LAB METHODS / BIOMARKERS

**SP122**

**COMPARISON OF ATHEROMATOUS DISEASE IN HIGH RISK POPULATIONS REVEALS A DISTINCT ASSOCIATION OF RISK FACTORS AMONG PATIENT POPULATIONS AND A STRICKING RELEVANCE FOR GLYCEMIC CONTROL IN DIABETIC NEPHROPATHY**

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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, HbA1 is a better understanding of specific risk factors that distinctly modulate the incidence of atheromatous disease in diabetic nephropathy.

**Conclusions:** Our findings confirm the high prevalence of atheromatous disease in asymptomatic high CV risk patients with a distinct association of risks factors among patient populations. Importantly, in diabetic nephropathy, HbA1c emerges as a main risk factor independently associated with the presence of carotid plaques.

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**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%) 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, urine protein (UPR, mg/24h), serum cholesterol, albumin (Alb), 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: 1.001-1.001, p=0.021) and VCAM-1 (RR: 1.0007 95% CI: 1.00-1.0013, p=0.026). For the renal outcome significant predictive factors were: eGFR (RR: 0.894, 95%CI: 0.844-0.947, p<0.001), UPR (RR 1.0005, 95% CI: 1.0002-1.0007, 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.
In multivariate analysis, cIMT was the strongest determinant for renal progression rate (change in slope: -0.605, 95% CI -0.953 to -0.269).

Conclusions: Increased cIMT and carotid plaque were associated with rapid decline of renal function and progression to dialysis in CKD stage 3 and 4 patients. Measuring cIMT and detecting carotid plaque may help identify high-risk patients with rapid progression of renal dysfunction.

SP125 THE EFFECTS OF THE CKD-MBD (CHRONIC KIDNEY DISEASE-MINERAL AND BONE DISORDERS) 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), PTH (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 been 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 echocardiographic data and other clinical data was performed in 1231 participants of KNOW-CKD. LV muscle indexed by body surface area (LVMi) and relative wall thickness were used to define LV hypertrophy (LHV) and LV geometry according to the American Society of Echocardiography. As parameters of CKD-MBD, serum calcium (Ca), P, 25-(OH) vitamin D, 1,25(OH)2 vitamin D, vitamin D, and FGF23 were measured.

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 (87.5±24.0, 91.2±24.1, and 108.7±23.9 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 LHV increased (normal; 43.2%, eccentric LVH; 21.7%, concentric remodeling; 13.6%, concentric LHV; 21.4% in CKD 1 stage).

Conclusions: With Portabl compact digital recorder Mobil-O-Graph NG (I.E.M) By collecting 24 hours of urine, glomerular filtration rate and microalbuminuria values were measured. With progression of CKD, the frequency of normal LV geometry decreased and those of eccentric and concentric LHV increased (normal; 43.2%, eccentric LVH; 21.7%, concentric remodeling; 13.6%, concentric LHV; 21.4% in CKD 1 stage).
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 ± 650 nm where the colour intensity is directly proportional to the concentrations of dp-ucMGP.

Results: The assay range of the MGP ELISA is 100 to 700 μM with an analytical sensitivity of less than 50 pM. The performance of the MGP ELISA kit displays excellent intra-assay precision with samples reading across the assay range showing less than 15% CV. The assay also displays excellent intra-assay precision with samples reading from 127 pM to 423 pM showing an average precision on 10 replicates of 6.3% to 8.8%. The average recovery of samples spiked with synthetic material is 103%. High standards linearly shows excellent recovery when diluted in a low MGP sample across the assay range with an average observed / expected value of 106%. The correlation of 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 0.866. The assay shows a positive relationship increasing in dp-ucMGP levels and progressing CKD stage and shows the expected decrease in dp-ucMGP after vitamin K supplementation.

Conclusions: This new and novel MGP ELISA test kit is an accurate device for the detection of dephospho-ucMGP in CKD patients.

NUTRITIONAL EDUCATION FOR MANAGEMENT OF OSTEODYSTROPHY (NEMO) TRIAL: IMPACT ON QUALITY OF LIFE

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Introduction and Aims: Hyperphosphatemia 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: This 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:85.94±28.79 to 57.77±32.96) and bodily pain (experimental: 76.85±29.57 to 56.62±36.65, Control: 77.77±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 receive 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: Fibroblast growth factor 23 (FGF23) is a remarkable 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 disease (CVD) and mortality in patients with chronic kidney disease (CKD), however number of studies reported the association of high levels of FGF23 with cardiovascular events and deaths was recorded over 22±3 months.

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Introduction and Aims: For measurement of serum albumin two different assays are generally used: bromocresol green (BCG) and bromcresol purple (BCP). These assays provide different results, in particular in hemodialysis (HD) patients. Hence, when calcium levels are corrected for albumin (adjusted calcium=[total calcium] x 0.2046 x (40–[albumin])) are recommended by guidelines, results depend on the type of albumin assay used. The objective of this study was to evaluate whether the type of albumin assay has clinical implications in HD patients, especially on prescription of phosphate binding agents.

Methods: In this cross-sectional study, 503 patients were analysed from 24 Dutch dialysis centers, at entry in the Convective Transport Study between 2004 and 2008 (mean age 63.3 ± 14.1 yrs; 62% male). 9 centers used BCP [n=330]. 15 centers used BCG [n=173]. Plasma phosphate, calcium levels, albumin and use of phosphate binding agents were compared between the two assay types.

Results: Plasma albumin was lower in the BCP as compared to the BCG group (34.5 ± 4.2 g/l vs 40.4 ± 3.1 g/l; P = 0.000), while normalized (normalized nitrogen appearance, creatinine, cholesterol and body mass index) and inflammatory (hsCRP) parameters were similar. The measured calcium levels were similar in both groups (2.4±0.5 mg/dl for BCP vs 2.32±0.18 mg/dl for BCG; P=0.25). Corrected calcium was higher in the BCP group (2.46±0.2 mmol/l vs 2.33±0.2 mmol/l, P=0.000). More patients in the BCP group were hypercalcemic after correction for albumin (28.8% vs 13.1%, P=0.001). Phosphate levels were higher in the BCP group (1.74±0.4 mmol/l vs 1.57±0.4 mmol/l, respectively; P=0.006), which was not explained by patient- or treatment characteristics. Use of calcium-containing phosphate binders tended to be higher in the BCP group as compared to the BCG group (43.9% vs 50.9%; P=0.157). No difference in use of calcium-free containing binders was found (75.2% for BCP vs 75.1% for BCG; P=0.999).

Conclusions: Calcium concentrations after correction for albumin were higher in patients treated in centers using the BCP as compared to the BCG assay, in the BCP group patients were more likely to be hypercalcemic. Despite higher calcium levels after correction for albumin, more calcium containing binders tended to be prescribed in these patients, suggesting that calcium levels were not corrected for albumin. In addition, phosphate levels were higher in the BCP group. Keeping in mind these are observational data, it may be hypothesized that the latter is explained by less restrictive dietary measures due to apparent hypocalcemia in these patients.
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 thousands nine hundreds forty one random urine samples were tested for PCR and urinary dipstick, and 3,874 samples for ACR and dipstick.

Results: The median values of PCR and UCR were higher in samples of high grade TP and low SG. When DP ≥100 mg/dL and over or 1+ (30 mg/dL) with SG ≥0.10 or trace with ≤1.005 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%, 87.5% and 89.8% respectively. When more than trace was used, the sensitivity, specificity, PPV and NPV for detection of microalbuminuria (ACR ≥30 mg/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.

Conclusions: Our findings show that administration of ACE-I induces dose-dependent antiproteinuric effects only after several hours, and no residual effect lasts over the 24 hours. Also, this finding suggests that an antiproteinuric effect lasting 24-hour could be obtained administering the drug in two daily doses and that higher dosage induces higher effect.

Introduction and Aims: Tubulointerstitial injury is one of the common features of patients with chronic kidney disease (CKD). Advanced glycation end products (AGEs) are elevated in patients with diabetes mellitus and end-stage renal failure (ESRD), whose serum and tissue levels are strongly associated with mortality in these patients. Further, binding of AGEs to receptor for AGEs (RAGE) induces reactive oxygen species (ROS) generation and subsequently evokes tubular injury in experimental diabetic model. However, whether and how AGEs-RAGE system could be regulated in non-diabetic CKD model such as remnant kidney model has not been elucidated. Therefore, we investigated whether serum AGEs and intrarenal RAGE expression were increased and associated with tubulointerstitial injury in a mouse of subtotal nephrectomy (Nx), as a non-diabetic CKD model.

Methods: Ten-week old C57BL/6J mice were assigned to 2 groups (Nx; n=18 or sham; n=10). 5/6Nx was performed by surgical resection. Four weeks after the Nx, mice were euthanized and sacrificed for analysis. Urinary albumin and neutrophil gelatinase-associated lipocalin (NGAL) excretion and serum N-carboxymethyl-lysine (CML), one of the AGEs, were measured by enzyme-linked immunosorbent assay. RAGE and type-IV collagen expression was evaluated by western blotting and real-time PCR. Tubulointerstitial fibrosis was examined by periodic acid-Schiff and Masson’s trichrome staining, respectively.

Results: Subtotal nephrectomy significantly increased the levels of blood urea nitrogen and creatinine (Cr), and decreased Cr clearance levels. Circulating CML and renal RAGE expression levels were significantly increased compared with those in sham-operated (Ctrl) mice. (305.60 ± 54.58 vs 529.53 ± 50.31, p=0.083, 1.07 ± 0.11 vs 4.2 ± 2.01, p=0.028, respectively) Urinary albumin and NGAL excretion were significantly higher than Ctrl mice (4.02 ± 0.11 vs 4.83 ± 0.26, p=0.030, 4.07 ± 0.66 vs 5.71 ± 0.31, p=0.017, respectively). Furthermore, type-IV collagen mRNA expression was increased and tubulointerstitial fibrosis was exacerbated in the kidney of 5/6 Nx mice compared with Ctrl mice (1.05 ± 0.01 vs 2.04 ± 0.58, p=0.037).

Conclusions: We demonstrated that induction of renal dysfunction increased circulating AGEs levels, increased RAGE expression and tubulointerstitial injury in Nx mice. These observations suggest that AGEs-RAGE system and tubulointerstitial injury may be correlated with each other, thereby being involved in the progression of tubulointerstitial fibrosis in CKD.

Introduction and Aims: Non-invasive testing of the kidneys has a limited ability to describe the condition of the renal tissue. It is desirable that we are able to distinguish between patients with chronic, irreversible scarring of the kidneys from those with active and potentially treatable lesions. We tested the ability of urinary alpha 1-microglobulin (A1m) to distinguish among patients with different degree of renal tubulointerstitial fibrosis.

Methods: In this multi-center study, we included patients who underwent diagnostic renal biopsy, whose primary diagnosis was other than acute or chronic tubulointerstitial nephritis, who had proteinuria (protein/creatinine ratio ≥15mg/mmol) and whose A1m/albumin ratio did not exceed 0.5 (to exclude patients who are likely to have a primary tubulointerstitial disease). Urinary levels of A1m, albumin (alb) and creatinine (creat) were measured and urinary indexes A1m/albumin and A1m/creat were calculated. Tubulointerstitial (TI) fibrosis was graded 1 (0-5%), 2 (5-25%), 3 (25-50%) and 4 (>50%) in the renal biopsy samples. We tested if A1m/albumin and A1m/creatinine differ among patients with different grades of TI fibrosis. We used non-parametric tests: Mann-Whitney U test and Kruskal-Wallis ANOVA, and we performed ROC analysis to find the discriminating power of parameters.
Results: 137 patients were included in the analysis. T1 fibrosis was graded in 16 patients, 2 in 52 patients, 3 in 37 patients, 4 in 32 patients. A1m/creatinine were determined better among groups than A1m/albumin. Statistically significant differences of A1m/creatinine were found between grade 1+2 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 A1m/creatinine was good between grade 4 versus grade 1 with the sensitivity 76.1% and specificity 86.2% (AUC 0.795, cut-off = 28 mg/mmol), and between grade 4 and grade 1+2+3 with the sensitivity 71.9% and specificity 68.9% (AUC 0.718, cut-off = 34.07 mg/mmol).

Conclusions: We confirmed results of our small pilot study, that urinary A1m is strongly associated with the grade of T1 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.

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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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 and -1635G/A) of TLR-9 polymorphisms on 630 ESRD patients and 415 controls analyzed by real-time PCR assays. Plasma concentrations of interleukin-6 (IL-6) were analyzed by real-time PCR assays. Plasma concentrations of interleukin-6 (IL-6) were analyzed by real-time PCR assays. IL-6 was determined by ELISA. A luciferase reporter assay and real-time PCR were used to test the function of the associated promoter polymorphism. The genotype distributions were analyzed by chi-square tests. The genotype frequencies of all SNPs were in Hardy-Weinberg equilibrium. The odds ratios (OR) and corresponding 95% confidence intervals (CI) for effect of the genotype distribution and allele frequencies on ESRD were calculated by logistic regression analysis with the function of the associated promoter polymorphism. The genotype distributions were analyzed by chi-square tests. The genotype frequencies of all SNPs were in Hardy-Weinberg equilibrium. The odds ratios (OR) and corresponding 95% confidence intervals (CI) for effect of the genotype distribution and allele frequencies on ESRD were calculated by logistic regression analysis with the function of the associated promoter polymorphism.

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 compared with 34.6% in the controls (OR = 0.73, 95% CI = 0.60-0.88, p = 0.001). Using the ROC analysis we found that the discriminating power of A1m/creatinine was good between grade 4 versus grade 1 with the sensitivity 76.1% and specificity 86.2% (AUC 0.795, cut-off = 28 mg/mmol), and between grade 4 and grade 1+2+3 with the sensitivity 71.9% and specificity 68.9% (AUC 0.718, cut-off = 34.07 mg/mmol).

Conclusions: We confirmed results of our small pilot study, that urinary A1m is strongly associated with the grade of T1 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.

IDENTIFICATION OF COMBINED URINARY MRNA BIMARKERS FOR RENAL FIBROSIS IN IGA NEPHROPATHY WITH PC 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 semiquantitativly graded tubulointerstitial fibrosis area (%) as none (5%, n=7), mild (6 - 35%, n=11), moderate (36 - 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 urine 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 ΔΔCt method. Correlation between differentially expressed mRNA and clinical parameters and the ROC-curve analysis of differentially expressed mRNA were also determined. Linear discriminant analysis was used to weight those differentially expressed mRNA 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 regulators, and apoptosis related, respectively. Among these 20 differentially expressed mRNAs, 6 ones (ACE, CD71, FN1, PODXL, CCL5, VIM) 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), and calculated area under the curve (AUC) above 0.71 (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 discovered to the level of healthy controls (p > 0.3). The composite 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 an novel biomarker for RF of IgAN.

NON-TARGETED METABOLOMICS IN THE STUDY OF CHRONIC KIDNEY DISEASE

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Introduction and Aims: The progressive loss in renal function in chronic kidney disease (CKD) results in the accumulation of potentially toxic compounds. Early detection of an impaired kidney function and biomarkers predictive for the progression
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 joint study of concept method 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 metabolomics platform combining reversed-phase liquid chromatography coupled to high-sensitivity high-performance liquid chromatography (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 for both the MS and the LC-MS part.

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-hydroxyisopropionic acid and 2-hydroxyisopropionic acid (salicylic acid) (p < 0.001), hydroxyproline (p < 0.00005), urinary hydroxyproline (C11H15O5, p < 0.0005) and a heptase-based tetrasaccharide (C2H25O11, p < 0.0005).

Conclusions: Further targeted analyses in an increased study population will be performed to validate and quantify these novel, potential biomarkers across all CKD stages.

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 obstinately 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 nephrectomized kidneys 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 trypsin digestion for mass spectrometry (MS). Sections of nephron segments were taken by laser-microdissection from normal human kidney tissues, which were immunostained with anti-AQP1, calbindin and AQP2 antibodies, for identification 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 glomerular proteins showed approximately 50% of proteins that 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 proteomes. 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.

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 calcineurin inhibitors (CNI) remains the dominant causative factor for kidney failure in nonkidney organ transplant recipients, especially in liver transplant recipients. The possible influence of single nucleotide polymorphisms (SNPs) including cytochrome P450 3A4 (CYP3A4) subfamily, CYP2C8 and Fpg (ABCB1) on CNI induced renal injury in liver transplant recipients have recently been investigated as one of the most important factors. The purpose of this study was to explore the association between known ABCB1, CYP3A5 and CYP2C8 polymorphisms and the risk of developing tacrolimus (Tac) associated nephrotoxicity in liver transplant recipients.

Methods: A total of 136 living donor liver transplant recipients (107 men and 29 females) and 150 healthy controls (120 men and 30 females) were enrolled in this study. All the recipients had normal renal function (normal Cystatin C and normal serum microalbumin) before transplantation and received Tac-based 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 immunoassory technique (EMIT). We also detected serum creatinine C (Crys-C) and urine microproteins including α1 microglobulin (α1M), microalbumin (MA), transferring (TRU) and IgG (IgU) among 136 allograft 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*3*3 were significantly higher than that in those with CYP2C8*1*1 allele (p<0.05). Regarding MDRI SNPs C3435T and C1236T, no significantdifference 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*3*3 was associated with the risk of early tubulointerstitial injury. ABCB1 genotypes (both C3435T and C1236T) were irrelevant to the Tac-induced nephrotoxicity in liver transplant recipients.

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. However, it is performed poorly in patients with renal failure due to the renin-angiotensin-aldosterone system (RAAS) function especially in non-dialysis chronic kidney disease (NDCKD) patients, and few studies examined the risk of worsening renal function about tolvaptan. The aim of the study is to investigate the risk factors of worsening renal function by tolvaptan in NDCKD patients with CHF.

Methods: We administered tolvaptan (Doses 10.7±3.9mg) for 120 NDCKD patients (male/female: 72/48, 78.8±11.9 years old, estimated glomerular filtration rate (eGFR): 42.3±21.8 ml/min/1.73m2) 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. 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: Out of 124 patients (36.7%) developed the WRF. In univariate analysis, age (Odds ratio 1.43, 95%CI 1.11-1.65, 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=0.02), serum albumin (0.91, 0.83-0.95, P<0.03), cardiac ejection fraction (0.88, 0.72-0.93, p<0.01) remained significant after adjusted for age, eGFR, serum albumin, urine output, and bicarbonate. It suggests that diuretics in 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.
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 laboratory 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 (33-73.6) kg/m². At baseline 55.6% had BP > or =140/90mmHg, and 45.8% had type 2 diabetes. During the 10.4±5.5 months of follow-up (postoperatively), a decrease occurred in BMI (44.2±5.6 kg/m² to 30.7±4.2 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±39 to 169±36,3 mg/dl; p=0.04), triglycerides (166±64,6 to 77.4±76,0 mg/dl; p=0.01), hypertensive medication (1.3±1.4 to 0.4±0.8; p<0.0001), 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 postoperative albuminuria lowered their albumin excretion levels (urinary albumin:creatinine ratio [UACr]) from a median of 52.1 mg/m² to a median of 12.3 mg/m²; p<0.0001. All parameters improved at 12 month after BS. There was no significant difference in UACr reduction between diabetics and non diabetics (pNS). In multivariate analysis (binary regression), there was a significant association between higher percentage of weight reduction (>18%) and higher UACr reduction at 6 months (p=0.007, Exp(B): 3.6, CI 0.41-7.24), even when adjusted for age, diabetes mellitus and hypertension.

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. Simultaneously, this surgery had a positive impact in major cardiovascular risk factors, such as BP, dyslipidemia and type 2 diabetes.

Interventions and Comparisons: The patients in the BS group were compared with healthy controls (HC) and patients with chronic kidney disease (CKD), hypertension (HTN) and diabetes (DM) with similar age, BMI and sex distribution.

**Results**

- **BMI:** 44.2±5.6 kg/m² to 30.7±4.2 kg/m²; p<0.0001
- **UACr:** 52.1 mg/m² to 12.3 mg/m²; p<0.0001
- **SBP:** 134±23.9 to 116±11.5 mmHg; p=0.01
- **DBP:** 81±13.2 to 67±4.9 mmHg; p=0.04
- **TC:** 182±39 to 169±36.3 mg/dl; p=0.04
- **TG:** 166±64.6 to 77.4±76.0 mg/dl; p=0.01
- **BMI-weight loss:** 1.3±1.4 to 0.4±0.8; p<0.0001
- **ORA:** 0.9±1.2 to 0.3±0.6; p<0.0001
- **Dyslipidemic medication:** 0.6±0.7 to 0.5±0.4; p<0.0001

**Conclusions**

- There was a significant reduction in BMI, systolic and diastolic BP, total cholesterol, triglycerides, and percentage of overweight patients.
- There was a significant reduction in UACr in patients who lost more than 18% of their body weight.
- The study suggests that Bariatric Surgery is an effective treatment for weight loss and improvement of cardiovascular risk factors.
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 chronic kidney disease (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; cFLC + λFLC + κFLC), 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: In the UHB population (median follow up 1483 days [range 22-2906]), cFLC levels were associated with reduced time to ESKD (HR=1.09, 95%CI 1.005-1.012, 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 identified 7 risk factors (including cFLC, ACR, phosphate and eGFR) being associated with progression to ESKD. Combining the 3 datasets, the algorithm identified 138/561 (25%) patients with no risk factors, with no risk of progression within 12 months and 180/561 (32%) patients with 1 risk factor and a 2.8% risk of progression who could be returned to primary care for 6-12 months. Combined with the eGFR, 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.

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 Allogro 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 (G3 – G5) 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.

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 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 EDTA-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±7 years. Inter and intra- assay CV’s 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=0.35, p<0.05). BMD was better correlated with 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= 0.040 ; LS r=0.34, p=0.006 cf r= 0.29, p =0.02).

Conclusions: PTH and calcium concentrations are normally very tightly coupled. The intact PTH results provide a skewed view of overall levels of calcium metabolism. The more physiologically relevant improved correlations between plasma PTH (but only when measured by the biointact assay) and bone mineral density also point to more relevant functional
SP150

'H'-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 ('H'-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 'H' 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 parts 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 (adenosine, ATP, ...).

Conclusions: Our results suggest that 'H'-NMR-based detection of urinary nucleic acids could discriminate patients with glomerular injury vs. tubular injury. Since nucleic acid signal promote tubular inflammation through purinergic receptors, our findings provide a new hypothesis regarding the negative impact of proteinuria on tubulo-interstitial inflammation and fibrosis.

SP151

ASYMMETRIC DIMETHYLMORPHINE 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 y, BMI 33.5±6.3 kg/m²). Exclusion criteria were CKD III-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 insulin, 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 (0.77±0.19 umol/l vs. CKD I 0.58±0.11, 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 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 µU/ml, b = 1.52±0.040), HOA index (3.3±1.7, b = -0.49, p=0.001) and ADMA (0.62±0.12, b = 0.46, p=0.038).

Conclusions: In obese patients stages of progressive early 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.

SP152

EFFECT OF ACUTE KIDNEY INJURY EPISODES ON PROGRESSION OF CHRONIC KIDNEY DISEASE IN EARLY STAGE CKD PATIENTS

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Introduction and Aims: Although episodes of acute kidney injury (AKI) is a well-known risk factor for progression of chronic kidney disease (CKD), most studies have been performed in in-hospital or intensive care unit settings. We designed this study to assess the contribution of AKI episodes on progression of CKD in a stable ambulatory, early stage CKD patient setting.

Methods: We retrospectively assembled a cohort of 458 ambulatory patients with stage 2 and stage 3 CKD and analyzed the risk of CKD progression as a function of AKI episodes using acute kidney injury network (AKIN) criteria. Primary outcome (progression of CKD) was defined as more than 15 ml/min/1.73m² decline of estimated GFR (eGFR) from the baseline.

Results: Over a median follow-up of 902 days, 134 (29.3%) patients had AKI episodes. We observed no mortality in our cohort during the follow-up period. Patients with AKI episodes were older and more likely to have diabetes and lower baseline eGFR. There was no difference in the proportion of gender and hypertension. Significantly more patients with AKI episodes reached primary outcome than patients without AKI episodes (29.16% vs. 15 (4.6%), p<0.001). In multivariate-adjusted Cox proportional hazard analysis, age, baseline eGFR and episodes of AKI were independent predictors of CKD progression. Among these, episodes of AKI was the most powerful predictor (hazard ratio, 3.517 vs. age 1.031 for baseline eGFR). Subgroup analysis including only patients with episodes of AKI stage 1 AKI and patients without AKI episodes also revealed the important contribution of minor elevation of serum creatinine on progression of CKD (hazard ratio, 2.852 for AKI episode vs. 1.046 for age vs. 1.043 for baseline GFR).

Conclusions: Even in stable stage 2 and stage 3 ambulatory patients, silent AKI episodes are also thought to be a powerful risk factor for progression of CKD. Multi-sided approach to develop tools for prevention, early detection, or stratification should be continued to improve the ultimate prognosis.

HbA1c IS AN INDEPENDENT RISK FACTOR FOR MORTALITY BUT NOT FOR END STAGE RENAL DISEASE IN NON-DIABETIC CKD PATIENTS

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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 higher 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-dialysis 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 42.3±19.8 ml/min/1.73 m² and 5.5±0.5%. HbA1c values were significantly associated with age, BMI, systolic blood pressure, mGFR, albuminuria, fasting blood glucose, insulinemia and orosomucoid. The risk of ESRD was significantly decreased in patients with intermediate value of HbA1c even after adjusting for initial mGFR (HR 0.517 vs. 1.031 for age vs. 1.037 for baseline eGFR). Subgroup analysis 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)]. Mortality HR was associated with higher HbA1c values for both a continuous or categorical variables: for each increase of 1% in HbA1c HR=1.95 (1.32,1.91). 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 inflammation and oxidative stress, various hypothesis including metabolic or inflammatory pathway must be explored to better understand these results.

**SP154**  
**EFFECTS OF ZINC SUPPLEMENTATION ON PLASMA HOMOCYSTEINE LEVEL IN ESRD PATIENTS: A DOUBLE BLIND RANDOMIZED CLINICAL TRIAL**

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**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 hCys. 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±11.9 μg/dl versus 120.8±26.9 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 13.2±3.5 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 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<0.013), plasma Zinc level at 43 days (r=0.446; P<0.0001) and mean percentage reduction of Zinc (r=0.327; P<0.001). Mean percentage reduction of hCys level positively related with baseline hCys (r=0.251; P<0.013), plasma Zinc level at 43 days (r=0.446; P<0.0001) and mean percentage reduction of Zinc (r=0.327; P<0.001).

**Conclusions:** Zinc supplementation leads to a reduction in serum hCys levels in ESRD patients with Zinc deficiency.

**SP155**  
**INFLUENCE OF RENAL DYSFUNCTION ON CLINICAL OUTCOMES IN PATIENTS WITH CONGESTIVE HEART FAILURE COMPLICATING ACUTE MYOCARDD Infectious**

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**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, statins, and ACE inhibitors or ARBs reduced 1-year mortalities, while diuretics increased the risk of 1-year mortality in Cox proportional hazard analysis. Moreover, postdischarge use of aspirin, beta-blockers, CCBs, ACE inhibitors, or ARBs and statins, which had been prescribed at discharge, significantly reduced the 1-year mortality rate for those with renal dysfunction; such reduction was not observed for those without renal dysfunction, except in the case of aspirin, which did have a positive impact on 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.

**SP156**  
**ARE GFR ESTIMATING FORMULAS INACCURATE IN OBESE PATIENTS?**

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**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 ± 6.4 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 57.7 ± 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 mgFRreal was significantly lower than the formulas (p < 0.01). Bias and accuracy are 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 insulin 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.

<table>
<thead>
<tr>
<th></th>
<th>Accuracy%</th>
<th>Bias (mL/min/1.73m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDRD</td>
<td>79.3%</td>
<td>82.1</td>
</tr>
<tr>
<td>CKD-EPI</td>
<td>72%</td>
<td>84.4</td>
</tr>
<tr>
<td>mgFRreal</td>
<td></td>
<td>+5.9</td>
</tr>
<tr>
<td>mgFRideal</td>
<td></td>
<td>-4.2</td>
</tr>
<tr>
<td>a = p &lt; 0.01 vs mgFRideal</td>
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<td>b = p &lt; 0.01 vs MDRD</td>
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**SP157**  
**NUTRITION ASSESSMENT AND RISK PREDICTION IN DIALYSIS PATIENT - A NEW INTEGRATIVE SCORE**

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**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 before 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=0.842, 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=0.77, 95% CI 0.72-0.828, p<0.0001). A unit increase of 3 monthly scores at beginning of study significantly reduced mortality and hospitalization risk (mortality:HR=0.485, 95% CI 0.278-0.847, p<0.011; hospitalization frequency: HR=0.77, 95% CI 0.72-0.828, 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, Cockcroft-Gault formula corrected by body surface area (CG), the abbreviated Modification of Diet in Renal Disease (MDRDa) equation and the Mayo Quadratic (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 carefully instructed about the 24h urine output collection by the same nurse. GFR was estimated using five methods: CCr, CKD-EPI, CG, MDRDa 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 MDRDa. 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 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^{-6} for creatinine-based eGFR, P= 1.0 x 10^{-4} for cystatin C-based eGFR and presence of CKD (eGFR < 60 ml/ min/1.73 m², P= 1.1 x 10^{-11}). 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^{-6}). 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...
serum creatinine (mg/dl) x fasting insulin concentration (μU/mL)]/22.5.

Elisa, CRP by nephelometry and glucose by routine method. Homeostasis model
assumption index of insulin resistance (HOMA-IR) was calculated as (fasting glucose
concentration (mmol/l) / fasting insulin concentration (μmol/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.

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
homocysteine metabiltie 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
glomerular filtration rate (GFR) according to the MDRD equation. This equation was
out-performed by the recent introduction of the 2012 CKD-EPI creat-cys equation.

Methods: We studied 186 patients whose plasma LCAT activities were
measured by enzymatic method from 2011 to 2012 at a single center. Other parameters
known. The aim of this study was to evaluate whether LCAT activities also decrease in
patients of the 1 LIKE HOME study. GFR was estimated according to the
MDRD and the 2012 CKD-EPI creat-cys equation. The SAM/SAH ratio was calculated
for assessing methylation capacity as a major determinant of epigenetic gene
regulation.

Results: SAH levels inversely correlated with eGFR estimated with both the MDRD
(r = -0.302, p < 0.001) and the 2012 CKD-EPI creat-cys, equation (r = -0.327, p < 0.001).
Compared to SAH, homocysteine showed a weaker inverse correlation with eGFR
(MDRD: r = -0.227, p < 0.001; 2012 CKD-EPI creat-cys: r = -0.252, p < 0.001). The
SAM/SAH ratio positively correlated with eGFR (MDRD: r = 0.001, 2012 CKD-
EPI creat-cys; r = 0.213, p < 0.001). Finally, in contrast to homocysteine (r = 0.018,
p = 0.720), SAH positively correlated with the IMT (r = 0.119, p = 0.017).

Conclusions: In subjects from the general population, gH2A and subclinical
atherosclerosis are more strongly associated with SAH than with homocysteine.
These associations are more evident when using the 2012 CKD-EPI creat-cys equation.
Interestingly, recent studies indicate that vitamin therapy for homocysteine reduction
(comprising folate, vitamin B12 and B6) does not lower SAH levels. Thus, SAH should
be considered as a more promising target in cardiorenal syndrome than homocysteine.
CIRCULATING ANGIOTENSIN-CONVERTING ENZYME 2 IN CHRONIC KIDNEY DISEASE 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-dialysed 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, and plasma ACE2 activity.

Results: Patients on dialysis had higher levels of ACE2 activity compared to CKD3-5 patients (38.46 ± 6.36 IU/l/lou/hr 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 (31.86 ± 5.58 vs 22.82 ± 1.41 p < 0.05), DM patients (33.49 ± 2.41 vs 26.32 ± 1.25, p < 0.05) and patients with hypertension with mortality on dialysis, as reported on 3 Registries (Italy, France, USRDS), both comparing the age-adjusted rates and considering only the follow-up of cases with GFR <15mL/min.

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.
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%) patients. 15 suffered from both depression and stress, while 10 experienced either stress or depression. A major chronic stressor, such as loss of a child, was present in 20 patients. Participants 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=40.6 ± 16 vs eGFR2=45.8 ± 17, p<0.01). Patients suffering from both stress and depression had a significant eGFR decline (eGFR1=43 ± 18 vs eGFR2=39 ± 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=0.03).

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.
copper 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/μl 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<0.05). Data obtained follows normal distribution. Paired t-test showed no significant (α=0.05) difference between results obtained by two methods (t=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 from normal kidney (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: C0+, no changes; C1+, <25% damage to the glomerulus; 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 myofibroblasts and glomerular parietal epithelium.

Results: In NS, most glomeruli (>95%; G0) showed no sclerotic damage, calponin-positivity at its periglomerular area (<97%; 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 of the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (2013002683)).

SP172

ADVANCES IN KIDNEY FOCAL LESIONS-USE OF CONTRAST ENHANCED ULTRASONOGRAPHY

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1Internal Medicine University of Medicine and Pharmacy Târgu Mures Mures Romania, 2Hippocratean Dialysis Center Târgu Mures Mures Romania, 3Pathology University of Medicine and Pharmacy Târgu Mures Mures Romania, 4TOPMED Medical Center Târgu Mures Romania

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 was performed and the vascular pattern was studied, results were different: three malignant lesions and two benign lesions were classified as malignant. Conclusions: CEUS is a noninvasive, harmless, high tech investigation of kidney focal lesions, with an excellent positive predictive value and can be performed also in kidney failure.

SP173

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 GFR (+7.19 vs -3.47 ml/min/yr, p<0.05) [Figure 1], nutritional parameters, body weight (+3.0 vs -1.0 kg, p<0.05), LBM (+1.0 vs -2.8 kg, p<0.05), and MAMC (+1.1 vs -0.34 cm, p<0.05).

**Conclusions:** Correcting metabolic acidosis (via bicarbonate supplementation) may preserve renal function and improve nutritional parameters in CKD patients, and adjusted by beta-actin band density in the setting of same beta-actin band density. We measured serum creatinine and spot urine albumin/creatinine ratio as a marker of renal damage, and compared correlation of urinary podocyte protein between disease groups or renal disease progression.

**Results:** 15 Patients were diabetes, 25 were glomerulonephritis and others were unspecified chronic kidney disease. Mean age was 34±15.8 years old, mean serum creatinine was 2.01±1.37 mg/dl, mean albumin/creatinine ratio was 4.65±3.60. Urine albumin excretion showed no difference between diabetes and non-diabetes (p=0.26), and that showed no correlation with serum creatinine level (p=0.81). The reference beta-actin band density showed no significant difference between diabetes and non-diabetes (p=0.60), and band density of podocalyxin/actin and nephrin/actin and showed no significant difference between patient group (p=0.31, 0.58). However, synaptopodin/actin and podocin/actin ratio between diabetes and non-diabetes showed remarkable difference (6.43±3.79 vs. 2.79±3.29, 8.46±9.43 vs. 4.47±7.67, respectively, p<0.01). Serum creatinine level showed significant correlation only with urinary synaptopodin/actin ratio (r=0.58, p<0.001) in contrast to nephrin, podocalyxin and podocin showed no significant correlation.

**Conclusions:** In conclusion, amount of urinary synaptopodin excretion is increased in diabetic kidney disease comparing with glomerulonephritis, and it showed significant correlation with serum creatinine elevation in glomerulonephritis. We suggest that urine synaptopodin level can be a predictor of glomerular damage regardless of urine albumin excretion.
Center. Small for gestational age (SGA) babies were defined as gestational-age adjusted <10th 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), GFR 75 (20-135), proteinuria 2.5 g/24h (0.6-2.3) 8/21 diabetes-3/21 kidney graft-2/21 interstitial-8/21 glomerular diseases). We identified 14 controls (median age 31 yrs (22-39), sCr 1.4 mg/dL (1.1-2.9), GFR 51 ml/min (24-60), proteinuria 0.6 g/24h (0.1-2) 1/14 kidney graft-3/14 glomerular diseases-10/14 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 child, 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, 4/19 singletons were SGA (2<5th centile, 2 5-10th centile). Conversely in the control group, with pre-term deliveries 9/14 cases, SGA was recorded in 7/14 (2<5th centile, 5 5-10th centile). Mean follow up of the children born from mothers in the diet group was of 33 months (1-96) and 28 months (6-108) in the control group. At the end of each observation period, none of the children had major auxologic profile in the long term.

Introduction and Aims: Chronic kidney disease (CKD) results in negative effect of albumin on tubular cells. The reduction of the transport function mediated by Pgp leads to intracellular accumulation of drugs and toxic compounds resulting in increased tubular cells toxicity. This could be a further factor of progression of kidney damage linked to inflammation, tubular degeneration, and fibrosis. Furthermore, a large number of genes encoding membrane transporter proteins of tubular cells was found to be up- or down-regulated by albumin. The aim of the study was to establish accuracy and safety of RFR definition after low dose dopamine load test to establish renal function reserve (RFR). Oral meat production could have negative effect of albumin on tubular cells. The influence of albumin on Pgp gene expression of Pgp with ensuing impairment in the membrane transport function. In the kidney, Pgp is mainly expressed in the proximal tubule. The influence of albumin on expression and function of Pgp in HK-2 proximal tubular cells has previously been demonstrated. Aim of this study was to assess the influence of various drugs on Pgp expression in HK-2 cells exposed to albumin. Methods: Tubular cells were cultured in presence of albumin (15 mg/mL) for 72 hours. Myocophenolic acid (MPA, 100 mM), paracalcitol (PAR, 100 mM), and celecoxib (CEL, 20 mM) were added to culture medium. Pgp protein expression was assessed by Western Blot (WB). To study the ABCB1 Pgp encoding gene expression semi-quantitative RT-PCR was employed. Pgp transport function was evaluated by intracellular accumulation of rodamine-123 test (R-123).

Results: In cells exposed to albumin a reduction in Pgp expression to 33.9% respect to controls (Western blot) was found (p<0.001). ABCB1 gene expression showed a reduction to 66 % of controls (p<0.02). Pgp mediated transport assessed by the R-123 test was also impaired. In fact, the fluorescence of HK-2 cells resulted 1.5-fold higher than that of controls (p<0.05). MPA added to the medium increased Pgp expression to 56% of controls, while the fluorescence was reduced to 1.37-fold. In presence of PAR Pgp expression increased to 44% of controls. Instead, CEL induced a reduction of Pgp expression to 19.6% of controls, higher than that caused by albumin alone.

Conclusions: Tubular cells exposed to albumin present a reduction in both protein and gene expression of Pgp with ensuing impairment in the membrane transport function. The reduction of the transport function mediated by Pgp leads to intracellular accumulation of drugs and toxic compounds resulting in increased tubular cells toxicity. This could be a further factor of progression of kidney damage linked to proteinuria. The results of this study show that the albumin induced down-regulation of Pgp can be reversed by MPA and PAR and point out a negative perspective of limiting the influence of albumin on tubular cells.
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 been a serious problem which threatens the problem 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 sodium Cytidine C (Cys-C) and normal urine microalbumin before transplantation and received Tac-based immunosuppressive regime (Tac+MMF+ prednisone) afterwards. A human-10 antibody bead kit (BioSource, Camarillo, CA) was used to measure the levels of 10 cytokines and chemokines in 50 ml of serum from each transplant patient and controls. After transplantation, Tac, Cys-C and urine microalbumin were measured every 3 months. In all recipients except 28 recipients were excluded from the analysis.

Results: The levels of IL-6, IL-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 onethundreth (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 (cilM>12.5 mg/L) was much higher compared with the group without injury (cilM<12.5 mg/L).

Conclusions: IP-10 may be the important cytokine leading to chronic CNI-induced nephrotoxicity, especially the tubulointerstitial injury. Alto-liver recipients with high serum IP10 posttransplant levels might develop severe chronic CNI-induced nephrotoxicity due to increased immune activation.

HIGH SENSITIVITY TROPONIN T IN CHRONIC KIDNEY DISEASE

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Introduction and Aims: Chronic kidney disease (CKD) is an independent risk factor for developing coronary heart disease (CHD). The cardiac troponins are structural proteins predictors of (CHD). It has been demonstrated that high sensitivity Tropinin T (hs-TnT) has greater predictive value than conventional Troponin T in the development of CHD in the general population. However, its usefulness in patients with CKD is unclear.

Objectives: To study the influence that the degree of renal function has on levels of hs-TnT and its possible association with other cardiovascular risk factors.

Methods: We conducted a prospective study including 563 patients: 58% male, 32.5% diabetics, aged 64 ± 17 years, at different stages of CKD. We collected clinical history, routine laboratory parameters and hs-TnT. 20% had CHD history and 9.2% of acute myocardial infarction (AMI). Glomerular filtration rate was 50 ± 29 ml/min/1.73m2 (MDRD-4) and 51 ± 29 ml/min/m2 (CKD-EPI). In 408 patients an echocardiogram was performed simultaneously.

Results: The mean hs-TnT was 18.5 ng/ml. Plasma concentrations of hs-TnT were directly relate to age (r = 0.643, P <0.001) and inversely with the MDRD 4 (r = -0.674 P <0.001). The hs-TnT is higher in men than in women (20.4 vs 15.9 ng/ml, P <0.01), is significantly higher in patients with history of CHD (p = 0.032) and especially in patients with a history of myocardial infarction (p <0.01). The mean hs-TnT according to stages of CKD was: Stage 1: 3.97 ng/ml, stage 2: 6.03 ng/ml, stage 3: 18.94 ng/ml, stage 4: 30.93 ng/ml, stage 5: 45.56 ng/ml, with a statistically significant difference in the variance analysis (P <0.01). When we divided the patients with and without history of CHD, the differences remained significant (p <0.01 and p <0.001 respectively), although the values were significantly higher in those with a history. 19.1% of patients had left ventricular hypertrophy in this group, the values of hs-TnT were higher (40.4 vs 13.8 ng/ml, p <0.001). In a multivariable model, remain as predictors of high hs-TnT values the loss of renal function, history of CHD and LVH.

Conclusions: The hs-TnT levels increased as the severity of CKD, even without evidence of acute myocardial damage, so the value of this marker must be adjust according to the degree of renal function. hs-TnT concentrations are higher as in men, patients with history of CHD and those with LVH.

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 an increase in number of patients sent back to general practitioners. This study was done in order to clarify whether the treatment of the eGFR of the patients 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<0.0001). 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 33.8ml/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).

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.

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Methods: Healthy 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 skeletal muscle mass (SMM) were estimated (using segmental and whole body calculations were performed. Blood pressure, serum creatinine and albumin were measured, eGFR was estimated using the CKD epidemiology collaboration equation (CKD-EPI). CKD stages (revised KDIGO classification based on eGFR [Levey et al in Kidney Int 2011]) were compared by ANOVA or Kruskal Wallis tests.

Results: Forty five subjects were studied (age 52 [range 45-61] years, 60% women, body mass index (BMI) 27.0±4.1 Kg/m², eGFR 82.1±16.8 ml/min/1.73 m²). Subjects were divided into three groups: G1 ≥90 ml/min/1.73m² (n=16), G2 60-89 ml/min/1.73 m² (n=24), G3a 59-45 ml/min/1.73m² (n=5). The ECV/ICV ratio was divided into three CKD stages: G1 SBP (mmHg) 119.2 Age (years) 46.5 (43-53.5) 54.5 (47-62) 70 (69-74) 0.004

Methods: 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 estimate BCM in obese patients an effort to reduce the bias (electrodes repositioning?).

Results: In general measurement of ICV 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 ECW compared to the Fresenius device (41 ± 35.8 kg; p = 0.04 and 22 ± 17.2; p = 0.01 respectively). A comparison of results from patients with BMI ≤25 vs ≥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), ECW (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), ICV (0.32; p=ns), BCM (0.15; p=ns), ECW (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 (28.7 ± 23 ±p=0.05) than Fresenius device.

Conclusions: Since estimates of TBW, ICV 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.

Introduction and Aims: There is no precise information on body composition with hydration and nutritional status in non-dialyzed patients with chronic kidney disease (CKD). So we decided to investigate ambulatory renal patients (P) at different levels of renal function: KDOQI-eGFR stage 1, 2, 3, 4, or 5-non D. The primary objective was to evaluate the hydration status of these P.

Methods: We used the Body Composition Monitor® (from Fresenius Medical Care Germany Inc.), based on multifrequency (50 measurements from 5 to 1000 kHz) 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 (ECW), intracellular water (ICW), and BCM were compared. Thirty patients with chronic kidney disease (stage III-V) with mean age 45.8±8.8 y, 19 men and 17 women, who had a wide range of BMI (17.3-42 kg/m²) were recruited to this study.

Methods: We evaluated the hydration status of these P. in an ambulatory renal patient study in Turkey and calculate a correction coefficient to obtain a better estimate BCM in obese patients an effort to reduce the bias (electrodes repositioning?)

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 estimate BCM in obese patients an effort to reduce the bias (electrodes repositioning?) and finally comparison to gold standard should be undertaken.
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 inpatients with chronic kidney disease as well as healthy volunteers. Iohexol clearance was measured and the precisions and biases 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 Cockroft-Gault, Mawer, Bjornsson 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 Mawer and MDRD 2 formulae. Bias and random error for the IDMS-traceable MDRD equation were 11.33±8.97 mL/min/1.73 m² and 14.21±1.73 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.
**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:** Cystatin 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 cystatin 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 eGFRcr and eGFRcy. 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:** 81.7% had undetectable HIV-RNA level. Prevalence of eGFRcr and eGFRcy < 60 ml/min/1.73 m² was 8.6% and 3.5%, respectively. 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.

**SP192 MDRD VERSUS CKD-EPI EQUATIONS TO ESTIMATE GLOMERULAR FILTRATION RATE IN OBESE 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, apparent increase of UV, but improved clinical symptoms associated with 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.

**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.

**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 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(UAV, ml/d) in stages G3b, G4 and G5 were 966±1250(P=0.19), −38±73(P=0.87) and 678±474(P=0.05), respectively, which showed significant increase of UV in CKD stage G5 at the end of the study. Increment of serum creatinine levels(ΔsCr, mg/dL) in each stage were 0.02±0.14(P=0.79), 0.48±0.47(P=0.05) and −0.11±0.44(P=0.53), respectively, showing no significant WRF except in stage 4. Changes in blood pressure(ΔBP, 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.

**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 colchicine treatment in renal amyloidosis in the frames of Familial Mediterranean Fever (FMF) depending on colchicine daily dose and the stage of nephropathy on 23 December 2018.

**Methods:** We studied 41 FMF patients with amyloid nephropathy. All patients were taking colchicine: 18 patients began the treatment in protenuric stage (I subgroup), 15 – in the stage of nephrotic syndrome (NS) (II subgroup), and 8 - in the stage of mild (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 41 investigated patients (26,8%). The essential inclusion criterion for the participation in the study was the duration of colchicine treatment not less than 2 consequent years.

**Results:** In 1 subgroup colchicine 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 increase tendency – in 12, and increase in creatinine level – in 3 patients. 5 patients in I subgroup were treated adequately. In 3 of them colchicine was efficient, however the rest 2 patient developed RF. In the majority (7) of inadequately treated patients in this subgroup (10 patients) colchicine 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 colchicine efficacy in III subgroup regardless of preparation dosage.

**Conclusions:** Our investigation has shown that colchicine in the most efficient in the terms of early prescription (protenuric stage of amyloid nephropathy) and in adequate dosage. The efficacy of colchicine tends to decrease in NS, and even full colchicine dose is not able to prevent the progression of amyloidosis. In the stage of RF colchicine 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 applanation 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). Glomerular filtration rate and fibulin-1 were inversely correlated (r=−0.57; p=0.022). There was a positive correlation between fibulin-1 and central pulse pressure (r=0.44; p=0.011) and central augmentation pressure (r=0.55; p=0.033).

**Conclusion:** Fibulin-1 is involved in the pathogenesis of cardiovascular disease observed in chronic kidney disease.

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**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 Gemcitabine (Gem) and who had never manifested proteinuria before it. Proteinuria was defined as +1+, persistent in at least two consecutive examinations within six months following Gem administration.

**Results:** Of 53 patients, 18 (33.9%) patients developed proteinuria during the follow-up period (median follow-up time 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.

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**SP197** CONVERSION FROM ALLOPURINOL TO FEBUXOSTAT IS BENEFICIAL 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 progressions 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 potentiates 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 – 40)mg/day of febuxostat for 10±5.6 (3 - 19) months. Out of 139, 63 patients (0toF group) had not been treatment with any XOI. 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 to -0.63±0.8 ml/min/month. After initiating febuxostat, decline of eGFR was significantly diminished as 0.03±0.8 ml/ min/month (p=0.01). 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.
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 habits 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. 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%). 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, parathryoid and sex hormones were highly interrelated with ions metabolism, stone formation and urinary tract infections.

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 Sperman’s method showed a strong correlation (r ≥ 0.5) between laboratory and morphometric parameters in patients with nephrolithiasis (p ≤ 0.05). Diameter of tubules 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-β (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 uTGF-β (r = 0.77; p = 0.036), and negatively with the concentration of VEGF in serum (r = -0.9; p = 0.018). 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.