CLINICAL NEPHROLOGY - EPIDEMIOLOGY I

PLASMA RENIN ACTIVITY AND ALDOSTERONE-TO-RENIN RATIO ARE ASSOCIATED WITH THE DEVELOPMENT OF CHRONIC KIDNEY DISEASE: THE OHASAMA STUDY

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Introduction and Aims: Aldosterone-to-renin ratio (ARR) is believed to be a more robust screening test than aldosterone levels for primary aldosteronism, and it could be an index for inappropriate aldosterone activity and salt sensitivity. Recently, in a community-based longitudinal study in the United States, aldosterone was associated with incident CKD and microalbuminuria independent of traditional risk factors. However, the influence of ARR on the development of CKD has not been reported previously. Therefore, the present study was conducted to examine the association of plasma renin activity (PRA), plasma aldosterone concentration (PAC) and ARR with the development of CKD in a general Japanese population.

Methods: We conducted a longitudinal observational study involving 689 participants from a general Japanese population (mean age 58.2 years; 68.5% women) who did not have CKD and were not receiving antihypertensive medication at baseline. The estimated glomerular filtration rate (eGFR) was calculated from serum creatinine levels and CKD was defined as eGFR < 60 ml/min/1.73 m2 and/or dipstick-positive proteinuria. The associations of baseline plasma renin activity (PRA), plasma aldosterone concentration and ARR with the development of CKD were examined using Cox proportional hazard regression analysis adjusted for sex, age, body mass index, smoking, drinking, history of hypercholesterolemia, diabetes mellitus, and cardiovascular disease, systolic blood pressure, and baseline eGFR.

Results: During a mean 9.1-year follow-up, 118 subjects developed CKD. Mean values were 127.9 ± 13.2/71.9 ± 8.7 mmHg for systolic/diastolic blood pressure levels, 0.82 ± 0.13 mg/dl for serum creatinine by the Jaffe assay, and 87.3 ± 17.5 ml/min/1.73 m2 for eGFR. The median (25–75th percentiles) values were 1.1 (0.6–1.9) ng/ml/h for PRA, 65 (50–81) pg/ml for PAC, and 56 (35–97) pg/ml per ng/ml/h for ARR. A 1-standard deviation increment in the natural log-transformed (ln) ARR was 97 (0.78–1.15) pg/ml per ng/ml/h for PRA, 65 (50–81) pg/ml for PAC, and 56 (35–97) pg/ml per ng/ml/h for ARR. The adjusted HRs for death were 0.85 (95% CI 0.70–1.03), 1.03 (0.85–1.25), and 0.94 (0.78–1.15) for water intakes of 2.0–2.4 l/day, 2.5–3.0 l/day and >3.0 l/day when compared to <2.0 l/day, respectively. There was similarly no association between cardiovascular mortality and water intake across quartiles of daily consumption.

Conclusions: This population-based cohort study in adults finds that daily water intake is not associated with survival. Randomized trials of targeted water consumption are now required if specific water intake is to be recommended to the general population.

DAILY WATER INTAKE AND RISK OF MORTALITY: LONGITUDINAL COHORT STUDY

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Introduction and Aims: Drinking eight glasses of water each day to improve health is a widely-held belief. Previous observational data exploring the association between fluid intake and risks of mortality are sparse and conflicting. We examined the association between water intake and risks of all-cause and cardiovascular death in a census-based population.

Methods: We examined adults ≥49 years identified by a population census in an urban area west of Sydney, Australia. Daily water intake was measured using a self-administered food frequency questionnaire and death was defined from the Australian National Death Index. Cumulative incidence rates for all-cause and cardiovascular mortality were calculated according to quartiles of daily water intake. We applied univariate and multi-variable-adjusted Cox proportional hazard models to assess the relationship between all-cause and cardiovascular mortality and total daily water consumption while controlling for the effects of age, gender, smoking status, history of myocardial infarction, prior cancer, cerebrovascular disease, employment, serum glucose, high density lipoprotein, serum cholesterol, triglycerides, platelet, white cell counts and fibrinogen levels. Hazard ratios (HRs) and their 95% confidence intervals (CI) with higher water intake (≥2.0 l/day, in quartiles) were then compared with those drinking < 2.0 l/day in the unadjusted and adjusted multivariable models.

Results: We had follow-up data for 2897 of 3654 recruited individuals (mean age 66.2 ± 9.8 years) during a median follow-up of 13.1 (11.1–13.9) years. The average reported daily water consumption was 2.48 l/day. Upper and lower quartiles of water intake corresponded to more than 3 l (12.5 glasses) and less than 2 l per day (8 glasses), respectively. There were 1047 deaths and 691 cardiovascular deaths. As compared with the lowest intake of water, the adjusted rate for death from any cause did not differ significantly for each quartile of increasing daily water intake. The adjusted HRs for death were 0.85 (95% CI 0.70–1.03), 1.03 (0.85–1.25), and 0.94 (0.78–1.15) for water intakes of 2.0–2.4 l/day, 2.5–3.0 l/day and >3.0 l/day when compared to <2.0 l/day, respectively. There was similarly no association between cardiovascular mortality and water intake across quartiles of daily consumption. There was also no indication of a dose-response relationship between increasing daily water consumption (in 100 ml increments) and either all-cause (1.01 (95% confidence interval 0.99 to 1.02) or cardiovascular mortality (1.05 (0.89 to 1.21)) when compared to less than 2 l/day.

Conclusions: This population-based cohort study in adults finds that daily water intake is not associated with survival. Randomized trials of targeted water consumption are now required if specific water intake is to be recommended to the general population.

META-ANALYSIS: STATIN THERAPY TO PREVENT DEATH AND MAJOR CARDIOVASCULAR EVENTS IN PEOPLE WITH CHRONIC KIDNEY DISEASE

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Introduction and Aims: Cardiovascular events are the most frequent cause of death and morbidity in people with chronic kidney disease (CKD). Statins lower cardiovascular events in people with CKD, although trial data are conflicting and treatment benefits of statins may depend on severity of CKD. Individual randomized trials may have insufficient power to determine treatment effects according to stage of CKD. We aimed to summarize the effects of statins on mortality, major cardiovascular events, and withdrawal of treatment due to adverse events using random-effects meta-analysis and explored the effects of stage of kidney disease on treatment effects using subgroup analyses.

Methods: We conducted a systematic review and meta-analysis of randomized controlled trials that included adults with chronic kidney disease and that compared statins with placebo, standard care, or no treatment. We systematically searched Cochrane and EMBASE databases to December 2011 without language restriction. Multiple reviewers extracted details on participant characteristics, interventions, and risk of bias. We summarized treatment effects on mortality, major cardiovascular events, and withdrawal of treatment due to adverse events using random-effects meta-analysis and explored the effects of stage of kidney disease on treatment effects using subgroup analysis.

Results: We included 80 trials including 51 099 participants including 48 comparisons (39 820 participants) with earlier stages of CKD, 21 comparisons (7982 participants) on dialysis and 17 comparisons (3297 participants) in kidney transplant recipients. Data for people with CKD in 10 studies (30 897 participants) were sourced from post hoc subgroup analyses. There was evidence that statins effects on mortality differed significantly according to stage of CKD. Statin treatment reduced death in people with earlier stages of CKD (relative risk [RR] 0.81 [95% CI 0.74–0.88]), but had little or no effect in people on dialysis (RR 0.96 [0.88–1.04]) and uncertain effects in kidney transplant recipients (RR 1.05 [0.84–1.31]) for subgroup
Serum Creatinine is Associated with Carotid Intima-Media Thickness in Males: Results of a Population-Based Study (SHIP)

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Methods: The Study of Health in Pomerania (SHIP) is a cross-sectional, population based study in the North East of Germany. Data from 2,267 individuals (1,199 males) aged 45 years or older were available for analysis. Creatinine clearance was calculated by the Cockcroft-Gault, Jelliffe, Wright and the abbreviated Modification of Diet in Renal Disease formulae. Women and men were analyzed separately.

Results: 240 males (20.0%) and 244 females (20.9%) showed serum creatinine values above the normal range. Males and females with high serum creatinine had higher serum HbA1C levels, pulse pressure, BMI, and serum uric acid after adjusting for confounding factors, multivariable analysis revealed that in males, raised serum creatinine levels were independently associated with carotid IMT (non-standardised β-coefficient 0.0274, 95% CI 0.005-0.050, p=0.018). However, we could not find an association for raised serum creatinine levels in women nor for reduced values of calculated creatinine clearances in either sex.

Conclusions: We found a gender-specific relation between impaired renal function and carotid IMT with subclinical atherosclerosis as depicted by carotid intima media thickness (cIMT). The aim of the present study was to examine the association of cIMT with various serum markers of renal function in a large population based study.

Introduction and Aims: Chronic kidney disease (CKD) remains asymptomatic until its late stage. There is only little information on the association of renal function with subclinical atherosclerosis as depicted by carotid intima media thickness (cIMT). The aim of the present study was to examine the association of cIMT with various serum markers of renal function in a large population based study.

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Conclusions: The result of this study demonstrates that decreased GFR and increased level of serum homocystein were independently associated with arterial stiffness only in CKD group, after adjustment for other confounding factors. However, in CKD group, not only age (β = -0.235, p = 0.001) and serum cystatin C, and aortic pulse wave velocity in 200 patients with stage 3 & 4 chronic kidney disease, and then serially in a subgroup of 65 patients over 36 months. We compared baseline biochemistries to a group of 152 healthy controls.

Results: Serum matrix metalloproteinase-2, cathepsin S, elastin-derived peptide levels were higher in CKD patients compared to healthy controls of similar age, and levels increased at a higher rate than in non-CKD suffers. All 3 markers of elastin degradation were independently associated with baseline aortic pulse wave velocity and changes in stiffness over the follow-up period. Higher matrix metalloproteinase-2 (odds ratio per 1SD increase = 3.11, p < 0.001) and elastin-derived peptide levels (odds ratio per 1SD increase = 1.98, p < 0.018) were also independently associated with pre-existing cardiovascular disease. In multivariable Cox regression analysis, higher serum elastin-derived peptide levels were associated with increased all-cause mortality (hazard ratio per 1SD increase = 1.74, p < 0.021) after adjustment for known cardiovascular and renal risk factors.

Conclusions: In pre-dialysis chronic kidney disease, elastin degradation is a major determinant of aortic stiffness and is associated with all-cause mortality.

Introduction and Aims: Brachial-ankle pulse wave velocity (BaPWV) is a measure of arterial stiffness and known to be an independent predictor of cardiovascular disease (CVD) in several disease populations including chronic kidney disease (CKD). But little is known about which individual factors are associated with arterial stiffness in CKD patients.

Methods: We retrospectively reviewed the 293 patients who had visited health promotion center in a single community. The patients were divided into 2 groups which are CKD group (n=99, estimated glomerular filtration rate (eGFR): 15-59 mL/min) and non-CKD group (n=194, eGFR = 60 mL/min) and non-CKD group (n=194, eGFR = 60 mL/min). Baseline characteristics (age, sex, diabetes, hypertension, smoking, eGFR, ankle-brachial index (ABI), intimal thickness (IMT) of carotid artery, systolic/diastolic blood pressure, body mass index (BMI) and various biochemical blood examinations including cystatin C, cathepsin S, elastin- derived peptides, their endogenous inhibitors, tissue inhibitors of metalloproteinase-1 and -2, cystatin C, and aortic pulse wave velocity in 200 patients with stage 3 & 4 chronic kidney disease, and then serially in a subgroup of 65 patients over 36 months. We compared baseline biochemistries to a group of 152 healthy controls.

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Introduction and Aims: Many authors have questioned Body Surface Area (BSA) as a normalisation index of Glomerular Filtration Rate (GFR). We investigated whether there are clinically significant differences between measured BSA indexed and absolute GFR values in 895 adults suffering from cancer in those cases of extreme body sizes. We also test the hypothesis that height is a better parameter for GFR indexation. All patients had their renal function measured with 51 chrome ethylene diamine tetraacetic acid (51Cr-EDTA).

Methods: Cross sectional study of 895 adults diagnosed with cancer, before they started treatment with chemotherapy.

Results: BSA-GFR in the subgroup with a BSA = 2 m² underestimated GFR with a bias up to -20.76 ml/min (-23.59%), and the opposite effect occurred in the subgroup of BSA < 1.60 m² where it causes an overestimation of GFR with a bias of 10.08 ml/min (11.46%). Indexing GFR for height also causes bias but to a much lesser extent. Bias in the subgroup of BSA = 2 was -6.67 ml/min (-7.59 %) whereas bias in subgroup with BSA < 1.6 was 3.99 ml/min (4.53%). GFR increased with BSA in men but not in women. There was an overall correlation between BSA and m-GFR of 0.52 and 0.44 between Height and m-GFR. Intercept was BSA = 1.4881 + 0.004 x ABS-BSA and Height = 156.63 + 0.114 x ABS-BSA.

Conclusions: BSA is not a good normalisation index in patients with extreme body sizes. Therefore, we recommend clinicians to use the GFR as ml/min values instead of ml/min per 1.73m² when treating individuals.
Abstracts

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HOW ARE EARLY CKD PATIENTS REFERRED TO NEPHROLOGISTS BY OTHER SPECIALTIES?

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Introduction and Aims: Chronic Kidney Disease (CKD) is an emerging public health problem worldwide. Nevertheless, the pattern of patients with CKD evaluated by nephrologists and the assessment of complications such as Secondary Hyperparathyroidism (SHPT) remains country and many times physician specific. PRESTAR sought to assess the characteristics of the CKD stages 3-5 (not on dialysis) population that is followed up in Nephrology clinics in Greece. Secondly, we examined the habitual clinical practices related to patient referrals and PTH measurement frequency in the same patient population.

Methods: This is a multicentre, epidemiological cross-sectional study conducted in outpatient nephrology clinics at different geographic regions in Greece during 2009-10. Data on referral patterns, demographics, medical and medication history, blood pressure, blood urea, creatinine blood levels, PTH blood levels and estimated creatinine clearance were collected. The Cockroft Gault rather than the MDRD equation was selected because at the time of the study, it was the most commonly used estimating method to assess renal function and CKD stage by Greek nephrologists. Adult consecutive CKD patients followed in Nephrology outpatient clinics, older than 18 years of age, able to give informed consent were included; patients with acute kidney injury or any serious disease with expected survival of less than 12 months were excluded. Continuous variables were summarized with means and standard deviations, while categorical variables were presented with frequency tables. Associations between variables were assessed with t-tests and chi-square statistics.

Results: 1501 patients in 9 clinics were included. Patient’s demographics were as follows: 45.1% (677/1501) were female, age 66.2 ± 14.6 years, BMI 28.8 ± 5.5 kg/m2, Systolic Blood Pressure: 137.1 ± 17.8 mmHg, Diastolic Blood Pressure: 80.5 ± 10.4 mmHg, Serum Creatinine: 2.0 ± 1.1 mg/dl. A sizeable minority of patients (26.7%) had early CKD (stages 1-2). The remaining population was: 59.9% CKD stage 3, 33.6% CKD stage 4 and 6.6% CKD stage 5. Four renal diagnoses accounted for 75.3% of CKD cases: diabetic nephropathy (29.7%), vascular disease (25.3%), glomerular disease (16.3), interstitial nephritis (5%). 36.5% of patients were self referred, while the remaining had been referred by a physician of another specialty. Four specialties accounted for the bulk of referrals: Internal medicine (48.9%), Diabetology (10.1%), Cardiology (6.9%) and Urology (6.9%), with no relationship between CKD stage and referring specialty. PTH was assessed in 46.6% of patients and the likelihood of obtaining a PTH measurement was higher in advanced CKD stage (37.1, 43.8, 57.2 and 70.6 in stages 1-3 respectively, p<0.001). PTH progressively increased with advancing stage of CKD 65.4 ± 41.4, 73.0 ± 50.4, 108.6 ± 73.7, 178.4 ± 149.4, 296.1 ± 236.3 (p<0.001).

Conclusions: A large minority of Greek patients present as self referrals to Nephrology clinics, while a large number of patients exhibit laboratory evidence of SHPT even in early CKD stages. Public Health initiatives are urgently required to raise awareness of CKD and its complications (SHPT) among non-nephrologists in the Greek healthcare system.

fp156 Table 3 Comparison of correlation between body surface area and glomerular filtration rate as absolute and indexed values

* p<0.05; ** p<0.01; *** p<0.001; NS not significant

GFR: glomerular filtration rate; BSA: Body surface area; BMI: body mass index; Mean Height in centimeters.
**Oxidative Stress and Kidney Effects in Workers with Low Occupational Exposure to Cadmium**

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**Introduction and Aims:** Brazing with cadmium (Cd) containing silver solder exposes workers to Cd. Recent studies suggest adverse health effects at Cd concentrations in urine below 2.8 μg/g creatinine. The aim of this study was to assess Cd, renal markers, and oxidative stress markers in workers.

**Methods:** Concentrations of Cd in blood (Cd-B) and urine (Cd-U) were determined in 36 refrigeration industry workers frequently brazing with cadmium containing silver alloys and in 29 non-exposed control subjects. Concentrations of renal markers (NAG, IAP, μ-ArB, β2-MG, BBP in urine) and oxidative stress markers (MDA, GPX, SOD in blood and 8-OHdG in urine) were measured as well.

**Results:** Exposed workers had significantly higher concentrations of Cd-B and Cd-U as compared with non-exposed subjects: 1.63 μg/l (95% CI: 1.29-2.06) and 0.82 μg/g creatinine (95% CI: 0.52-1.27), respectively, versus 0.21 μg/l (95% CI: 0.15-0.29) and 0.14 μg/g creatinine (95% CI: 0.10-0.19), respectively. Pearson correlation analysis showed a statistically significant positive correlation between Cd-B and Cd-U (r = 0.82, p < 0.001) and the "sit-to-stand" test performance (r = 0.82, p < 0.001), respectively. In contrast, an inverse, significant correlation was observed between Cd-G and GPX concentrations. Multiple regression analysis with adjustment for age, pack-years of smoking and hypertension indicated that Cd-B and Cd-U concentrations were both significantly associated with Cd-B and Cd concentrations. The GPX concentrations were inversely and significantly associated with only Cd-U concentrations.

**Conclusions:** Significant associations between Cd-B concentrations in blood and urinary function on the one hand and renal dysfunction on the other side were found. This suggests adverse effects and offers opportunities to develop biomarkers of oxidative stress and early markers of renal injury as tools for health effect surveillance.

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**Physical Function at Start of Renal Replacement Therapy - Independent Predictor of Survival**

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**Introduction and Aims:** Patients with chronic kidney disease (CKD) benefit from regular exercise training and a high level of physical function with positive effects on cardiovascular risk factors, health related quality of life and nutritional parameters as was stated in a recent Cochrane review. The aim of the present study was to examine whether physical function at start of renal replacement therapy (RRT) affects survival and further any specific functional test has greater predictive value.

**Methods:** In this retrospective longitudinal study, 134 patients starting RRT at our department between 01-01-1998 and 31-12-2006 were observed. Data were retrieved from medical reports and the Swedish Renal Registry. Comorbidity was categorized according to Davies et al. (2002) and the "sit-to-stand" test performed. The standardized functional test program comprised hand grip strength, isometric quadriceps strength, standing heel rise, toe lift, functional reach and stair climbing and was performed by the same physiotherapist. The patients were followed until death or until the end of the observation period.

**Results:** At the end of the observation period 112 (84%) patients were still alive and none were lost to follow-up. Univariate Cox regression analysis showed, as expected, a significant effect of age (p<0.0001) and comorbidity (p=0.028). Furthermore, hand grip strength (right p=0.005), left p=0.0039), functional reach (p=0.015) and standing heel rise (right p=0.011, left p=0.004) all reached statistical significance in univariate analysis. In a subsequent multivariable Cox regression analysis, taking gender, age and comorbidity into account, hand grip strength left (p=0.023) achieved statistical significance. We found hand grip strength to be an important predictor of mortality, a reduction of hand grip strength by 50% increased the hazard ratio for death fourfold.

Between patient groups (alive versus deceased) there were no statistically significant differences in as found between concentrations of Cd-U and β2-MG, 8-RDM, SOD, and 8-OHdG, respectively. It is uncertain which is more associated with CKD, the liver enzyme or alcohol consumption.

**Conclusions:** A personalized, home-based, low intensity exercise program improves physical performance in dialysis patients. The simplicity and adaptability of this exercise program makes it well suited to the needs of a high risk population like dialysis patients. The EXCITE (Exercise Introduction To Enhance performance in dialysis) study is a randomized multicentric trial aiming to test whether a simple personalized walking exercise program prescribed in the dialysis centre but performed at home improves the degree of fitness in dialysis patients.

**Methods:** Patients were randomized (randomization stratified by NYHA class) to normal physical activity (control group) or to two daily 10-minute walking sessions at home (exercise group). Exercise intensity in this group was guided by a metronome and gradually increased according to a predefined protocol. Functional capacity was assessed at baseline and after 6 months by the 6-minutes walking test (walk-T) and the "sit-to-stand" test.

**Introduction and Aims:** Dialysis patients are characterized by poor physical performance and reduced quality of life. The EXCITE (Exercise Introduction To Enhance performance in dialysis) study is a randomized multicentric trial aiming to test whether a simple personalized walking exercise program prescribed in the dialysis centre but performed at home improves the degree of fitness in dialysis patients.

**Methods:** Patients were randomized (randomization stratified by NYHA class) to normal physical activity (control group) or to two daily 10-minute walking sessions at home (exercise group). Exercise intensity in this group was guided by a metronome and gradually increased according to a predefined protocol. Functional capacity was assessed at baseline and after 6 months by the 6-minutes walking test (walk-T) and the "sit-to-stand" test.

**Results:** 486 patients (43.9% of the total population of 1241) met the eligibility criteria. 318 patients (65.4%) providing informed consent were randomized to the exercise group (baseline 326±116 m; 6 months 364±113 m) but not in the control group (baseline 320±107 m; 6 months 324±116 m) (P between groups<0.001). Similarly, Sit to Stand time improved in the exercise group (baseline 20.5±5.0 sec; 6 months 18.3±5.1 sec) but again no change was observed in the control group (baseline 20.8±6.1 sec; 6 months 19.7±6.7 sec) (P between groups<0.009).

**Conclusions:** A personalized, home-based, low intensity exercise program improves physical performance in dialysis patients. The simplicity and adaptability of this exercise program makes it well suited to the needs of a high risk population like dialysis patients.
Results: Age of both genders were median 66 (interquartile range 60 - 70) years, and eGFR of males and females were 74 ± 16 and 76 ± 16 ml/min/1.73m², respectively. Prevalence of proteinuria was 3347 (8.1%), 7045 (7.5%), 5617 (3.9%), and 1809 (2.3%) in male non-drinkers, male drinkers, female non-drinkers, and female drinkers, respectively. In male drinkers, multivariate models identified GGT, AST, and ALT as a proteinuria-associated factor (per 1 standard deviation (SD) log IU/L, PR 1.20 [1.18 - 1.23], P<0.001; 1.14 [1.12 - 1.16], P<0.001; 1.07 [1.05 - 1.10], P<0.001, respectively), along with age and eGFR. The model adding on GGT showed the lowest AIC (47315), compared with AST (47395) and ALT (47509), indicating that GGT was more effective in identifying the participants with proteinuria. Results were similar to the other subgroups. Male moderate drinkers with lower GGT (<24 IU/L) had the lower probability of proteinuria (vs. male non-drinkers with the lowest GGT (<24 IU/L); PR 0.75 [0.65 - 0.86], P<0.001; 0.90 [0.82 - 0.98], P=0.011, respectively), whereas male moderate drinkers with higher GGT (>75 IU/L) had the higher probability of proteinuria (PR 1.36 [1.24 - 1.48], P<0.001) (Figure A). The similar associations with proteinuria were observed in females (Figure B).

Conclusions: This study suggested that participants with liver dysfunction were possibly at higher risk of proteinuria and therefore needed further examinations for CKD, irrespective of drinking status.

FP162 | RENAL DYSFUNCTION IN A COHORT OF MARFAN SYNDROME PATIENTS

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Introduction and Aims: Albuminuria and proteinuria are markers of vascular and renal dysfunction, as well as independent predictors of increased risk of cardiovascular morbidity and mortality. Marfan syndrome (MS) is an autosomal dominant disorder caused by mutation of the gene encoding fibrillin, affecting the connective tissue and typically the cardiovascular, ocular and skeletal systems. There have been very few a report of renal involvement in Marfan’s syndrome. The aim of the present study was to assess the prevalence of proteinuria and albuminuria as predictors of renal dysfunction in Marfan syndrome.

Methods: We performed an observational analysis of patients with MS according Ghent criteria diagnosed in two Hospitals (H. 12 de Octubre and Hospital Vall d’Hebron). The following baseline data were compiled from medical records: age, gender, blood pressure, albuminuria, proteinuria, serum creatinine (SCr), and glomerular filtration rate (GFR) by MDRD-4, hematoma and immunological parameters.

Results: Seventy-seven patients (41 M, 36 F) with MS have been evaluated to assess renal function. Mean age was 32.3 ± 10.6 (14-65) years. Renal function of patients was: serum creatinine 0.8 ± 0.2 mg/dL and a GFR (MDRD-4): 105.6 ± 26.1 mL/min/1.73 m². 3 patients (3.9%) had GFR<60 mL/min. Albuminuria levels was 16.6 ± 34.5 mg/24 hrs and proteinuria 0.13 ± 0.08 mg/24 hrs. 9 patients (12%) had proteinuria>0.2 mg/24 hrs. 9 patients (12%) had microscopic hematuria. 10 patients (13%) were hyper- or hypertensive. 35 patients (45.5%) were receiving beta-blockers and 17 renin-angiotensin system blockers (22%). 10 patients (13%) had elevated levels of serum IgA. The group of hypertensive patients (N = 10), had worse renal function (Scr 0.9 ± 0.2 vs 0.7 ± 0.2 mg/dL, P=0.012 and GFR 88.9±32.2 vs 108.3±24.5 mL/min, P=0.039) than non-hypertensive. The total number of patients with renal impairment (GFR<60 mL/min) was located in hypertensive patients. The percentage of patients with elevated levels of IgA was also higher in the hypertensive group (30 vs 10.9%, p=0.101).

Conclusions: The prevalence of proteinuria and albuminuria in patients with MS is higher than in the general population. Although renal function was not affected, these markers could be an early indicator of renal dysfunction. The alteration of fibrillin might be involved in the genesis of these renal effects.

FP163 | DI PYRIDAMOLE IMPROVES PATIENT AND RENAL SURVIVAL IN CHRONIC KIDNEY DISEASE STAGE 3-5 PATIENTS

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Introduction and Aims: Dipyridamole has inhibitory effects on cell proliferation and extracellular matrix accumulation and has been shown to reduce proteinuria in a variety of renal diseases such as diabetic nephropathy and IgA nephropathy. However, the role of dipyridamole for renal function preservation is still controversial. Additionally, the effects of dipyridamole for mortality and end-stage renal disease (ESRD) are not well studied. The aim of this retrospective analysis is to evaluate the association of dipyridamole therapy with long-term clinical outcomes.

Methods: Among 3,749 patients joined the IKCD (Integrated CKD care program Kaohsiung for delaying dialysis) between November 11, 2002 and July 31, 2009, 3074 CKD stage 3-5 patients who received medical prescription more than 3 months were divided into dipyridamole treated and untreated groups. We used propensity-score weighting to adjust for difference in all covariates (sex, age, primary renal diseases, comorbid diseases, life styles, baseline clinical characteristics and laboratory data, and drugs) between the two groups. Cox proportional hazard models were used to evaluate the association of dipyridamole and outcomes after adjusting propensity score and all covariates.

Results: Among the total 3074 subjects analyzed, 871 patients (28.3%) had been treated with dipyridamole. After adjustment by inverse probability of treatment weighted (IPTW) estimator, the baseline characteristics between the two groups were similar except the causes for primary renal diseases and alcohol use. The medication of renin-angiotensin blockage, other antihypertensive treatment, statin and oral antidiabetic treatment were also similar between two groups. Majority of patients were female (64%) with mean age of 63.0 years, and averaged eGFR of 25.5 ml/min per 1.73 m². During a median 2.7-year follow-up, 941 (30.6%) and 441 (14.3%) patients reached ESRD and mortality, respectively. Dipyridamole treatment had significantly associated reduced all-cause mortality by 15.5% (HR= 0.845, 95% CI=0.732-0.976). Dipyridamole treatment was also associated with slower GFR decline. The dipyridamole treated subgroups with advanced ESRD by 15.5% (HR= 0.845, 95% CI=0.732-0.976). Dipyridamole treatment was also associated with slower GFR decline. The dipyridamole treated subgroups with advanced ESRD by 15.5% (HR= 0.845, 95% CI=0.732-0.976). Dipyridamole treatment was associated with slower GFR decline. The dipyridamole treated subgroups with advanced ESRD by 15.5% (HR= 0.845, 95% CI=0.732-0.976).

Conclusions: In a cohort of advanced CKD patients, we observed the association of dipyridamole therapy with decreased all-cause mortality and ESRD. Further randomized controlled trial is suggested.
Introduction and Aims: International treatment guidelines suggest achieving target levels of serum phosphorus, parathyroid hormone (PTH) and calcium in people with chronic kidney disease (CKD). We evaluated the evidence that specifically targeted biomarker levels (serum phosphorus, parathyroid hormone, and calcium) improved clinical outcomes in people with CKD.

Methods: We conducted a systematic review of randomized controlled trials that reported achievement of serum targets for phosphorus, PTH, and calcium in adults with CKD and that reported relevant clinical outcomes (mortality, fracture, kidney function, and withdrawal due to treatment toxicity). We systematically searched Cochrane and Embase databases without language restriction to September 2010. We also included randomized trials of interventions (vitamin D compounds, calcimimetics, and phosphate-binding agents) that reported serum biochemical for phosphorus, PTH, and calcium at study end in people with CKD and that reported relevant clinical outcomes. We summarized the effects of specific biochemical targets on specified outcomes as randomized interventions using random-effects meta-analysis. We also summarized the non-randomized associations between the proportion of participants achieving biomarker targets and clinical outcomes using two-dimensional arrow plots. Subgroup and meta-regression analyses to evaluate the effects of patient and intervention characteristics on treatment effects were not possible due to insufficient data. Trial risk of bias was evaluated using standard methods.

Results: On the basis of 158 trials (24,965 people with CKD) evaluating interventions on serum biomarker values, no consistent associations between the proportion of participants achieving a biomarker target and clinical outcomes (total and cardiovascular mortality, fracture or end-stage kidney disease) were observed in low-quality or insufficient evidence. Similarly, no consistent associations between biomarker values at study end and clinical outcomes were observed. Specifically, an increasing proportion of participants achieving a serum PTH target with treatment was not consistently associated with lower mortality (Figure) but may be associated with increased withdrawal from treatment due to adverse events.

Conclusions: Targeting specific levels of phosphorus, PTH, and calcium is not consistently associated with improved clinical outcomes in adults with CKD. Treatment to specific PTH targets may be associated with treatment-related toxicity.
such as radiation exposure and inconvenience. Our aim was to identify a more readily-measurable predictor of incident CVD among four vascular calcification-related factors, osteoprotegerin (OPG), fibroblast growth factor 23, fetuin-A, and fetuin-mineral complex (FMC).

Methods: In this prospective cohort study, we enrolled 97 diabetic outpatients with chronic kidney disease (CKD) in a nephrology department in Japan. We measured CACS by multi-detector computed tomography. The endpoint was defined as a fatal or non-fatal CVD requiring hospitalization. Multiple imputation method was carried out for missing values. After confirming that CACS predicts CVD with adjustment for conventional risk factors, additional adjustment of which biomarker changed the coefficient of CACS by >15% was scrutinized in Cox proportional hazards models. We compared model performance between models with either that biomarker or CACS by employing C-statistics, Bayesian information criterion (BIC), net reclassification improvement (NRI), and integrated discrimination improvement (IDI).

Results: Median estimated GFR (eGFR) was 25.0 mL/min/1.73m². During a median follow-up period of 5.0 (IQR, 2.0-5.8) years, 32 patients developed the endpoint. At baseline, only OPG and FMC were associated with CACS. In a multivariable Cox model, CACS, treated as continuous or categorical variable, was significantly related to CVD after adjustment for sex, age, prior CVD, eGFR, urinary protein, duration of diabetes, and systolic blood pressure (hazard ratios (HRs) [95% confidence intervals (CI)], 1.75 [1.03-2.99] per SD increase in ln (CACS+1) and 4.40 [1.10-17.7] in the highest versus lowest quartile. Among four factors of our interest, only OPG adjustment changed the coefficient of CACS by >15% (22.9%), leading to the elimination of its significance. Comparing the models including either CACS or OPG, the effect sizes were much higher for OPG than for CACS (HRs [95%CI], 2.14 [1.35-3.39] per SD increase of OPG and 2.06 [2.14-200] in the highest versus lowest quartiles). Unadjusted Kaplan-Meier curves (Figure) showed that patients in higher quartiles of CACS or OPG were in higher risk for CVD event. The separation of curves for OPG quartiles were observed much earlier than that for CACS quartiles, indicating a higher resolution in risk stratification by OPG. From the perspective of C-statistics, BIC, NRI, and IDI, model performance was better with a model containing OPG than with that CACS.

Conclusions: In predicting incident CVD, OPG rather than CACS should be measured in diabetic patients with CKD.

**FP168 INDICES OF INSULIN RESISTANCE AND RISK OF TOTAL AND CARDIOVASCULAR MORTALITY IN DIALYSIS PATIENTS**

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Introduction and Aims: Insulin resistance (IR), either measured by the state of art technique of hyperinsulinemic euglycemic clamp, or by HOMA and other simple indexes is an established cardiovascular (CV) risk marker in the general population. Whether IR predicts all causes and CV deaths and which is the best predictor of these outcomes among insulin resistance indexes in Stage 5 CKD-D patients is still unsettled.

Methods: In this study we tested the relationship between several indexes of IR [the Homeostatic Model Assessment of Insulin Resistance (HOMA), Quantitative Insulin Sensitivity Check Index (QUICKI), McAuley index (McA), HOMA index adjusted for adiponectin (HOMA-HOMA_AD) or leptin/adiponectin ratio (LAR)] and all cause and CV mortality in a prevalent-incident cohort of 537 prevalent-incident dialysis patients (age: 63 ± 15 years; 310 M and 227 F; diabetics: 16%).

Results: During a 46 month follow-up, 308 patients died (CV 54%). In analyses adjusting for age, sex, smoking, cholesterol, C-reactive protein, waist circumference and BMI, both HOMA IR and HOMA-AD predicted all cause (P=0.003 and P=0.01) and CV mortality (P=0.001 and P=0.004). All other indexes of IR (QUICKI, McA, HOMA-LAR) had no independent predictive power for study outcomes.

Conclusions: Independently of other risk factors, two simple indexes of insulin resistance, HOMA and HOMA-AD adjusted for adiponectin, predict all causes and cardiovascular mortality in stage 5D CKD patients. These relationships points to insulin resistance as a relevant pathway conducive to adverse clinical outcomes in this population. HOMA per se (without adjustment for adiponectin) holds predictive power at least equal to that of adiponectin- adjusted HOMA and may be applied in large scale epidemiological studies in this population.

**FP167 HEMATURIA IS A RISK FACTOR FOR END STAGE RENAL DISEASE IN CHRONIC KIDNEY DISEASE PATIENTS**

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Introduction and Aims: Isolated hematuria is not considered as a prognostic factor for developing end stage renal disease (ESRD) in early literature. Some recent studies addressed hematuria as a risk factor for the development of renal insufficiency in selected populations with IgA nephropathy, lupus nephritis, after kidney transplantation, or even in general population. However, the relationship between hematuria and long term clinical outcomes in chronic kidney disease (CKD) population was not known. Hence, we evaluate the risk of ESRD in CKD patients with hematuria.

Methods: Between November 2002 and June 2009, 3659 patients received the integrated CKD care program (ICKD) in Kaohsiung Medical University Hospital. Hematuria was measured by urine dipstick and confirmed by microscopic examination. Chi-square test, t-test, Kaplan-Meier survival analysis and Cox proportional hazards models were used and P value less than 0.05 was considered as significant.

Results: The mean age was 62.3 years, 59.1% were female, and the mean estimated GFR was 30.7 mL/min/1.73m². During a median follow-up of 2.7 years, 346 (9.5%) patients died and 1076 (29.6%) commenced renal replacement therapy (RRT). In logistic regression, hematuria had significant correlation with below listed clinical variables of urinary tract infection [OR 1.35, 95% CI, 1.04-1.74], hypertension [OR 1.42, 95% CI, 1.16-1.69], serum phosphatase [OR 1.15, 95% CI, 1.04-1.27], serum CRP [OR 1.13, 95% CI, 1.03-1.25] and proteinuria [OR 2.86, 95% CI, 2.33-3.36]. In contrast, hematuria had no significant association with mortality or cardiovascular events with hematuria. Hematuria was significantly associated with the rapid decline of renal function (eGFR slope less than -6 mL/min/1.73 m²/yr) in logistic regression with the odds ratio 1.29 [95% CI, 1.03-1.62]. The associations between hematuria and ESRD were more accentuated in subgroup of patients with hypertension [HR 1.30, 95% CI, 1.03-1.65], with advanced CKD (stage 4-5) [HR 1.24, 95% CI, 1.01-1.50], without chronic glomerulonephritis [HR 1.44, 95% CI, 1.18-1.85], and without proteinuria [HR 1.78, 95% CI, 1.80-3.16].

Conclusion: Hematuria is an independent risk factor for rapid decline of renal function and the commencement of RRT, but not for mortality in CKD patients.

**FP169 MONITORING OF INTRA OCULAR PRESSURE CHANGES IN HEMODIALYSIS PATIENTS**

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Introduction and Aims: Chronic renal failure (CRF) and imposed hemodialysis (HD) induce interesting effects on visual system. This study was planned to evaluate the effects of different changing metabolic parameters on intra ocular pressure (IOP) in hemodialysis patients.

Methods: This descriptive cross sectional study was conducted on 65 HD patients. Demographic information including age, gender, underlying systemic or ocular diseases or surgeries, HD duration and frequencies in addition to levels of blood
pressure (BP), body weight, blood urea, sodium (Na), potassium (K) blood sugar (BS), before and after HD and KTV values were recorded. Patients with any glaucoma medications or conditions were excluded. Results: In presence of 130 eyes of 65 HD patients (38 male and 27 female) with the age range of 24-90 (mean 60.26±16.66) years were evaluated. Mean pred HD, IOP (12.73 mmHg) were significantly lower than mean pre HD, IOP (13.50 mmHg) respectively (P=0.023). Mean IOP levels in the first and second hour (12.32 and 11.83 mmHg respectively) of HD sessions was significantly lower than the mean pred diaylsis IOP (13.50 mmHg) (P=0.000 and 0.000 respectively). In addition mean IOP in second hour (11.83 mmHg) was still significantly lower than the first hour of HD (12.32 mmHg) (P=0.000). In non-diabetic (but not in diabetic) patients, IOP significantly decreased after HD. Mean pred BS levels were significantly higher after HD (P=0.000) and there were meaningful relationship between IOP and BS changes after HD (P=0.040). Conclusions: BS changes significantly decreased IOP in HD patients without glaucomatous disorders. There weren’t any meaningful relationship between changes of serum Na and K, BP, blood urea, KTV, weight, duration of HD and underlying diseases with IOP changes before and after HD.

**FP170** EVALUATION OF AN INSTRUMENT FOR SCREENING PATIENTS AT RISK FOR CHRONIC KIDNEY DISEASE: TESTING SCORED (SCREENING FOR OCCULT RENAL DISEASE) IN PORTUGUESE POPULATION

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Introduction and Aims: The prevalence of chronic kidney disease (CKD) is increasing worldwide and represents a social and economic burden in many countries. Since it is asymptomatic until late stages, CKD is underdiagnosed and referral to the nephrologist occurs late in the progression of the disease resulting in poor outcomes. Identification of individuals at risk of CKD becomes important in this scenario, allowing early implementation of strategies that improve survival. In 2007, Bang et al. developed a screening tool, SCORED (Screening for Occult Renal Disease), that identifies individuals with high probability of occult CKD based on the answer to 9 clinical and demographic questions. Our aim was to analyze the performance of SCORED in identifying subjects at risk of CKD in a sample of Portuguese population.

Methods: The SCORED tool was applied to volunteers that attended the World Kidney Day 2011 event in Torres Vedras, Portugal. Demographic and clinical data were collected, and the SCORED questionnaire was filled in. Individuals with SCORED score ≥4 were considered at risk of CKD. Within 3 months, the volunteers had an appointment in the Nephrology Department in which blood and urine samples were collected. Glomerular filtration rate (GFR) was estimated according to the CKD-EPI equation and Urinary albumin-to-creatinine ratio (UACR) were accessed. The prevalence of chronic kidney disease (CKD) and urinary protein were compared with the presence of CKD after GFR and UACR were accessed.

Results: Eighty-eight volunteers were evaluated, 60 (68.2%) of whom were identified as being at risk of CKD according to the SCORED. Only 47 (53.4%) subjects attended the appointment at the Nephrology Department. When considering CKD in the presence of GFR<60mL/min/1.73m2, SCORED had a sensibility of 100%, specificity of 24.3%, positive predictive value of 26.4% and negative predictive value of 100%. Considering CKD if GFR<60mL/min/1.73m2 or UACR>30mg/g were present, this tool obtained a sensibility of 89.5%, specificity of 21.4%, positive predictive value of 43.6% and negative predictive value of 75.8%.

Conclusions: Our results suggest that SCORED, besides inexpensive and easy to perform, seems to be effective in the recognition of subjects that, according to their clinical condition, have high probability of CKD and should proceed to further clinical assessment. The small size of the sample does not allow us to conclude whether or not SCORED should routinely be used as a screening procedure but it may represent a useful tool for primary care physicians before referral to nephrologists.

**FP171** SUBENDOCARDIAL VIABILITY RATIO AND ALBUMINURIA IN CKD PATIENTS

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Introduction and Aims: Using applanation tonometry, pulse wave analysis (PWA) can be performed. PWA derived from radial artery can provide information about hemodynamic parameter subendocardial viability ratio (SEVR) or the Buckberg index, which is a non-invasive estimate of myocardial workload and perfusion and is measure of the ability of the arterial system to meet the heart’s energy requirements. Albuminuria and chronic kidney disease (CKD) are associated with increased risk of clinical cardiovascular disease (CVD). The purpose of our study was to evaluate the relationship between SEVR and albuminuria in CKD patients.

Methods: PWA and SEVR measurements using applanation tonometry were performed (SpynoMed, ATCor Medical, Ltd., Sydney, Australia). For PWA, an average radial pressure waveform was generated from at least 10 seconds of sequential radial pressure waveforms. PWA was used to determine SEVR in 63 patients (45 men, 18 women; age 22-88 years; mean 61±13±12.27) with different stages of CKD (cystatin C 0.66-4.02 mg/L, mean 2.11±0.86). Four (6.3%) patients were habitual smokers, 23 (36.5%) patients were former smokers and 17 (27%) patients were diabetics. Albuminuria was determined with the urinary albumin/creatinine ratio (UACR). 24-hour ambulatory BP measurements (ABPM) were performed using a non-invasive ABPM monitor (Schiller BR-102 plus, Schiller AG, Switzerland).

Results: The SEVR was between 82 and 235 % (mean 150.6±33.8), UACR from 2 to 642.5 mg/g (mean 66.6±1108.5). The mean 24-hour systolic/diastolic ABPM was 137±6/76±10 mmHg. Also with multivariate regression analysis SEVR turned out to be statistically significant associated with UACR (p<0.001). Age, cystatin C, smoking, cholesterol, triglycerides and 24-hour systolic/diastolic ABPM were not associated with SEVR.

Conclusions: SEVR as estimate of myocardial perfusion was associated with UACR in CKD patients.

**FP172** FROM NEWLY DIAGNOSED SYSTEMIC LUPUS ERYTHEMATOSUS TO DIALYSIS AND THEN ALL-CAUSE MORTALITY: A NATIONWIDE COHORT STUDY IN TAIWAN

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Introduction and Aims: The incidence and prevalence of systemic lupus erythematosus (SLE) in the Asian population are higher than those in the Caucasians. The survival of SLE patients has been improving, whereas lupus nephritis may still progress to end stage renal disease (ESRD) even if the treatments are aggressive. This study aims to investigate the incidence of ESRD and then all-cause mortality in newly diagnosed SLE patients.

Methods: This was a nationwide cohort study in Taiwan from National Health Insurance Research Database (NHIRD). 4130 newly diagnosed SLE patients who were at risk for ESRD were identified during 2000-2002. Among them, 103 patients developed ESRD by the end of 2008. Additional 412 age- and sex-matched incident ESRD cases without SLE were included as controls in the survival analysis post the development of ESRD. We selected age, gender, malignancy, and SLE as predictors. ESRD and all-cause mortality were primary outcomes. Kaplan-Meier survival curve and Cox proportional hazard model were performed as data analysis.

Results: Age (HR 0.66, 95% CI 0.47-0.94) and gender (HR for men vs. women is 2.24, 95% CI 1.4-3.6) were significantly associated with the development of ESRD among newly diagnosed SLE patients and the overall 6-year incidence rate is 2.5%. In the survival analysis post the development of ESRD, patients with SLE revealed a higher hazard (HR 1.3, 95% CI 0.71-2.39). In particular, patients with SLE demonstrated a significant hazard (HR 2.73, 95% CI 1.22-6.07) in end stage renal disease (less than 40 years old). Our limitation included registration bias, lack of laboratory data, and exact cause of death from the national database.

Conclusions: Age and gender were risk factors for the development of ESRD among newly diagnosed SLE patients. Female patients, compared with male patients, were less likely to develop ESRD and had better survival post the development of ESRD. After entering ESRD, SLE patients younger than 40 years old had the worst 5-year survival rate.

**FP173** THE SIGNIFICANCE OF HYPERURICEMIA ON NEPHROCALCINOSIS BY ULTRASONOGRAPHY IN NON-PROTEIURIIC CKD OF GENERAL POPULATION

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Introduction and Aims: There are some reports that hyperuricemia is related as the predictor to hypertension, metabolic syndrome and CKD. Moreover, lowering of uric acid shows the slowing of renal dysfunction. CKD is defined as the abnormality of urine, especially proteinuria and/or low eGFR(<60mL/min/1.73m2). In the general
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health check population, non-proteinuric individuals with low eGFR were not observed scarcely. But the pathogenesis was not clarified. We reported the hyperuricemia is the the risk factor for non-proteinuric CKD by cohort study. The deposition of uric acid crystals in the kidney is considered. It is reported in experimental study that hyperuricemia increases intracellular Ca2+ in mesangium cell. So, we investigated the relation between the nephrocalcinosis by ultrasonography and hyperuricemia in CKD.

Methods: 1973 non-proteinuric subjects (male:13320, female:6419, age 46.0±10.2) who had the first health check at Health Management Center, Toranomon Hospital during 1997-2005, were investigated. Serum uric acid(SUA), uric acid, body mass index(BMI), systolic blood pressure(SBP), triglyceride, HDL cholesterol(HDLc), and fasting blood glucose(FBG) were the risk factors to non-proteinuric CKD, and evaluated. Moreover, the relation between CKD and nephrocalcinosis was estimated by multivariable logistic regression analyses. The association between nephrocalcinosis and the values noted above was also estimated by longitudinal analysis during 5 years using multivariable Cox proportional hazard model. The value of eGFR was calculated by using the formula for Japanese people as follows, eGFR(ml/min/1.73 m2) = 194 × Cr−1.094 × age−0.287 (× 0.739 if female). The nephrocalcinosis was diagnosed by renal ultrasonography.

Results: As the risk factors for non-proteinuric CKD odds ratio of SUA, uric acid, BMI, SBP, triglyceride, HDLc, and FBG were the followings respectively 1.735 (P<0.001), 0.826 (P<0.01), 1.013 (P<0.163), 1.050 (P<0.001), 0.999 (P<0.011), 0.993 (P<0.023), 0.99 (P<0.002) after adjusted for age and gender. The prevalence of nephrocalcinosis in subject with non-proteinuric CKD (eGFR<60) was 6.7%, and higher than the prevalence (4.9%) in non-CKD health check population, non-proteinuric individuals with low eGFR were not observed scarcely. But the pathogenesis was not clarified. We reported the hyperuricemia is the the risk factor for non-proteinuric CKD by cohort study. The deposition of uric acid crystals in the kidney is considered. It is reported in experimental study that hyperuricemia increases intracellular Ca2+ in mesangium cell. So, we investigated the relation between the nephrocalcinosis by ultrasonography and hyperuricemia in CKD.

In the multivariable logistic analysis for nephrosclerosis, SUA, SBP, and urine pH were the risk factors to nephrocalcinosis. The prevalence of nephrocalcinosis was 6.3±1.4mg/dl, 1.02±0.18mg/dl respectively. In the group of CKD, these are 6.7%, and higher than the prevalence (4.9%) in non-CKD (eGFR<60) was 6.7%, and higher than the prevalence (4.9%) in non-CKD health check population, non-proteinuric individuals with low eGFR were not observed scarcely. But the pathogenesis was not clarified. We reported the hyperuricemia is the the risk factor for non-proteinuric CKD by cohort study. The deposition of uric acid crystals in the kidney is considered. It is reported in experimental study that hyperuricemia increases intracellular Ca2+ in mesangium cell. So, we investigated the relation between the nephrocalcinosis by ultrasonography and hyperuricemia in CKD.

Conclusions: Only SUA had a significant hazard ratio, 1.204 (P=0.015), for nephrocalcinosis.

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Introduction and Aims: Cardiovascular disease is the leading cause of death in patients with chronic kidney disease (CKD). Increased inflammation is common in patients with CKD and is associated with increased cardiovascular (CV) events. Numerous biologic markers of inflammation including C-reactive protein (CRP) and interleukin-6 have been studied with an attempt to prognosticate patients in terms of adverse cardiovascular outcomes. Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were used to predict survival in patients with cardiovascular diseases and malignancy. We aimed to evaluate if PLR would provide additional data regarding development of cardiovascular events in addition to inflammatory markers such as CRP in patients with stage 3 to 5 CKD. We also investigated relation of PLR with endothelial function.

Methods: 242 subjects with stage 3-5 CKD were followed for a mean of 39 months. There were 77 patients with stage 3, 79 patients with stage 4, and 86 patients with stage 5 CKD. All stage-5 patients were predialytic. Fatal and nonfatal CV events were recorded during this period. PLR at baseline was determined from complete blood count differential. Endothelial function (flow mediated dilation, FMD) and CRP were determined along with routine biochemistry.

Results: A total of 72 composite (20 fatal and 52 nonfatal) CV events occurred during the follow-up period. Cardiovascular mortality CV n=20 was defined as death due to coronary heart disease (13), sudden death (3), stroke (3) and complicated peripheral vascular disease (1). In addition to cardiovascular deaths, 52 non-fatal cardiovascular events were registered as follows: stroke (18); myocardial infarction (29); peripheral vascular disease (4) and aortic aneurysm (1). PLR as well as platelets and lymphocytes particularly showed significant decrease from stage-3 CKD to stage-5. Univariate and multivariate cox analyses showed that PLR was a significant independent predictor of composite CV events. Univariate analysis demonstrated that higher PLR predicts composite FMD, lymphocytes and history of diabetes (hazard ratio 1.08; 95% CI; P<0.001). The hazard ratio was 1.03 for PLR after adjustment for age, sex, eGFR, CRP, haemoglobin, platelet, lymphocyte, diabetes, and medical history of cardiovascular disease at baseline. PLR was inversely correlated with FMD (r=-0.34; CI 95%; p<0.001). Kaplan-Meier analysis showed that PLR = 0.147 was related to a significantly increased survival time. The survival rate was significantly higher in the group with PLR < 0.147 compared to 84% in the arm with PLR ≥ 0.147 (p<0.001 by log-rank test).

Conclusion: PLR is independently related to endothelial dysfunction and can predict composite CV endpoints independent of traditional confounding factors in patients with moderate to severe CKD. PLR greater than 0.147 may be used as a complementary prognostic marker for predicting cardiovascular events in patients with CKD.

Introduction and Aims: It is well known that hyperkalemia is associated with the progression of chronic kidney disease. Hypokalemia-induced tubulointerstitial disease was also documented in basic research and hyperkalemia was reported to be associated with adverse outcomes in patients with cardiovascular diseases and recently in chronic kidney disease (CKD). However, in earlier CKD stages, the role of serum potassium and the reason for the prognostic value of hyperkalemia are less understood. Thus, we investigated whether hyperkalemia or hypokalemia is a risk factor for adverse outcomes in mild-moderate CKD population.

Methods: Between November 2002 and June 2009, 3659 patients received the integrated CKD care in Kaohsiung Medical University Hospital. A total of 2505 subjects in CKD stage 1-4 were classified into five quintiles based on serum potassium: Q1 to Q5 with the cut-off level at 3.82, 4.1, 4.33, and 4.62 mmol/L, respectively. Chi-square test, t-test, Kaplan-Meier survival analysis and multivariate cox regression analysis were used and p value less than 0.05 was considered as significant.

Results: Majority of patients were female (64%), had diabetes (41.8%) with mean age of 62.4 years, and averaged eGFR of 40.6 ml/min per 1.73 m2. During a median 2.7-year follow-up, 299 (12.0%) and 223 (8.9%) patients reached end-stage renal disease (ESRD) and mortality, respectively. There was a robust trend of higher mean BP, more common use of diuretics, and less frequent use of anti-hypertensive medication and renin-angiotensin inhibitors in patients with lower serum potassium. The prevalence of nephrotic range proteinuria was higher in both the lowest and highest quintiles. Serum potassium was inversely correlated with female gender, diuretics use, eGFR, mean BP, bicarbonate, CRP and hemoglobin. Hypokalemia (<4.1 mmol/L) was significantly associated with ESRD even after adjustments for baseline variables and nutritional factors with hazard ratios (HR) of the lower quintiles (Q1 vs Q3) 1.63 [95% CI, 1.02-2.59, p=0.03] and (Q2 vs Q3) 1.58 [95% CI, 1.02-2.45, p=0.03], respectively. The lowest quintile (Q1) was significantly associated with faster yearly decline in eGFR with the odds ratio 1.54 [95% CI, 1.07 to 2.22, p=0.01]. The risk of hypokalemia remained borderline significance for mortality and cardiovascular events but the association was mitigated with the adjustment for serum albumin. Hyperkalemia was associated with elevated risk of ESRD but adding nutritional and inflammatory covariates to the model decreased this association. The associations between hyperkalemia and mortality and cardiovascular events were not significant.

Conclusions: Both hyperkalemia and hyperkalemia were significantly associated with increased risk of progression towards ESRD in our mild to moderate CKD population. Whether over-diabetes use, under-renin-angiotensin blockade and malnutrition are related to the prognostic value of hypokalemia may need further study.

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Introduction and Aims: Roma people are 5% of Bulgarian population. Until now there is complete lack of proven data of frequency of Chronic Kidney Diseases (CKD) among this minority. The task of the screening program was to investigate frequency of CKD as well as some of risk factors for their occurrence in roma people in Bulgaria.

Methods: After receiving informed consent 365 roma people (88 male and 277 female, from 18 to 88 y.o. were screened. Studied parameters were: fasting blood sugar, serum creatinine, total cholesterol, urine sample for creatinine and microalbuminuria/albuminuria (MA/A). We collected data for educational level, presence of arterial hypertension and diabetes. Arterial pressure was measured and BMI was calculated. As presence of data for CKD we accepted MA/A (UACR>2.5

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mg/mmol in male and >3,5 in female) and/or GFR <60ml/min/1,73m². Control group was 1261 non-roma (486 male and 775 female), from 18 to 89 y.o. every one of them was studied for same parameters and in same conditions as roma people. Statistical data were obtained using SPSS 13.0 through Descriptive analysis, Logistic regression analysis, Diagnostic analysis, Student’s t-test, Chi-square test with Kendall tau rank and Cramer’s V correlation coefficient.

**Results:** Roma people group is younger compare to control group – mean age 42,6 ±15,8 vs. 51,2±13,6 y.o. (p<0,001). Older than 60 y.o. are 17,5% vs. 26,1%. According to BMI roma people were distributed as follows: normal BMI 30,7%; overweight 33,1% and obese – 36,2%. In control group distribution was 38,9%; 37,5% and 23,6% respectively. 9,3% of roma people were with diabetes (7,1% known and 2,2% newly established); diabetics in control group were 7,3% (6,2% known and 1,1% newly established). Arterial hypertension was found in 45,5% of roma and in 41,6% of non-roma. With MA/A were 15,4% of roma and 9,1% of non-roma (p<0,002). Main risk factor for presence of MA/A in roma as well as in non-roma is existing of diabetes. With low GFR were 4,7% of roma and 4,2% of non-roma people (n.s.). Generally with MA/A and/or low GFR were 18,7% of roma and 11,4% of controls (p<0,002). In younger people than 60 y.o. with no risk factors (diabetes and arterial hypertension) the difference was even bigger. Roma people (n=166) with 15/111 and/or low GFR were 22,9% vs. non-roma 11,1%. Roma people under 60 y.o. were divided into two groups considering their education level and social status. In group 1 were included individuals with less than elementary school level. In group 2 were people with elementary or upper education. Distribution according BMI in group 1 was: 25,6% overweight and 50,4% obese – 24,2% respectively were 33,5%, 38,1% ± 28,4% (p<0,001). With diabetes were 13,9% in group 1 and 6,8% in group 2 (p<0,001). With MA/A and/or low GFR were 19,4% of roma people in group 1 and 13,1% – in group 2 (n.s.).

**Conclusions:** Our results demonstrate that roma people in Bulgaria have higher frequency of CKD as well as risk factors for them compared to non-roma people. For this difference are socio-economic factors such as: level of education, unemployment, access to medical care, weight gain and its associated cardiovascular and mortality risks, as well as in CKD and congestive heart failure patients to manage hypertension and resorb edema.

**FP177**

**RDX5791, A NON-SYSTEMIC NHE3 INHIBITOR FOR THE TREATMENT OF FLUID AND SODIUM OVERLOAD, SHIFTS SODIUM EXCRETION FROM URINE TO FECES IN HEALTHY SUBJECTS**

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**Introduction and Aims:** RDX5791 is a first-in-class minimally systemic, small molecule NHE3 inhibitor in clinical development for the treatment of sodium (Na) and fluid overload-related diseases. The intestinal Na+/H+ antiport protein NHE3 plays a key role in the uptake of Na from the intestinal lumen. RDX5791 decreases NHE3-mediated intestinal Na transport leading to enhanced fecal excretion and reduced urinary excretion. In a randomized, double-blind, placebo-controlled 2 ascending-dose study, RDX5791 was very well tolerated and exhibited minimal to no systemic absorption. The purpose of this study was to evaluate the safety, tolerability and pharmacodynamics (PD) of different RDX5791 dosing regimens.

**Methods:** A randomized double-blind, placebo-controlled study was performed in 16 healthy volunteers treated for 7 days either with 30 mg QD, 15, 30, or 60 mg bid, or 30 mg tid (12 treated, 3 placebo/cohort) RDX5791. An additional cohort was examined where the dose was escalated to 60 mg. Safety assessments were performed and included vital signs, ECGs, hematology, serum chemistry evaluations as well as adverse event assessments. The PD of RDX5791 was assessed by measuring stool and urine Na, stool frequency, weight, and consistency.

**Results:** RDX5791 was very well tolerated and there were no SAEs observed and very few adverse events; urine and serum electrolyte values within the normal range. RDX5791 induced a significant increase in stool Na with a concomitant decrease in urine Na (shown below). At a total dose of 30 mg/day, 15 mg bid produced 3-fold greater stool Na excretion than 30 mg QD. For the bid dose regimen, the dose response relationship was flat at 15 mg produced higher stool Na output than 30 mg. When calculated over the 7-day period and corrected from baseline, the cumulated stool Na output was 21 mmol for placebo and between 205 to 345 mmol for bid administration and the cumulated Na urinary output was 166 mmol for placebo, and between 363 and 591 mmol for bid administration.

**Bid administration, response rates among subjects on fixed dose regimens ranged from 50-60%. In the treat-to-effect cohort, 92% of the subjects (11 of 12) responded to dose escalation. Except for the 60 mg bid dose, all doses produced stool frequency and stool consistency within the normal range; stool weight correlated with stool Na output.**

**Conclusions:** RDX5791 dosed bid or tid was well tolerated, increased fecal Na by 30 mg QD, 15, 30, or 60 mg bid, or 30 mg tid (12 treated, 3 placebo/cohort) RDX5791. An additional cohort was examined where the dose was escalated to 60 mg. Safety assessments were performed and included vital signs, ECGs, hematology, serum chemistry evaluations as well as adverse event assessments. The PD of RDX5791 was assessed by measuring stool and urine Na, stool frequency, weight, and consistency.

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explore the effects of specific patient and study characteristics on the risks of depression and associated clinical outcomes.

Methods: We conducted a systematic review and meta-analysis of observational studies (cross-sectional, case-control, and cohort studies) reporting prevalence of or clinical outcomes related to depression in people with CKD. English-language studies were identified from systematic searching MEDLINE through September 2010. Multiple reviewers extracted details on participant characteristics, tools used to measure depression, details of statistical analysis, including adjustment for confounding, and study risk of bias. Estimates of prevalence and associations with clinical outcomes were summarized using random-effects meta-analysis. The effects of participant and study characteristics on prevalence and associations with outcomes were explored using subgroup and univariate meta-regression.

Results: 201 studies (263 cohorts) including 121,648 people with CKD were analyzed. Depression was generally identified by self-rating questionnaire. In 163 cohorts (112,577 participants) the prevalence of depression measured by any tool was 35% (95% confidence interval [CI] 32–39%). Stage of chronic kidney disease was an effect modifier; people on dialysis experienced a higher prevalence of depression (40% [CI 36–44%]), compared to those with earlier stages of CKD (27% [CI 17–40%]) and kidney transplant recipients (23% [CI 16–31%]). P for subgroup difference <0.001). Cohort size was the only other effect modifier identified. People with CKD and depression experienced higher risks of mortality (15 studies, 82,240 participants; risk ratio 1.68 [CI 1.39–2.04]) and hospitalization (6 studies, 16,662 participants; risk ratio 1.17 [CI 1.06–1.30]) compared to people with CKD who were not depressed. Overall study quality was low, and subgroup analysis incompletely explained differences between studies; analyses may be limited by confounding.

Conclusions: Overall, approximately one-third of people with CKD may be depressed. Prevalence of depression may be higher in people on dialysis and lower in people with earlier stages of CKD. Depression is associated with adverse clinical outcomes in observational analyses. Randomized controlled trials on the effects of screening and treatment for depression on patient-relevant outcomes in people with CKD are now needed.

Introduction and Aims: Renal biopsy registries are valuable pool of clinical, laboratory and histological data for understanding epidemiology of renal disease as well as for clinical research. In this abstract we will present epidemiological data gathered from Renal biopsy registry of our Hospital, where almost two-thirds of all native renal biopsies in adult Croatian patients were done.

Methods: Using Microsoft Office Access Database, a relevant demographic, laboratory and histological data were collected from 831 adult patients who had undergone kidney biopsy during period of 1997–2011. Data included gender and age, weight and height, blood pressure, serum creatinine concentration, maximal 24-hour proteinuria level and therapeutic modalities. Indications for renal biopsy were defined as an asymptomatic hematuria and/or proteinuria syndrome, acute or chronic nephritic syndrome, acute renal failure of unknown etiology, nephrotic syndrome, revision of previous biopsy and suspected inherited renal disease. Tissue samples for histopathological analysis were obtained by ultrasound-guided percutaneous renal biopsy performed in local anesthesia using 16-gauge core-needle (automatic biopsy device Biopsy Bard, USA). All samples were analyzed by light, immunofluorescence and electron microscopy.

Results: From 831 analyzed patients, 470 (56.6%) were male and 361 (43.4%) female, aged between 16 and 80 years (mean 47.2 years). The most frequent indication for renal biopsy was nephrotic syndrome founded in 335 (40%) patients, followed by asymptomatic hematuria and/or proteinuria syndrome in 240 (29%) patients, chronic nephritic syndrome in 106 (13%) patients, acute nephritic syndrome and acute renal failure of unknown etiology, each in 50 (6%) patients. The revision of previous biopsy was done in 40 (5%) cases. The primary glomerulonephritis was found in 50% of patients, secondary type of glomerular disorders in 25%, hereditary disorders in 6%, tubulointerstitial diseases in 5% and end stage kidney disease in 1% of patients. The most common primary glomerulonephritis was IgA nephropathy diagnosed in 19% of all patients, followed by focal segmental glomerulosclerosis (17% of all patients) and membranous nephropathy (9% of all patients). Among secondary glomerular disorders, pauci-immune crescentic glomerulonephritis and lupus nephritis (both in 7% of all patients) were most observed, followed by diabetic nephropathy (4.2% of all patients) and plasma cell dyscrasias (2.7% of all patients). The chronic interstitial nephritis was the most common of the tubulointerstitial nephropathies. Acute postinfectious glomerulonephritis and hypertension nephropathy were found each in 1.5% of patients. Male gender was predominant in most diagnosed entities, except in minimal change disease, lupus nephritis and thin basement membrane disease.

Conclusions: This is the first renal biopsy registry in the Republic of Croatia and should serve to improve understanding of renal disease epidemiology in Croatia and help creating the National registry of renal biopsies.