranged: 3 to >15 years. The eGFR on establishing therapy was calculated at 12.1±3.12mls/min/1.73m2. Pretransplantion patients had an identitied by 40.7%, 55% of these received transplants either pre-emptively or within a year of transplants reaching end stage, 9 started pre-planned peritoneal dialysis, 1 conservative care, 13 started haemodialysis, 6 had preformed functioning fistulae & 3 tunnelled lines because of imminent transplants, 2 were unexpected failures and 1 was excluded from analysis as was lost to follow-up & presented via intensive care in end stage.

Conclusions: These patients have special needs and may require psychological input in addition to the attention given to nutrition, biochemistry, anaemia and medical co-morbidities. By establishing a special focus clinic to cohort patient care we have been able to provide management, which meets the standard of care requirements of the RA and other established guidelines for managing ESRF patients due to other causes. We support development of guidelines for managing this unique group of patients, as they represent a growing population.

**MP665 DENGUE INFECTION IN PATIENTS WITH RENAL TRANSPLANT: A REAL PROBLEM IN PARAGUAY**

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Introduction and Aims: Dengue fever infections can be asymptomatic, or can produce undifferentiated fever, Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS). The virus transmission by blood products or by organs of a donor in transplant is a possibility that has been reported in the medical literature before. The goal of this work has been to evaluate the behavior of the Dengue Fever in kidney transplanted patients with a compromised immune system, in an endemic zone as Paraguay.


Results: From a total of 135 patients that had kidney transplantation, 8 (6%), presented dengue fever infection in this period of time. There were 3 female and 5 male patients with an average age of 45.6±15.1 years old and a time of presentation of the disease of 41.8±80 months after the renal transplant. 2 (25%), presented the disease in the immediate post-transplantation period. All cases were seen in their first transplant, 3 out of living donors and 5 of cadaveric donors immune suppression: Miconofolic Acid-Prednison (100%), Cyclosporine (38%), Tacrolimus (62%). The symptoms were: Fever (100%), malaise (80%), myalgia (80%), headache (66%), shock (38%), bleeding
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PRE EMPTIVE KIDNEY TRANSPLANTATION

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Introduction and Aims: This study was to investigate the outcome of native kidney originated pre-transplant proteinuria after transplantation. Methods: Forty eight adult patients (33 men, 15 women; transplanted between 1999-2011) with proteinuria ≥500 mg/day within preceding 3 months before transplantation were included. Data was collected from the medical records. Results: The median pre-transplant proteinuria was 1953.29 mg/day (500-7006.6). One month after transplantation more than 50% decline in proteinuria (proteinuria reduction ratio;PRR≥50%) was observed in 43 (89.6%) patients. One patient had 76% decrease and 1 patients had a fall of 66.8%. Four patients died, PRR of these patients were lower than 20%. Infection was the cause of death in 3.3% of the patients and type 1 diabetes was the most common cause of death. Conclusions: Proteinuria immediately after renal transplantation may originate either from native kidneys in patients with residual renal function at the time of transplantation or from diseases emerging in the allograft. Knowing the source and course of post-transplant proteinuria is essential for proper management. The aim of this study was to investigate the outcome of native kidney originated pre-transplant proteinuria after transplantation.

EFFICACY AND SAFETY OF OUTPATIENT RABBIT-ANTITHYMOCYTE GLOBULIN INDUCTION IN DE-NOVO KIDNEY TRANSPLANT RECIPIENTS

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Introduction and Aims: In an effort to minimize hospital length of stay (LOS), our center instituted outpatient (outpt) administration of rabbit antithymocyte globulin (ATG) post transplant. Methods: We included 63 patients who were PTK and compared them with 84 patients on dialysis for > 6 months between Feb 2010 and April 2012. All patients had follow up of minimum 6 months. Immunosuppression protocols in PTK was tacrolimus+mycophenolate and steroids in 34 (52%) of patient, steroid free (SF) protocol with antibody induction+Tac and MMF in 27 (44%) and Tac+ara aza+ steroids in 2 patients. Immunosuppression in dialysis group was Tac+MMF+St in 56 (66.8%), steroid free protocol in 18 (21.6%) patients, Cyclosporin+MMF+St in 5 (5.7%) and 5 patients received Tac+Aza+ Steroids. They were started on tacrolimus at a dose of 0.1 mg/kg or cyclosporine 7 mg/kg in two divided dose and MMF/Mycophenolate sodium at doses of 1000 mg/d transplanted on day 1 of transplantation. All patients required hemodialysis up to 60 ml/m2. In dialysis group methylprednisolone 500 mg perioperatively. In SF group tab prednisolone was initiated on day 1 at a dose of 40 mg, tapered and stopped on day 5. In steroid group prednisolone was gradually tapered to a dose of 5-7.5 mg at 3 months. Graft biopsy was done when rejection was suspected. Target trough level of tacrolimus was kept between 8-12 ng/ml in first three months, 6-8 ng/ml for next 6 months and 3-6 ng/ml thereafter. Outcomes were evaluated in terms of acute rejection, infections, new diabetes after transplant, and graft or patient loss.

RESULTS: The baseline characteristics like age, sex, duration of follow up, donor’s age, HLA mismatch and basic disease were similar in both groups. Antibody use for induction was similar in both groups 42/63 in PTK vs 46/84 (p=0.14). Significantly higher number of patients in dialysis group had pre transplant hepatitis C, 10(13%) as compared to only 1 (1.5%) in PTK group (p=0.019). The incidence of acute rejection was 15% in PTK vs 16% in dialysis group (p=0.81) in both groups. In PTK group 1 patient lost his graft and one died (survival 98.4%), as compared to 4 graft loss and 4 deaths (survival 95.2%) in other group.

Conclusions: PKT is associated with less chances of dialysis related complications like chronic viral hepatitis and CAD. However there was no difference in graft and patient survival in this short term study. Longer follow up is required to see difference in these outcomes.

REFERENCES

transplantation from a HBSAg (+) donor to a HBSAg (-) recipient. Methods: Transplant candidates without protective titer (≥10mIU/ml) of anti-HBs antibody were given hepatitis B vaccination to develop protective level of antibody. Virus DNA quantitate to be undetectable by real time PCR before transplantation. Recipients were also given entecavir before and during 3 months after transplantation for prophylaxis. Hepatitis B immune globulin was injected intravenously to recipients in the morning of transplant day. Results: Six living donor kidney transplantations in 5 patients from HBsAg (+) donor to HBSAg (-) recipient were performed. In 5 transplantations, recipient had protective titer of antibody at initial presentation. One patient had a low titer of anti-HBs (7mIU/ml), which was raised by hepatitis B vaccine to protective level (15mIU/ml) before transplantation. All the recipients had undetectable HBV DNA after transplantation and remained HBSAg (-) anti-HBs (+) during the median follow up of 25(8-48) months. Conclusions: Kidneys from HBsAg (+) living donors can be safely transplanted to HBSAg (-) recipients.

**NUTRITIONAL STATUS AND CARNITINE LEVEL IN KIDNEY TRANSPLANT RECIPIENTS**

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Introduction and Aims: Overweight and obesity are common in subjects after kidney transplantation. On the other hand, signs of malnutrition and abnormalities in carnitine metabolism are recognized in this group of patients. The aim of the study was to evaluate the prevalence of nutritional status abnormalities in a cohort of stable kidney transplant recipients (KTx). We also investigated associations between nutritional status, graft function and carnitine concentrations.

Methods: 80 (55m/35f) prevalent kidney transplant patients 52.4 ±13.9 years of age (without carnitine supplementation). Body composition (% of fat, lean body mass (LBM), water content) was measured by multifrequency bioelectrical impedance (Body Composition Monitor). Nutritional status was determined by a 7-point Subjective Global Assessment (SGA), anthropometric measurements and s-albumin concentration. C-reactive protein (CRP), IL-6 and plasminogen activator inhibitor - 1 (PAI-1) were used as markers of inflammatory status. Urinary excretion and serum concentration of total (TC), free (FC) carnitine were measured using enzymatic methods according to Cederblad.

Results: Diabetes mellitus was present in 29% (n= 23) of KTx patients. Mean KTx vintage was 82.5±56.5 months (median = 73 months). Mean eGFR was 41.7±14.9 ml/min/1.73 m2), BMI was 25.7 ± 4.2. Overweight and obesity were noticed in 41% and 14% of pts, respectively. Malnutrition was observed in 21.3% of the KTx subjects. Signs of malnutrition was present in 64% (21/33) of the overweight patients and in 91% (10/11) of the obese patients. KTx patients with malnutrition (SGA ≤ 5 points) were significantly older, with longer transplantation vintage, presented lower level of eGFR, higher BMI, higher body fat and decreased hand grip strength in comparison to KTx patients with good nutritional status. In 8.6% of KTx patients deficiency of FC (in serum and urine) was observed Carnitine (TC and FC) and PC/TC ratio not correlated with anthropometric and laboratory parameters of nutritional status. Serum levels of TC and FC were negatively correlated with graft function (eGFR).

Conclusions: 1. The prevalence of overweight/obesity was high in the studied cohort of KTx recipients. 2. In spite of overweight/obesity KTx patients showed signs of malnutrition.3. KTx patients need thorough nutritional evaluation and appropriate nutritional interventions.

**ANALYSIS OF CORPORAL COMPOSITION BY BIOIMPEDANCE SPECTROCOPY IN KIDNEY TRANSPLANT PATIENTS**

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Introduction and Aims: Kidney transplantation is often associated with weight gain, increased fat tissue and sometimes with metabolic syndrome. The objective of the study is to analyze the effect of renal transplantation on patient's body composition.

Methods: This is a retrospective study in which we analyze a population of 169 patients with functioning kidney graft and a mean age of 56.2±13.6 years, of whom 56.2% were male. 48.8% were diabetic and 31.3% had received another kidney transplant. 21% had had at least one episode of acute rejection and 27% were treated with ESAs. In 47 patients (27.8%), steroids were discontinued completely during the follow-up period. In all patients, we analyzed body composition using bioimpedance spectroscopy (BCM, FMC - ’), collected data on overweight (OH) with respect to the water content of normohydrated tissues, total body water (TBW), extracellular water (ECW), and intracellular (ICW) as well as body composition data: lean mass (LTM) and adipose mass (ATM). Differences were calculated with respect to reference values
adjusted for age, sex, body composition. Lean tissue (LTI) and fat tissue indexes (FTI) were calculated (kg/m²). Renal function is determined by the CrCl.

**Results:** Patients had an average OH 0.91 ± 1.65 liters, equivalent to a state of relative overhydration (OH / Hb% 4.9 ± 8.9%). The OH is inversely related to the fat content (r = -0.405, p < 0.001) and CrCl (r = -0.20, p = 0.019), but unrelated to blood pressure. Patients exhibited a higher FTI 5.0 ± 5.8 Kg/m² vs reference values. Relative adipose tissue ratio (ATM / weight %) directly correlates with the CrCl (r = -0.196, p = 0.057). ATP is unrelated to the duration of steroid therapy. The FTI and adipose tissue differences with respect to the reference were significantly higher in patients in whom steroids had been withdrawn, which can be interpreted as a prescription bias in drug withdrawal. Decreased renal function is significantly associated with increased hydration (p = 0.013), higher systolic BP (p = 0.003) and lower fat mass (p = 0.023). We did not find differences in body composition when comparing between patients with or without previous acute rejection history.

**Conclusions:** We conclude that renal transplantation has an important impact on body composition, and is related to moderate hyperhydration and increased fat mass. Controlled studies are needed to assess possible interventions in order to modify these changes.
polyethiologal infection (3-4 microorganisms) and 16.2% had pulmonary tuberculosis. The most common clinical signs of PI were fever (100%), dyspnea (61.3%), and general fatigue (54.8%). Chest CT scan most often revealed consolidation (74.4%), ground-glass opacity (73.7%), local pneumothorax (45.4%) and mediastinal lymphadenopathy (45.5%). Overall mortality rate was 35.5%. The highest mortality was observed in patients with severe polyethiologal pneumonia. PI had a great negative impact on recipients and RT survival. Significant risk factors for PI were delayed graft function (OR 3.31, p = 0.014), chronic graft dysfunction (OR 3.48, p = 0.002), acute rejection of RT (OR 3.72, p = 0.004), treatment with antilymphotic antibodies (OR 2.96, p = 0.011), CMV infection (OR 4.39, p = 0.002), EBV infection (OR 3.49, p = 0.009) and leukaemia (OR 5.76, p = 0.0002).

Conclusions: Identifying patients with risk factors and careful clinical monitoring, posttransplant chemophrophylaxis with valganciclovir and trimethoprim-sulfamethoxazole, early diagnosis and early treatment are necessary to decrease the incidence of severe pneumonia and mortality from PI in RT recipients.

WHY ARE PATIENTS UNDER 60 YEARS NOT WAIT-LISTED FOR TRANSPLANT? A RETROSPECTIVE SURVEY

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Introduction and Aims: Patients under 60 who require renal replacement therapy (RRT) have longer survival and improved quality of life with transplantation. However, not all patients under the age of 60 are put on the transplant waiting list. Many of these patients will be unsuitable due to co-morbidities such as heart disease, obesity, diabetes or malignancy. We were interested to see on what grounds patients were not being listed and if these were improving. We are also looking at any improvements in the care of patients suitable for transplantation are offered appropriate treatment options.

Methods: We looked at patients under 60 years old newly started on RRT at our hospital from 1st January 2005 to 31st December 2008. This list was obtained from the PROTON data recording system. The gold standard for comparison was the Renal Association/British Transplant Society Module 4: Assessment for renal transplantation. We used PROTON to find patient demographics (age and sex), co-morbidities (diabetes, cardiovascular disease, respiratory disease, malignancy and obesity) and time between starting RRT and becoming active on the transplant waiting list. Where data entry on PROTON was limited we reviewed the patient’s written notes for further information.

Results: 221 patients fitted the entry criteria. Of these, 137 (62.0%) were wait-listed within 2 years of starting RRT. However, 84 (37.9%) were not wait-listed within 2 years of starting RRT. There was a significant difference in age between those listed (average age 44.4 years, SD 10.9 years) and those not listed (average age 48.7 years, SD 9.2 years). 30 (42.1%) of those not listed had diabetes (type 1 or type 2) as their primary renal disease, compared to 28 (20.4%) of those suitable for listing. Of the 42 type 1 diabetics, 27 (64.2%) were wait-listed, but only 19 (70.3%) of these were listed within 2 years of starting RRT.

Conclusions: Patients with under 60 years of age who require renal replacement treatment but are not wait-listed for transplantation should be reviewed urgently. It is important that all patients who require RRT are assessed for transplantation appropriately.

CONCORDANCE OF ESTIMATED GLOMERULAR FILTRATION RATES BY DIFFERENT FORMULAS IN RENAL TRANSPLANT RECIPIENTS

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Introduction and Aims: Different equations have been used to estimate the glomerular filtration rate (GFR) in renal patients, including kidney transplant recipients. A controversy exists concerning which of these equations is more precise and exact to determine the degree of kidney failure. To analyze the concordance (bias, variability and exactness) of the GFR as estimated by the Modification of Diet in Renal Disease (MDRD4) and the Chronic Kidney Disease Epidemiology (CKD-EPI) equations using the Cockcroft-Gault (CG) method as the reference.

Methods: This observational, cross-sectional study included 153 clinically stable patients who received a kidney transplant between 2007 and 2009. The GFR was estimated 12 months after the transplantation by MDRD and CKD-EPI formula, using CG as the reference.

Results: The mean GFR for the various methods was: CG=65.6±23.3 ml/min/1.73 m², MDRD=54.5±19.3 ml/min/1.73 m², and CKD-EPI=55.8±19.6 ml/min/1.73 m². Good correlations were found between CG–MDRD4 (r=0.84; P<0.001), CG–CKD-EPI (r=0.87; P<0.001), and MDRD4–CKD-EPI (r=0.98; P<0.001). The analysis of concordance detected a bias (normal difference/SD) of –10.6±12.7 vs. –9.8±11.3 ml/min/1.73 m² (P<0.001), a variability (interquartile range of the differences) of 14.3±15.4 vs. 13.6±14.5 (P<0.001), and an exactness (P30) of 81.7% vs. 86.9% (P<0.001) of CG–MDRD versus CG–CKD-EPI, respectively. For a GFR>60ml/min/1.73 m² the exactness was 75.3% vs. 83.5% (P<0.001) for CG–MDRD versus CG–CKD-EPI, and for a GFR<60 ml/min/1.73 m² the exactness was 89.7% vs. 91.2% (P<0.01).

Conclusions: In our population the CKD-EPI method most approached the CG values. This was more evident when the patients had a GFR>60 ml/min/1.73 m².
Abstracts

**PD 48.8 (37-76) 1.3 (28/22 4.31±3.22 259.5 22.5 7.76±1.18 7.420**

**HD 49.8 (22-75) 0.92 (24/26) 14.09±17.24 220.5 23.1 7.92±1.19 7.658**

Inflammatory cytokines levels were increased in recipients. Use of CNI in these patients

**Conclusions:**

There has not been a study on this subject in kidney transplant recipients. In experimental studies, regulatory and conventional T cell homeostasis effects of CNI’s

**Conclusions:**

In this study we retrospectively investigated 200 CKD patients consists of 50 stage 3-4 CRF patients, 50 HD patients, 50 PD patients and 50 Rtx patients. Included
patients were between 18 and 76 years of age who followed in our outpatient nephrology clinic. The collected data included demographic properties, platelet count, MPV, C- reactive protein (CRP), hemoglobin, ferritin, body mass index. The patient groups were matched in age and sex. All of the patients were at least 6 month of therapy of either renal replacement modality.

Results: Patient characteristics and results were given in Table 1. Mean CRP value of HD, PD, Rtx and CRF stage3-4 were detected as 14.09±17.24, 4.31±3.22, 5.99±6.88 and 7.62±8.63 accordingly. Mean CRP value was detected statistically significantly higher in HD patients compare to PD, Rtx and CRF stage3-4 patients (p<0.001, p<0.001 and p=0.005 in orderty). There was no statistically significant difference detected among mean MPV value of all the patient groups (p=0.05).

Conclusions: In conclusion, we detected that hemodialysis patients were in an increased state of inflammation compare to other groups of the patients according to CRP. We did not detect such a significant difference for MPV between the groups. We speculated that hemodialysis patients had an increased inflammatory state and MPV does not have a predictive value to indicate this inflammation in CKD patients.

**IMPACT OF RENAL IMPAIRMENT ON LIVER TRANSPLANT PATIENTS - THE BONN EXPERIENCE**

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Introduction and Aims: Orthotopic liver transplantation (OLTx) nowadays is a common treatment for patients with end stage liver disease. However, renal insufficiency may be crucial for the outcome. We performed a retrospective study to evaluate the impact of renal function before and after OLTx on patients mortality.

Methods: In this study we identified a cohort of 146 patients with end stage liver disease who underwent OLTx between 2004 and 2011 at our centre. Mean age was 51.6 years (18 to 71 years). Patients with polycystic liver disease were excluded. Follow up was 12 months. We assessed renal function using modification of diet in renal disease (MDRD IV) formula prior and after OLTx. Renal function was considered mildly impaired when glomerular filtration rate (GFR) was 60-89 ml/min, moderately impaired when GFR was 30-59 ml/min and severely impaired with GFR<30 ml/min. Patients outcome was analyzed with Kaplan-Meier survival curves and multivariate Cox hazard analyses.

Results: Prior OLTx the majority of patients (73.7%) had a GFR < 90 ml/min, of those 26.5% were on dialysis and 27.8% had a GFR < 30 ml/min. The remainder (26.3%) had normal renal function (GFR > 90 ml/min). Average eGFR of non-dialysis patients was 69.7 ml/min/min +/- 33.1 (median: 61.7 ml/min; 95% CI: 52.2-69.4 ml/min). During the observation period 58.4% of patients required dialysis therapy. Mortality was 69.7 ml/min +/- 33.1 (median: 61.7 ml/min; 95% CI: 52.2-69.4 ml/min). During

Conclusions: The study demonstrates that there are discrepancies between MRA and operative findings. Although there are no national recommendations, we believe that our study demonstrated that there are discrepancies between MRA and operative findings. Although there are no national recommendations, we believe that our study demonstrated that there are discrepancies between MRA and operative findings. Although there are no national recommendations, we believe that our study demonstrated that there are discrepancies between MRA and operative findings. Although there are no national recommendations, we believe that our study demonstrated that there are discrepancies between MRA and operative findings. Although there are no national recommendations, we believe that our study demonstrated that there are discrepancies between MRA and operative findings. 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Methods: All kidney transplants performed in type 2 diabetic patients, from July 1983 to December 2009 in our centre, with a graft survival over 3 months, were included. Non-diabetic controls were individually matched with diabetic patients with respect to gender, age, year of transplantation, number of donor HLA mismatches and dialysis vintage. The two groups were compared concerning patient and graft survival, delayed graft function (DGF) and prevalence of acute rejection (AR).

Results: We included 62 type 2 diabetics and 62 non-diabetic patients who were followed for a mean period of 102±64 months after KT. Diabetic patients and controls were similar for the matched variables. Graft survival censored for patient death for diabetics and non-diabetics was 70 and 83% at 5 years and 54 and 71% at 10 years, respectively (log rank test p=0.38). Occurrence of DGF did not differ (X² test p=0.12). Using multivariate Cox’s proportional hazards analysis, DM (HR=7.72, p=0.001) and hepatitis (HR=4.16, p=0.02) correlated with reduced patient survival.

Conclusions: Diabetic patients’ survival after KT was reduced when compared with non-diabetic matched patients. However, censored graft failure was similar between the two groups. Concerns about graft survival should not prevent KT in diabetic patients with kidney failure.

Introduction and Aims: Hypomagnesaemia is a known side effect of immunosuppressive regimes, especially calcineurin inhibitors, and has been associated with new onset diabetes after transplantation (NODAT), decreased graft survival in chronic cyclosporine nephrotoxicity and vascular stiffness. Proton pump inhibitors-induced hypomagnesaemia has been described recently, although its relevance in renal transplant recipients is still unknown.

Methods: We conducted a single center cross-sectional retrospective study of renal transplantations performed between 2006 and 2011 in order to evaluate the impact of low serum magnesium (Mg) levels in patient and graft outcomes. Serum Mg levels 1-year after renal transplantation were available for 316 patients.

Results: The median follow-up was 1062 days (range, 284 – 2287). Patients were divided into four groups, based in quartiles of serum Mg levels, and no significant differences were found regarding sex, age, pretransplantation cholesterol, albumin, triglycerides, body mass index, donor age and type, immunosuppressive regimen, use of Mg supplements, delayed graft function, acute rejection, CMV and HCV infection, or NODAT development. Patients with Mg < 1.6 mg/dL (n=81) had a higher frequency of prolonged (> 1 year) proton pump inhibitors use (90% vs. 81%, p=0.04), when compared to patients with Mg > 2 mg/dL (n=81). Using Cox multivariate regression analyses, adjusted for recipient age, donor age and type, immunosuppressive regimen, diabetes, NODAT and presence of acute rejection, graft survival was significantly reduced in the low Mg group after 4.6 years posttransplantation (p=0.001).

Conclusions: Hypomagnesaemia 1-year posttransplantation, possibly related to prolonged use (> 1 year) of proton pump inhibitors, is associated with decreased graft survival in renal transplant recipients.

Introduction and Aims: People information is the most important thing to obtain their participation in transplant process. We designed an outreach project about transplant-donation aimed to inform about the process at high school students in our province: Girona (Spain).

Methods: We developed our project over 8 years (2002-2010), offering our informative lesson performed by health professionals: nurses and doctors from the coordination department to high-school students. We went to the classrooms of students seeking a direct approach sometimes accompanied by transplant recipients talking about their own experience. We used blackboard and chalk as a communication way with students and we seek their participation conducting a seminar on the topic.

Results: Throughout this period we visited 46 different public and private institutes in 175 occasions. 418 lessons (83.6 every course) were given. We analyse the opinions of our high school students through 16.842 inquiries collected: 9140 before the briefing and 7702 after it. We compared results between gender, place of residence (urban or rural), isolated mountain areas or coastal areas with greater population mix.

Conclusions: Females, students from public institutes and urban population near mountain areas are more favourable to donation. Our method has been well received by students and teachers. 86.9% of the institutions asked for the lessons to be repeated 3 or 5 times more. The method is close, direct, easy and participative, with a greater impact on their mind. Additionally, in these times of crisis, the method is less expensive compared to others using modern technology.
the practice patterns for transplant wait-listing that exist across the UK, and understand the perceived barriers of key stake holders.

Methods: Semi-structured interviews were conducted with 45 ‘key stakeholders’ involved in transplant listing (including clinical directors, physicians, surgeons, and nursing staff) in a purposive sample of nine renal units across the UK. Units were stratified by data on degree of listing for transplantation, whether a transplant or dialysis centre and geography to include spread of deprivation and ethnicity. Interviews were recorded and transcribed verbatim. Double coding was performed to improve validity of coding and thematic analysis undertaken using NVivo 10.

Results: Thematic analysis identified a series of themes which included the role of cardiac services, with recipient cardiac work-up being a major source of ambiguity and delay. Variation in cardiac service delivery and granularity seen in both interpretation of test results and management strategies, were also seen as a source of strain on interpersonal relationships and subject to variable resource issues. Pathways of care involving living donation and pre-emptive transplantation was another major theme which was seen to pose ethical and financial dilemmas, and was a source of both dispute and innovation. Staff fatigue was another major theme seen across many professional ranks, often linked to resource shortages, feeling unappreciated and helpless whilst receiving little professional support.

Conclusions: Reaching a consensus on cardiac work up and resolving areas of contention surrounding living donation are important in improving access to transplantation and equity. There is also a need to address the causes of staff fatigue in renal services and improving support provisions whilst promoting innovation. It is hoped that the results of this study will inform a national survey aimed at identifying centre practice patterns influencing access to transplantation.

MP692 A SURVEY OF DIALYSIS PATIENTS ATTITUDES ON ORGAN DONATION AND KIDNEY TRANSPLANTATION IN A TURKISH COMMUNITY

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Introduction and Aims: The most outstanding of renal replacement therapy is kidney transplantation (KT). However, there is no adequate information about dialysis patients’ thoughts on KT. This study investigated the opinions of chronic dialysis patients about KT. This study investigated the opinions of chronic dialysis patients about KT.

Methods: The study was performed in all dialysis centers in Bursa, Turkey, from January to December 2010. The response rate was 40%. 597 dialysis patients (547 on HD, 50 PD) were included in the study. We designed a questionnaire with many questions on attitudes toward organ donation and KT. The questionnaires were filled out in the course of face-to-face interviews by the same author.

Results: Chronic dialysis patients who wants KT was 414 (69.3%) and did not want KT was 183 (30.7%). Totally, 31 patients (14 - 2.3% had live donor KT and 17 - 2.8% had cadaveric KT) had a history of KT. While 60 patients (10%) did not want to have KT, 299 of them (50.1%) wants to receive from live donors and 238 of them (39.9%) wanted to receive from cadaveric donor. 70 (11.7%) patients had a live donor. Specification of live donor candidates stated in Graphic 2. Patients registered in the waiting list are 179 (30%) and the average waiting time of 2.84±2.1 years. While 90 of waiting list patients was stated that they did not called for any donors, 32 of them stated that they were called but they were found not suitable for KT nad 55 of them did not know the reason why they were not transplanted. While 212 patients (35.5%) wanted to donate their organs, 385 (64.5%) patients did not want. 342 (57.3%) patients thought that they could save the lives of other people by their bodies. Others states that they were on dialysis and their organs were not robust anymore. Dialysis because of kidney disease and solid organ others had already noted that entered. 38 (6.4%) patients’ relatives prepared organ donor card (10 mothers, 7 fathers, 10 siblings, seven wives and 4 others).

Conclusions: In spite of improvements in graft and patient survival rates, the number of cadaveric organ KT has not reached the desired level, and the number of patients on the waiting lists is increasing rapidly. Organ donation and KT will become our major concern in the very near future. As a result, dialysis patients are more informed for this issues. Organized training programs about KT should be organized for dialysis patients.
PAEDIATRIC NEPHROLOGY II

MP693
MATRICES METALLOPROTEINASES AND THEIR EXTRACELLULAR INDUCER (EMMPRIN) IN THE URINE OF CHILDREN WITH CHRONIC KIDNEY DISEASE

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Introduction and Aims: Renal interstitial fibrosis is a final common pathway in chronic kidney disease (CKD) progression, independent of its origin. Matrix metalloproteinases (MMPs) are known for their proteolytic activity, regulating extracellular matrix content and tissue remodeling. The increased serum levels of MMPs have been described both in children and adults with different stages of CKD, showing their role in arterogenesis, apoptosis and inflammatory cell migration. However, the knowledge about MMP excretion with urine and its potential applicability as indicators of interstitial fibrosis in that group of patients is limited. There are no results of such investigation in children. There are either no data on the impact that EMMPRIN (extracellular matrix metalloproteinase inducer) could have on MMP urine excretion in CKD patients. The aim of the study was to assess the concentrations of MMP-2, MMP-7, MMP-9 and EMMPRIN both in serum and urine of prepubertal CKD children and to analyse the potential relations between these parameters.

Methods: 41 children with paediatric CKD stages III-V were enrolled in the study; 23 age-matched subjects with primary nocturnal enuresis and normal kidney function served as controls. The concentrations of MMP-2, MMP-7, MMP-9, e-selectin, sFas and sFlt1 were assessed by ELISA, hCRP by nephelometry.

Results: The median serum values of MMP-2, MMP-7, MMP-9, EMMPRIN, e-selectin, sFas/sFlt1, were significantly elevated in CKD patients vs. controls. The urinary concentrations of all MMPs and EMMPRIN were markedly increased in CKD children when compared to the control group. The MMP-2 and MMP-9 levels in urine correlated significantly with the corresponding values in serum, whereas MMP-7 and EMMPRIN urine concentrations did not. All parameters examined in urine were related to serum levels of sFas/sFlt, e-selectin and the lipid profile.

Conclusions: The increased urinary levels of examined MMPs and EMMPRIN may indicate enhanced proteolytic processes and renal tissue remodelling, responsible for progression of interstitial fibrosis in CKD. In the case of MMP-7 and EMMPRIN those disturbances seem independent of enhanced serum activity of the corresponding enzymes. Significant correlations with indices of inflammation, apoptosis and dyslipidemia suggest that urinary MMPs and EMMPRIN could serve as easily accessible markers of CKD-related disorders. Urine MMP-7 and EMMPRIN concentrations may be used as independent indices of kidney-specific fibrotic changes.

MP694
UK STUDY OF LATE REFERRAL OF CHILDREN WHO DEVELOP ESTABLISHED RENAL FAILURE: IMPACT ON TRANSPLANTATION AND SURVIVAL

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Introduction and Aims: Early referral of children with chronic kidney disease (CKD) to a paediatric nephrology centre is recommended to minimise clinical complications related to CKD in childhood, and improve pre-emptive transplantation. In the absence of any existing data, this study aims to define late referral rates in the UK paediatric renal replacement therapy (RRT) population, and highlight its impact on transplantation and survival.

Methods: Using UK Renal Registry data we analysed all incident patients starting renal replacement therapy (RRT) aged >3months and <16years between 1996 and 2010. Late referral was defined as seeing a paediatric nephrologist less than 3 months from commencing RRT. Late referral rates were analysed across different demographic characteristics and their impact on transplantation calculated. Survival analyses was adjusted for gender, ethnicity, RRT modality and age at start of RRT A chi-squared test was used for group analyses.

Results: Of 1554 eligible patients, data completeness of 86.7% allowed analysis of 1347 patients. Overall late referral was seen in 25.5% (n=343) of patients. Late referral was significantly lower in males 20.18% (n=156) than females 32.75% (n=188), P=0.0001, and highest in the 3-months-2 years age group 31.61% (n=49) p=0.0005. Children diagnosed with established renal failure (ERF) of unknown aetiology had the highest late referral rate at 78.9% (n=41), p=<0.0001. No significant differences in late referrals were noted amongst different ethnic groups, paediatric centres, or when comparing rates over time. The proportion of children transplanted at 1 year of start of RRT was reduced in the late referral group at 45.1% (n=155) compared to 66.9% (n=672) in the control group, p=<0.0001. No child presenting late underwent pre-emptive transplantation compared to 28.1% (n=282) in the control group. p=<0.0001. Survival analysis adjusted for gender, ethnicity, RRT modality and age at start of RRT did not show any significant difference between groups.

Conclusions: A quarter of all children who develop ERF are referred late to nephrology units, with significantly higher rates in girls and those under 2 years old. These children have lower transplantation rates at 1 year from start of RRT and are unable to benefit from pre-emptive transplantation. There is a need to understand the reasons behind late referral, to help reduce it, and the potential exposure of children to clinical complications that accompany late referral.

MP695
EFFECT OF COOLING DIALYSATE ON HEART RATE VARIABILITY IN CHILDREN ON REGULAR HEMODIALYSIS

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Introduction and Aims: Cardiac autonomic neuropathy is a common finding in uremic children. Heart rate variability (HRV) analysis is a useful non-invasive tool for assessment of cardiovascular autonomic input. Cardiovascular disease is associated with significant mortality and morbidity in dialysis patients. The aim of this study has been to determine the effect of using lowered-temperature (cool) dialysate on cardiac autonomic function and intradialytic hypotension among children with end-stage renal disease (ESRD) treated with maintenance hemodialysis.

Methods: Warm (37°C) and cool (35°C) dialysate were used, for 3 months each, in 28 children (4-16 yrs old) with ESRD. Patients were compared regarding dialytic hypotensive episodes, echocardiographic parameters and HRV; assessed using computerized analysis of short term heart rate samples (1024 beats).

Results: Cool dialysate was associated with reduction of intradialytic hypotensive episodes (from 8.18±3.06 to 2.95±1.87 /3 months, p=0.0001) and increase in fractional shortening (from 32.5±8.4% to 40.6±7.8%, p=0.01). Short-term analysis of HRV revealed reduced heart rate, significantly increased mean and median RR as well as mean deviation of RR interval. On cool dialysate, phase space plots showing poor and very poor dispersion decreased from 92% to 58% of cases.

Conclusions: In children with ESRD, using cool dialysate is associated with improvement in left ventricular systolic function, hemodynamic stability and some HRV parameters. The long-term impact of this needs further study.

MP696
HYPERVITAMINOSIS A IS PREVALENT IN CHILDREN WITH CHRONIC KIDNEY DISEASE AND CONTRIBUTES TO HYPERCALCAEMIA

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Introduction and Aims: Vitamin A accumulates in chronic kidney disease (CKD), but the prevalence of hypervitaminosis A in children with renal disease is not known. Current guidelines for vitamin A intake in CKD children allow twice the Reference Nutrient Intake (RNI), are not evidence based and may lead to elevated serum levels of vitamin A. Some case studies have linked hypervitaminosis A with hypercalcaemia. We aimed to study the relationship between vitamin A intake, serum retinol and associated retinoids and serum calcium levels.

Methods: Serum retinol, its carrier proteins (retinol binding protein [RBP] and transthyretin [TTR]) and its metabolite retinol acid (all trans [ATRA] and 13-cis) were measured in 106 children with CKD stage 2-5, dialysis and post-transplant. Dietary vitamin A intake was assessed through a 3 day food diary.

Results: 25 children were in CKD 2-3, 36 in CKD 4-5, 23 on dialysis and 22 post-transplant. 53% had vitamin A intake above the RNI. Children receiving supplemental or exclusive feeding compared to diet alone had higher median intake of retinoids and serum calcium levels.

Conclusions: Serum retinol levels were noted highest in the 3-months-2 years age group 31.61% (n=49) p=0.0005. Children diagnosed with established renal failure (ERF) of unknown aetiology had the highest late referral rate at 78.9% (n=41), p=<0.0001. Survival analysis adjusted for gender, ethnicity, RRT modality and age at start of RRT did not show any significant difference between groups.

Conclusions: A quarter of all children who develop ERF are referred late to nephrology units, with significantly higher rates in girls and those under 2 years old. These children have lower transplantation rates at 1 year from start of RRT and are unable to benefit from pre-emptive transplantation. There is a need to understand the reasons behind late referral, to help reduce it, and the potential exposure of children to clinical complications that accompany late referral.

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normal range post transplant (p<0.001). High retinol levels were present even in children who received less than twice the RNI for dietary vitamin A. There was also an independent and graded association between eGFR and retinol levels: for every 10ml/min/1.73 m² fall in eGFR there was a 13% increase in retinol (p<0.001). In contrast, an inverse correlation between RBP and eGFR was observed (r=-0.01, R²=0.62) with positive correlation and RBP (p<0.05, R²=0.4). This trend was also seen for TTR. ATRA showed an inverse association with eGFR (p=0.001). In a multivariate linear regression model only serum ATRA and vitamin A intake by weight were significant predictors of serum calcium (adjusted R² 0.58; p<0.001). Intake of calcium and vitamin D and eGFR did not show multivariate associations. Finally, there was a strong linear association between serum retinol levels and high sensitivity CRF (p=0.001).

Conclusions: Hypervitaminosis A is seen in early CKD and increases significantly with eGFR decline. Serum ATRA and vitamin A intake are associated with hypercalcaemia. Hypervitaminosis A may also be a risk factor for inflammation in CKD patients. Revision of RNI for vitamin A in CKD may be indicated to reduce the risk of hypervitaminosis A and associated hypercalcaemia.
definition of glucose intolerance and the diagnosis of diabetes mellitus were based on the American Diabetes Association criteria.

Results: Six patients (29%) showed post-transplant hyperglycemia (4 glucose intolerance, 2 diabetes mellitus). Of these, three had pre-transplant glucose intolerance. However, eight pre-transplant patients with glucose intolerance showed a normal post-transplant OGTT. There was no association between the presence of pre- and post-transplant glucose intolerance. Higher post-transplant fasting glucose were significantly associated with lower 25-OH vitamin D levels (r=−0.608, p=0.012). Higher post-transplant 2-hr glucose were significantly associated with higher PTH levels (r=0.456, p=0.038). Post-transplant HOMA-IR levels were significantly higher than the pre-transplant levels (1.93±1.02 vs. 1.42±1.04, p=0.019); post-transplant insulin resistance was present in 2 patients (9.5%). Higher levels of post-transplant HOMA-IR were independently associated with higher CRP (p=0.001), higher SD scores of BMI (p=0.003) and lower 25-OH vitamin D (p=0.019).

Conclusions: Post-transplant hyperglycemia seems to be associated with vitamin D deficiency and hyperparathyroidism, but not with the presence of pre-transplant glucose intolerance. Obesity, inflammation and vitamin D deficiency appear to be the risk factors for insulin resistance after transplantation.

**MP700**

**QIN-Kid - A GERMAN REGISTRY FOR PEDIATRIC DIALYSIS PATIENTS**

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Introduction and Aims: In Germany, 16 out of 17 pediatric dialysis centers in the country are run by an incorporated association with charitable status. All centers work with a common computerized documentation system, which can be used as a data base for scientific analyses. As soon as informed consent by a legal guardian is obtained, all data can be transferred automatically to QIN-Kid, a German registry for pediatric dialysis patients.

Methods: Based on the data transferred to QIN-Kid, we analyzed several parameters in order to give a representative overview on the situation of pediatric dialysis patients in Germany. For the present study, the following categories were looked at: renal disease, current age of the patient, current height of the patient, blood pressure (percentage of patients with hypertension), body mass index (BMI) (percentage of patients with obesity), comorbidities (n=97), height (n=121), blood pressure (n=130). Results: In 132 patients at least one dialysis was documented between January and September 2012. In these patients, the following clinical parameters were documented: renal disease (n=91), comorbidities (n=97), height (n=121), blood pressure (n=130). All patients were grouped according to the type of dialysis most often documented (peritoneal dialysis, n=77; hemodialysis, n=32; home hemodialysis, n=1; undetermined, n=2). Almost half of the patients (48%) had a height <2 SDS. Systolic blood pressure was >90. centile in 38,9% of the patients. Looking at anemia parameters, hemoglobin was >10 g/dl in 16,5 % of the patients and ferritin was <100 μg/l in 24% and >500 μg/l in 24,8% of the patients. As to renal osteopathy, parathyroid hormone >300 pg/ml in 21,6% of the patients. Albumin, reflecting the nutritional state, was <35 g/dl in 27,6% of the patients.

Conclusions: Based on a common documentation system installed in 16 pediatric dialysis centers, QIN-Kid was started as a national registry in Germany. Aimed from being an ideal data base for future scientific analyses, this will contribute to quality improvement efforts in the care of pediatric dialysis patients.

**MP701**

**CHRONIC KIDNEY DISEASE STAGES 3-5 IN IRANIAN CHILDREN**

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Introduction and Aims: There is scarce epidemiological data on early and asymptomatic stages of chronic kidney disease (CKD) in children, especially from developing countries. In this study we investigated the frequency of CKD stages 3-5 among general students of Isfahan (a large province of Iran), and compared the findings with those derived from the main pediatric nephrology referral center of province.

Methods: This study was performed among 712 Isfahan school students (377 boys) aged 7-18 years, as part of the baseline survey of a national surveillance system. Blood samples were analyzed for blood urea nitrogen, creatinine and cystatin C. Gomeralur filtration rate (GFR) was calculated based on two 2009 Schwartz equations (the ‘updated’ and the ‘new’). CKD was defined as GFR<60 mL/min/1.73m2. Additionally, a retrospective analysis of clinical records of children with stages 3-5 CKD patients referred to main referral center of province from November 2001 to December 2011 was made.

Results: The mean age of students was 12.2±2.4 years. In students' screening, the frequency of CKD was 1.3% and 1.7% based on the updated Schwartz and the new Schwartz equation, respectively. The referral center survey revealed an annual incidence of 14.5 per million age-related population (pmpr), and a prevalence of 118.8 pmpr in our province.

Conclusions: The prevalence of asymptomatic and undetected low GFR in Iranian children is higher than what is reflected from the reports of referral centers. Simple screening programs like annual urinalysis among high risk school students should be considered.

**MP702**

**CARPEDIEM (MINIATURIZED CRRT EQUIPMENT FOR INFANTS): THE FIRST APPLICATION**

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Introduction and Aims: Acute kidney injury (AKI) is an independent risk factor for morbidity and mortality in critical ill children. Renal replacement therapy (RRT) is a cornerstone of therapy to correct uremia and fluid overload. Provision of maintenance hemodialysis to neonatal and infants implicate many challenges: blood flow rate, UF settings and accuracy, catheter size and length, extracorporeal circuit volume, circuit functional survival and the anticoagulation strategy. We evaluated the technical aspects of the first world in-ovo treatment with the new cardio renal paediatric dialysis machine (CarPeDeM) specifically designed for infants.

Methods: Patients 38 week-old male infant weighting 3.2 Kg admitted at the PICU with sepsis and acute lung injury due to severe combined immunodeficiency syndrome, was treated with the CarPeDeM in CVVH pre dilution. Fluid overload was the main reason for RRT initiation. The extracorporeal circuit included a D50 hemofilter (polysulfone, 0.075m2) totalizing 27ml of priming volume (10% of total circulating blood volume). A 4.5 FR dual lumen catheter length 3.9 inch was placed in the femoral veins. Heparin was continuously infused of 10 U/kg/hr. Haemoglobin was 10 g/dl.

Results: A total number of 61 hours was done with 4 circuits. Arterial, Venous, Drop and PreFilter Pressures were stable during all treatment (see figure 1 for the first circuit, 1b).

Conclusions: Despite the negative data in literature (13.9±8.6 with 6.5 FR catheter for patients weighting <3Kg or circuit life < 20 h with 5 FR catheter, ppCRRT) our circuit life was quite long (17.5±6.24 h). In addition the reasons for downtime were clinical. Limitation on flow through a tube described by Poiseuille law and the need of laminar flow dictated by Raynolds, suggest the right blood flow need to optimize the circuit survival, in particular with small catheter. The Carpediem blood pump allows a wide and appropriate range (5-50ml/min) of flows. Fluid balance safety is moreover assured by a very high sensitivity, Ig, scale. The data of the first in vivo treatment, suggest that CRRT with Carpediem is safe and effective in neonates and infants weighing less than 10 Kg. Prolonged circuit survival with small catheter due equipped features, allows to explore all potential benefits of CRRT in infants without technical and clinical complications.
enoxaparin sodium at a dose of 1mg/kg as an anticoagulant and her anti-Xa activity was found to be as high as 1.79 ml (normal range 0.1-ml). After having a serious bleeding complication of enoxaparin in this case, we aimed to evaluate dose-dependent efficacy and safety of enoxaparin, and to assess plasma anti-Xa activity in patients receiving enoxaparin for their routine HD.

**Methods:** Nine children and adolescents (5 males; aged from 9 to 21 years) on maintenance HD were enrolled into the study. All patients were receiving HD thrice weekly for four hours. The vasoaccess of the patients was either an arterio-venous fistula or a venous catheter. Enoxaparin sodium was administered as a single bolus dose, 1mg/kg, 0.75 mg/kg, and 0.60 mg/kg in the consecutive sessions, at the beginning of the dialysis sessions. Anticoagulant effect was clinically monitored by visual inspection of HD line hourly and inspection of the dialyzer at the end of the session, and also laboratory monitored measuring anti-Xa levels at the end of each session.

**Results:** All HD sessions resulted in no fibrin/clot formation in the HD lines or in the dialyzers. There was no bleeding complication during or after the HD sessions. The mean plasma anti-Xa levels were 1.05±0.34, 0.81±0.27 and 0.50±0.23 ml at the end of the sessions followed by the decreasing doses of enoxaparin (1mg/kg, 0.75 mg/kg, and 0.60 mg/kg), respectively. The mean plasma anti-Xa levels after the dose of 1 mg/kg were significantly higher than the doses of 0.75 mg/kg and 0.60 mg/kg (p=0.028 and p=0.04), respectively. However, there was no significant difference in anti-Xa levels between the doses of 0.75 mg/kg and 0.60 mg/kg.

**Conclusions:** Enoxaparin seems to be efficient and safe as an anticoagulant at a single initial dose of 0.60 mg/kg for thrice weekly HD. On the other hand, the dose of enoxaparin should be adjusted in frequent dialysis because of its potential for accumulation and causing bleeding complications in the setting of renal impairment. Therefore, we recommend monitoring plasma anti-Xa activity in pediatric HD patients, especially in daily dialysis.

**MP705**  
RENAL EFFECTS OF IBUPROFEN DURING THE TREATMENT OF PATENT DUCTUS ARTERIOSUS IN LOW BIRTH WEIGHT PREMATURE INFANTS

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**Introduction and Aims:** Patent ductus arteriosus (PDA) is common in very premature infants. Pharmacological closure of PDA with ibuprofen is better tolerated. Aim of this study was to assess the efficacy and safety of oral ibuprofen and intravenous ibuprofen for the early pharmacological treatment of PDA in preterm infants.

**Methods:** A randomized, single-blinded, controlled study was performed on premature neonates at the neonatal unit tertiary care hospital, from January 2010 to December 2012. The study enrolled 68 preterm infants with gestational age between 28-32 weeks, birth weight ≤ 2000 g, postnatal age 48-96 h, and had echocardiographically confirmed significant PDA. The preterm infants received either intravenous or oral ibuprofen randomly as an initial dose of 10 mg/kg, followed by 5 mg/kg at 24 and 48 h. Serum creatinine (sCr), blood urea nitrogen (BUN) and urine output (UO) were recorded prior to start treatment, and after the course treatment.

**Results:** 36 patients were treated with oral ibuprofen and 32 with intravenous ibuprofen in this period. There was no difference between treatment groups in demographics or baseline renal function. After the first course of the treatment, the PDA closed in 30 (83.3%) of the patients assigned to the oral ibuprofen group versus 21 (71.8%) of those enrolled in the intravenous ibuprofen group (p=0.355). In the evaluation of renal tolerance, none of the patients had oliguria. The serum creatinine levels after the course treatment did not differ significantly from the baseline for each group.

**Conclusions:** Oral ibuprofen treatment seems to be as efficient as intravenous ibuprofen in closing PDA on the third day of life in low birth weight preterm infants and without significant changes of renal function.

**MP704**  
URINARY NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN AS AN EARLY BIOMARKER FOR PREDICTION OF ACUTE KIDNEY INJURY IN PRETERM NEONATES

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**Introduction and Aims:** Our aims are to determine whether the urinary neutrophil gelatinase-associated lipocalin (uNGAL) can predict acute kidney injury (AKI) development in non-septic and non-asphyxiated critically ill preterm neonates.

**Methods:** This case control study was performed on 50 preterm neonates whose gestational ages (GA) were between 28 and 34 weeks. AKI was diagnosed in six preterm neonates during the first 7 days. Blood and urine samples were taken on postnatal days 1 and 7. Urine and clinical data were collected and uNGAL levels measured by ELISA method.

**Results:** The median uNGAL levels were significantly higher in the preterm neonates with AKI than those of the controls on PND 1 and 7 (p=0.006 and p=0.023, respectively). The level of uNGAL was predictive of AKI (odd ratio=1.08; [95%CI 1.01-1.17], p=0.025), even after controlling for GA, birth weight, gender, and Apgar scores.

**Conclusions:** Higher uNGAL can predict AKI in non-septic and non-asphyxiated critically ill preterm neonates.
significant difference in the urinary levels of the marker was detected between different types of steroid responsive nephrotic syndrome (infrquent relapsers, frequent relapsers and steroid dependent). No significant correlation was detected between urinary A1BG and age, gender, serum albumin or total serum proteins.

**Conclusions:** Urinary A1BG is a promising, non invasive, prognostic biomarker that can predict steroid response during the initial phase of treatment of childhood nephrotic syndrome and is not apparently influenced by the degree of proteinuria. Further longitudinal studies are required to prove its efficiency in this field.

**MP707**

**EFFICACY AND SAFETY OF DARIEPOETIN ALFA (DA) FOR ANEMIA IN CHILDREN WITH CKD: A MULTICENTER PROSPECTIVE STUDY IN JAPAN**

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**Introduction and Aims:** DA is an attractive alternative to rHuEPO in managing anemia in pediatric CKD patients. Since the ability of DA to be administered at extended dosing intervals is a less clear, more data of DA treatment are needed to better treat anemia in pediatric patients. Therefore, we conducted a multicenter prospective study to examine the pharmacokinetics, safety and efficacy of DA in Japanese pediatric CKD patients.

**Methods:** The study was a multicenter, prospective, open-label study that enrolled pediatric CKD patients, including non-dialysis (ND), peritoneal dialysis (PD), and hemodialysis (HD) patients. [Pharmacokinetics study] Pharmacokinetic parameters were investigated in 16 patients who received single dose of DA intravenously or subcutaneously. Safety and efficacy study: DA was started with weekly dose for HD patients (n=2), and biweekly for PD patients (n=13) and ND patients (n=16). The doses were adjusted to maintain the target Hb range of 11.0 to 13.0 g/dL. Additionally, the ability of DA to be administered at extended dosing interval (once every 4 weeks) was examined in PD and ND patients during 24 weeks of study period.

**Results:** [Pharmacokinetics study] When administered intravenously, t1/2 was 26.3 ± 9.1 h (mean ± SD) and CL was 1.8 ± 0.7 mL/h/kg. These parameters were similar to those in adult CKD patients. When administered subcutaneously, t1/2 was 46.7 ± 19.7 h and Cmax was 1.7 ± 0.8 ng/mL. T1/2 was slightly shorter and Cmax was higher in pediatric patients than those in adult CKD patients. [Safety and efficacy study] After initiation of DA, the mean Hb increased from baseline of 10.5 ± 0.5 g/dL to reach the lower target Hb of 11.0 ± 0.5 g/dL at 4 week and maintained within the target range throughout the study. The mean rate of increase in Hb was 0.26 g/dL/week. All patients reached to the target Hb. The dosing frequency was extended to once every 4 weeks for 24% of patients, 3% for 4 weeks, and 1% for 5 weeks. The adverse events were noted in 39% of the patients, but no adverse drug reactions indicating causality with DA treatment were observed.

**Conclusions:** The results of this study suggest that extended dosing (once every 2 weeks or once every 4 weeks) regimens with DA are safe and effective treatment options for anemia in pediatric ND and PD patients.

**MP708**

**DO CHILDREN WITH STEROID RESISTANT NEPHROTIC SYNDROME NEED ARTERIAL STIFFNESS ASSESSMENT?**

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**Introduction and Aims:** Children with nephrotic syndrome (NS) are assumed to be at increased risk for atherosclerosis and coronary heart diseases (CHD), probably because of NS associated with hyperlipidemia, hypertension and steroid therapy. Aim of the study: This study was aimed at evaluation of the arterial stiffness as a predictor of developing atherosclerosis in children and young adolescents with steroid resistant nephrotic syndrome.

**Methods:** Twenty children were enrolled in this study. They were 11 males and 9 females with a mean of 10.75 ± 3.31 years. They were having proteinuria and depending on steroid therapy. Twenty healthy age and sex matched children served as a control group. All patients and controls were subjected to thorough history taking and clinical examination. All patients in the study underwent laboratory investigations including urinalysis, 24-hour protein in urine, serum urea and creatinine, triglycerides (TGs), cholesterol, low and high density lipoproteins (LDL and HDL). Renal biopsy was done to diagnose histopathological type of nephrotic syndrome. Doppler study for determination of Ankle Brachial Index (ABI) and carotid duplication.

**Results:** The results showed that ankle brachial index was significantly higher in nephrotic patients with steroid resistance than patients with steroid sensitive (P < 0.0001). There was a positive correlation between ankle brachial index and dose of steroids and duration of treatment (r = 0.69 and 0.61 respectively). The results showed that carotid intimal thickness was significantly higher in nephrotic patients with steroid resistance than patients with steroid sensitive (P < 0.001). Carotid intimal thickness was directly correlated to relapse rates and serum LDL, and cholesterol (P < 0.001 for each).

**Conclusions:** Ankle brachial index and carotid duplication are simple non invasive tools to assess arterial stiffness in steroid resistant nephrotic patients.

**MP709**

**LONG TERM FOLLOW-UP OF METAPHYSEAL SCLEROTIC LINES IN BIPHOSPHONATE THERAPY FOR STEROID INDUCED OSTEOPOROSIS IN CHILDREN WITH NEPHROTIC SYNDROME**

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**Introduction and Aims:** Bisphosphonates are widely used in the management of children with steroid induced osteoporosis (SIO). With the increasing use of bisphosphonates, there have been reports of abnormal radiological findings in the growing skeleton. Therefore, their use in pediatric patients remains controversial. The present study was conducted to evaluate the long term follow up results of radiographic features especially metaphyseal sclerotic lines, associated with pamidronate therapy in pediatric patients with nephropathy.

**Methods:** Twenty children with nephropathy receiving oral calcium and pamidronate (mean duration: 7.9 months, dose: 125mg daily) were evaluated retrospectively. All Patients had SIO because of chronic glucocorticoid therapy for the treatment of nephropathy. Biochemical tests, long bone radiography and bone mineral density (BMD) were performed before the treatment of pamidronate and followed up several years later. The physiological growth rates were estimated by measuring the distance that the sclerotic lines moved on the radiographs during the corresponding time intervals.

**Results:** The mean follow up period was 9.7 years. In all patients, the well-defined sclerotic lines at the metaphyseal ends were observed and progressively moved from physical plate to diaphysis on the radiographs of long bones. The mean moving rates of the sclerotic lines was 7.99 mm per year and in twelve patients, the lines disappeared. And the mean growth rate of height was 4.58 cm per year.

**Conclusions:** Our long-term follow-up results suggest that the metaphyseal sclerotic lines associated with pamidronate treatment tend to disappear without affecting the skeletal growth. Bisphosphonate treatment for SIO in pediatric patients with nephropathy seems to be safe although further studies for larger number of patients are needed.

**MP710**

**BIOIMPEDANCE ANALYSIS AND INFERIOR VENA CAVA DIAMETER FOR DRY WEIGHT ASSESSMENT IN PEDIATRIC HEMODIALYSIS PATIENTS**

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**Introduction and Aims:** Dry weight (DW) assessment is a common problem in the pediatric population on regular hemodialysis. Differentiating fluid overload from fluid underload is essential to avoid complications. The aim of this study was to assess and follow up DW in children on regular HD by various clinical and non-clinical methods and determine the effect of hemodialysis sessions on different body compartments.

**Methods:** A prospective follow up clinical study was conducted on 40 pediatric patients on regular hemodialysis. DW was assessed using the three methods at the beginning of the study and 8 months later. Clinical methods including pre and post-session blood pressure (BP), Ultrasonographic measurement of inferior vena cava diameter (IVCD). Multi-frequency bioimpedance spectroscopy (BIS) was done using the Body composition monitor to calculate hydration variables such as total body water (TBW), intracellular water (ICW), extracellular water (ECW), overhydration (OH) and ECW/ICW (E/I ratio). BIS also measured different body tissue parameters as lean tissue mass (LTM), lean tissue index (LTI), fat mass, fat tissue index (FTI) and adipose tissue mass (ATM). All measurements were applied immediately before and two hours after dialysis session. Study design: DW was assessed at the beginning and the end of the study by the three methods, then changed according to BIS recommendations. Patients were followed up clinically for 8 months. A concordance rate, between the three methods, was calculated.

**Results:** HD sessions caused a significant effect on ECG causing a significant reduction in IVCD, TBW, OH, E/I ratio, systolic and diastolic blood pressure at the beginning and the end of the study but not on ICW. Concerning body water parameters, LTM and LTI were significantly decreased at the beginning of the study due to the underestimation of our patients’ DW. After adjusting their DW via the BIS recommendations, HD sessions had no significant effect on both. Body fat parameters (fat, FTI and ATMI) were not affected by HD sessions at the beginning and the end of the study. The study found that the concordance between clinical recommendations and BIS recommendations was increased by the end of our study. Yet the concordance between BIS and IVCD recommendations slightly decreased. After adjusting the patients’ DW according to the BIS recommendations, the number of intradialytic hypotensive episodes decreased at the end of the study.
RENAL INVOLVEMENT IN CHILDREN WITH HENCH-MOONEIN PURPURA: HIGH LEVEL OF SERUM PENTRAxin 3 AND IgM IN LESIONAL SKIN

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Introduction and Aims: Renal involvement is the principal cause of morbidity and mortality in children with Henoch-Schönlein purpura (HSP). To date, some clinical and laboratory findings associated with renal involvement in patients with HSP were reported. However, there is no information about the association of HSP and pentraxin3 (PTX3) which is a novel biomarker of inflammatory vascular diseases. The aim of this prospective study was to investigate the risk factors associated with renal involvement in the patients with HSP at the presentation.

Methods: Sixty patients with HSP (according to the IFNB/Pres criteria) were included between February 2011 and November 2012. The patients were followed for at least six months for any signs of renal involvement. At the end of the study, clinical features, skin biopsy findings, laboratory parameters, and serum PTX3 levels were compared between patients with and without renal involvement.

Results: There were 60 patients, 33 male (%55) and 27 female (%45), the age ranged from 3 to 15 years (mean 8.01±2.52 years). Renal involvement was observed in 29 patients (48.3%), joint in 32 (61.7%), gastrointestinal tract in 30 (50%). The mean serum PTX3 level of the patients with renal involvements was significantly higher than those of the patients without renal involvement 2.2±1.3 vs. 1.0±0.85 mg/l, respectively P<0.004. Presence of IgM indirect immunofluorescence studies of skin biopsy specimens was found to be significantly associated with renal involvement (P<0.008). None of the patients with renal involvement reached end-stage kidney failure. Early systemic corticosteroid therapy, sex, age, skin relapses and severe abdominal pain were not statistically significant different between the patients with or without renal involvement.

Conclusions: We suggest that elevated serum PTX3 levels and IgM deposition in skin biopsy are closely associated with renal involvement in the children with HSP.

References:


MP714 CLINICAL CHARACTERIZATION OF RENAL CYSTIC DISEASES IN CHILDREN: A SINGLE CENTER EXPERIENCE

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Introduction and Aims: Renal cystic disease (RCD) constitutes an important and leading cause of end-stage renal disease in children. RCD can be acquired or inherited; isolated or associated with extra-renal manifestations. The precise diagnosis represents a difficult clinical challenge. The aim of this work was to study the epidemiology and clinical phenotypic features of RCD in Egyptian children based on examination of clinical features and survival characteristics in addition to renal imaging and histopathologic findings as helpful tools to categorize these diseases.

Methods: The study included all patients with renal cystic diseases presenting to, or being cared for at, the Center of Pediatric Nephrology and Transplantation, Cairo University through the period from April, 2009 to November, 2010. The clinical records, imaging studies and pathology reports of all patients with a diagnosis of renal cystic disease at the nephrology clinic were reviewed. Patients were subjected to:- Clinical assessment including history, age and pattern of presentation, renal, visual, hepatic and neurological symptoms etc.- Routine laboratory investigations and assessment of renal functions using estimated GFR by Schwartz formula and staging of CKD.- Abdominal ultrasonographic examination.- Abdominal CT examination was performed in some selected cases. - Additional imaging studies for the urinary tract (e.g. VCUG, MRU) and CNS abnormalities (brain CT or MR) when needed.- Ultrasound guided renal biopsy when feasible and required for definitive diagnosis and precise categorization of the renal disease.

Results: We have studied the clinical phenotypes of 105 children with RCD (45 of them had extrarenal manifestations). The most common disorders were inherited renal cystic diseases including nephronophthisis and related ciliopathies (36.2%), and polycystic kidney disease (31.4%). Multicystic dysplastic kidneys represented 19% of cases. Four syndromic cases were unclassified, not being previously reported. In our study, RCD was largely due to inherited disorders (70.5%).

Conclusions: While inherited disorders were the most common in this series, it might not reflect their prevalence in the community since the study was based on a
referred center. Extrarenal manifestations are common and may constitute well-defined syndromes or newly described constellations. Ultrasonography is a useful screening and initial diagnostic tool with a role for additional imaging, genetic studies and possibly biopsy in selected cases. We conclude an algorithm as a helpful tool for categorization of RCD.

**MP715**

LONG-TERM OUTCOME IN IDIOPATHIC NEPHROTIC SYNDROME (INS): FROM CHILDHOOD TO ADULTHOOD

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Introduction and Aims: Long-term outcome in children with INS is considered good, but reliable data on adults are scarce. Aim was to assess INS relapse (INSR) rate and risk factors, treatment adverse events, co-morbidities, social status in adults with INS in childhood.

Methods: In 61 adults (26male, 35female), aged 26.0±6.2 (18.5-51.5) yrs, with INS in childhood, we analyzed: age of INS onset, number and treatment of relapses <18 yrs, response to corticosteroids (CS), renal biopsy, number and treatment of relapses >18 yrs, final height, co-morbidities, age of menarche, offspring, educational status, occupation.

Results: Median age of INS onset was 3 (1.3-14.0) yrs, median number of INSR <18 yrs: 5 (1-20). Steroid-sensitive NS (SSNS) was diagnosed in 37, steroid-dependent (SDNS) - 18, steroid-resistant (SRNS) - 6 pts. Renal biopsy was performed in 28 pts; MCN was found in 10, MP-17, FSGS-1. All pts received CS, methylprednisolone pulses (MPS)-15, cyclophosphamide (CY)-3, chlorambucil (CHL)-11, cyclosporine A-2, levamisole-21. All pts achieved remission <18 yrs. In adulthood INS relapsed in 10 pts, mean age 28.2±5.1 yrs; 5 SSNS, 4 SDNS, 1 SRNS; observation time after INS onset 24.4 ±6.1 (13.5-32.7) yrs; median No of INSR: 2 (1-11). Relapses were treated with CS, MPS-5, CY-3, CHL-1. Pts with INS in adulthood had more (P=0.0001) INSR <18yrs (median: 10 (4-20) vs. median: 4 (1-16)). Arterial hypertension was diagnosed in 8/61 pts: 2 at age 15 and 17, 6 >18yrs, 3 of them had INS as adults. These 3 pts had more (P=0.05) relapses >18yrs than >7 normotensive pts (median: 10 (3-11) vs. median: 2 (1-2)). Overweight was found in 14/61, obesity in 3/61, 5 pts were growth-retarded, 4 with INS onset <3 yrs (1-8 relapses), 1 with SSNS (5 relapses) had height <3c. before treatment. No myocardial infarctions, strokes, severe infections, malignancies were noted; 12 pts had bone fractures. Mean menarche age: 12.9±1.4 yrs; 13 pts have children, 1 treated with CYP and CHL in prepubertal period. Elementary education was reported in 4, secondary - 32, higher - 25, 34 pts are occupied. 60 pts are alive, 1 with SDNS without relapses >18yrs died at age 29 due to alcohol abuse.

Conclusions: 1. High number of INS relapses in childhood is a risk factor for recurrences in adulthood. 2. Educational status and professional activity of adults with INS in childhood seems to be satisfactory.

**MP716**

ASSOCIATION OF ANGIOTENSINOGEN GENE (M235T) POLYMORPHISM WITH ANTHYPERTENSIVE EFFICACY OF ACE INHIBITORS IN CHILDREN WITH STEROID-RESISTANT NEPHROTIC SYNDROME

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Introduction and Aims: Hypertension has been generally recognized as an independent predictor of unfavorable long-term outcome in patients with various CKD. Angiotensinogen AGT (M235T) gene polymorphism associated with increased serum angiotensin level and hypertensive. The data on the potential association between AGT (M235T) gene polymorphism and BP lowering efficacy of ACE inhibitors (ACE-i) in children with steroid-resistant nephrotic syndrome (SRNS) is limited. The study was conducted to determine whether AGT (M235T) gene polymorphism associated with efficacy of antihypertensive treatment in Russian children with idiopathic SRNS.

Methods: We performed a retrospective study of ninety-two children (4M:58F) aged 15.5 (IQR: 11.3; 17.0) years with initial idiopathic SRNS in relation to response to antihypertensive treatment with ACE-i subject to AGT (M235T) gene polymorphism. Histological findings were FSGS in 41 (44.6%), mesangial proliferative glomerulonephritis in 21 (22.8%), membranoproliferative glomerulonephritis in 16 (17.4%), MCD in 8 (8.7%), membranous nephropathy in 6 (6.5%) patients.

Hypertension was determined during initial treatment with prednisolone - 2 mg/kg/d (maximum 60 mg/d) for 6-8 weeks before using other immunosuppressive treatment. Antihypertensive effect of treatment with ACE-i was determined as reduction of the BP (≥ 50th percentile for age, sex, and height of children. The AGT Gene (M235T) polymorphism (rs699) was determined by PCR and SSCP analysis in SRNS patients and 50 healthy subjects as controls. Results: Allele frequencies and genotype distribution of the AGT Gene (M235T) polymorphism in patients and controls were consistent with Hardy-Weinberg equilibrium (p=0.05). Median age, initial renal function, frequency of FSGS and hypertension did not differ significantly between patients with AGT (M235T) genotype (p=0.05). Antihypertensive effect of treatment with ACE-i was identified significantly often in children with M/M genotype in comparison with patients with T/T and T/M genotype of AGT (M235T) gene: 73.1% vs. 35% (p=0.01; OR=5.0, 95% CI: 1.4-17.8) and 30.2% (p=0.0086; OR=6.3, 95% CI: 2.1-18.5), respectively. Combined antihypertensive therapy with ACE-i and angiotensin-receptor blockers was needed significantly often in patients with T/T and T/M genotypes than in children with M/M genotype of AGT (M235T) gene: 55% vs. 22.2% (p=0.013), OR=5.1 (95% CI: 1.4-19.1) and 63.6% vs. 22.2% (p=0.0003), OR=7.4 (95% CI: 2.3-23.3).

Conclusions: Our results indicate that AGT (M235T) gene polymorphism associated with antihypertensive efficacy of ACE-i in children with SRNS. Patients with M/M genotype of AGT (M235T) gene had higher frequency of antihypertensive efficacy of therapy with ACE-i compared with children with T/T and T/M genotypes. This association can be speculated by severity of podocytes damage with involvement of expressed receptors to angiotensin.
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