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CARDIOVASCULAR COMPLICATIONS IN CKD 5D

FP461 CHRONIC PROTON PUMP INHIBITOR TREATMENT IS ASSOCIATED WITH AN INCREASED RISK OF VASCULAR CALCIFICATIONS IN CHRONIC KIDNEY DISEASE.

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Introduction and Aims: Proton pump inhibitors (PPIs) are extensively used for the chronic treatment of common gastrointestinal disorders. Chronic PPI use is associated with increased risk of fractures. The primary endpoint was the extent of aortic and iliac calcifications, in relation to PPI use.
Methods: Multicenter, cross-sectional study in hemodialysis patients, 18 hospital based dialysis centers. We included 387 hemodialysis patients (76.2% on chronic PPI treatment). Vascular (aortic and/or iliac) Calcification (VC) assessments were centralized. Witteman's method (Lancet, 1994) was used for blinded assessments in duplicate. VC were quantified by measuring the length of calcific deposits along the anterior and posterior wall of the aorta (mild 0.1-5 cm, moderate 5.1-10 cm and severe >10 cm). They also evaluated the presence or absence of calcifications of the iliac arteries in the same radiograph (mild 0.1-3 cm, moderate 3.1-5 cm and severe > 5 cm). Any differences were resolved by consensus.
Results: Bone markers were: Ca 9.15±0.68 mg/dl, P 4.8± 1.28 mg/dl, median ALP 83 U/L, median PTH 244, median 25(OH)D 28.9 nmol/L, median BGP 175 mcg/L, median ucBGP 10.95 mcg/L, median MGP 19.36 nmol/L, median PCR 1.6 mg/L. Prevalence of VC was 80.6% (mild 20.1%, moderate 30.8%, severe 29.7%) in the aorta and 55,1% in the iliac arteries. We found Arterial calcifications were significantly more common in the PPI group : 57.0% vs. 41.3% (p=0.0086). Also the rates of aortic and iliac calcifications considered separately were higher (+12.2% p=0.0254 and +13.6% p=0.0211, respectively). The proportions of patients suffering from angina and atrial fibrillation were significantly higher in the PPI group (+11.7% p=0.0083 and +8.8% p=0.0306, respectively). Severe aortic calcifications, as well as moderate and severe iliac calcifications, appeared to be significantly related to age, male gender, hypertriglyceridemia, warfarin treatment and also to PPI treatment, the latter with an odd ratio of 2.15-2.66 depending on calcification site.
Conclusions: In hemodialysis patients chronic treatment with PPIs is associated with vascular calcification, a known risk factor for cardiovascular events and mortality in hemodialysis patients, and for cardiovascular events in non renal elderly subjects. Additional studies are warranted to explore the association among chronic PPI treatment, vascular calcifications and cardiovascular events.

FP462 INFLAMMATION AND SERUM FETUIN-A LEVELS ARE ASSOCIATED WITH CARDIOVASCULAR CALCIFICATIONS IN CHRONIC HEMODIALYSIS PATIENTS

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Introduction and Aims: The aim of the study was to investigate the correlations of the inflammation which is associated with the uremic microenvironment, as expressed by the serum levels of CRP and interleukin-6(IL-6) and the calcification inhibitor fetuin-A, with the extent of cardiovascular calcifications in hemodialysis patients
Methods: 80 patients (44 male, mean age 59.8±15.8 years) with end-stage renal disease on chronic hemodialysis (median dialysis duration 88.4 months) consecutively entered the study. Twelve patients (15%) had a history of diabetes and 55 (68.8%) of cardiovascular disease (medical history of either coronary artery and/or cerebrovascular and/or peripheral arterial disease). Serum levels of IL-6 and fetuin – A were measured by ELISA. Vascular calcifications were evaluated using a semiquantitative score on plain abdominal X- rays, whereas calcifications of the cardiac valves with echocardiogram. We investigated the correlations of anemia and biochemical parameters of nutrition and bone- mineral metabolism with the aforementioned inflammatory markers, as well as the associations of their serum levels with the extent of vascular and valvular calcifications.
Results: CRP levels were significantly correlated with the levels of fibrinogen (r= 0.329, p= 0.003) and IL-6 (r= 0.409, p= 0.0001). Moreover, IL-6 levels had a significant positive correlation with alkaline phosphatase (r= 0.275, p= 0.014) and significant negative correlations with albumin (r= - 0.300, p= 0.007) and fetuin-? levels (r= - 0.304, p= 0.006). Finally, fetuin-?, apart from its negative correlation with IL-6, was significantly positively correlated with serum albumin levels (r= 0.233, p= 0.038). The extent of cardiac valve calcifications was associated with significantly increased serum levels of IL-6 (ANOVA, p=0.012) and significantly lower serum levels of fetuin-A (ANOVA, p=0.0001).
Vascular calcification score was significantly associated only with lower serum fetuin-A levels (ANOVA, p=0.0001), as levels of serum fetuin were inversely proportional to the extent of vascular calcifications.
No other parameter of bone metabolism was significantly associated with cardiac valvular or vascular calcification scores.
Conclusions: In chronic hemodialysis patients, inflammation and fetuin-A were closely associated with the presence and extent of cardiac valve calcification, as the latter was characterized by the presence of significantly higher levels of IL-6 and significantly lower levels of fetuin-A. Concerning vascular calcifications, fetuin-A was the only independent predictor of their extent, underlying its importance in the development of extraosseous calcification in these patients.

FP463 ASSOCIATIONS BETWEEN OSTEOPONTIN, INTERLEUKIN-6 AND HOMOCYSTEIN LEVELS AND MALNUTRITION, CALCIFICATION AND CAROTID INTIMA-MEDIA THICKNESS IN DIALYSIS PATIENTS

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Introduction and Aims: Progressive vascular calcification is a major cause of cardiovascular morbidity and mortality in patients with end-stage renal disease (ESRD). The underlying mechanism is quite complex with intricate associations between malnutrition, inflammation and atherosclerosis, namely the MIAC syndrome. Osteopontin (OPN) is an important regulator of arterial mineral deposition by acting as an inducible inhibitor of calcification. The aim of our study was to investigate OPN levels in relation to the markers of MIAC syndrome in dialysis patients.
Methods: 78 hemodialysis (HD) patients [52 (67 %) males and 26 (33%) females, mean age 48±17 years], 61 continuous ambulatory peritoneal dialysis (CAPD) patients [30 (48 %) males and 32 (52%) females, mean age 45,9±13,2 years] and 44 age and sex matched controls [23 (52%) males and 21 (48%) females, mean age 45.1 ±12.3 years] were included. End stage renal disease patients who had been on the same renal replacement therapy for at least 24 months were selected. Carotid intima media thickness (CIMT), serum levels of OPN, IL-6, homocystein were determined for each patient. Peripheral artery calcification scores were calculated using plain radiographic films of pelvis and hands. Valvular calcifications were assessed by echocardiography. Nutrition status was assessed by serum albumin and subjective global assessment (SGA).
Results: Serum OPN, IL-6 and homocystein levels were comparable between HD and PD patients while they were significantly lower in healthy controls (Table-1). OPN was positively correlated with the duration of dialysis (p=0,01, r=0,21), serum creatinine (p=0,04, r=0,17), phosphorus (p=0,001, r=0,27), CaxP (p=0,001, r=0,28), PTH (p=0,001, r=0,35), mitral valve calcification score (p=0,04, r=0,16) and negatively correlated with BMI (p=0,02, r=-0,18), age (p=0,008, r=-0,22), fasting blood glucose (p=0,03, r=-0,18) and LDL-cholesterol (p=0,02, r=- 0,18). While homocystein levels were correlated with hs-CRP (p=0,009, r=0,22) and IL-6 (p=0,000, r=0,59) levels, those inflammatory markers had no association with OPN. CIMT was positively correlated with vascular calcification (p=0,004, r=0,23), mitral and aortic valvular calcification (p=0,002, r=0,26 and p=0,008, r=0,22, respectively) and SGA (p=0,000, r=0,29) scores, however we did not find any association between OPN and CIMT, SGA and arterial calcification scores.
Conclusions: Dialysis patients with malnutrition and elevated markers of inflammation have a higher risk of premature atherosclerosis and vascular/valvular calcification. OPN seems to act directly through calcification rather than having additional effects on inflammation and malnutrition. Further studies are needed on the role of OPN on MIAC syndrome.

FP463 Table 1. Comparison of carotid intima media thickness and other parameters in study groups.

	HD group (n=78)	PD group (n=62)	Control group (n=44)
CIMT (mm)	1,01±0,30[a,c]	0,82±0,29[a]	0,184±0,25
Osteopontin (ng/ml)	33,42±18,44[a]	28,26±20,65[a]	9,58±8,88
IL- 6 (pg/ml)	10,42±23,80[b]	6,02±11,60[b]	0,69±2,63
Homocystein (µmol/L)	29,57±11,78[a]	26,88±11,30[a]	9,61±3,25

[a]p=0,001, compared to control group
[b]p=0,01, compared to control group
[c]p=0,001, compared to PD group

FP464 VALVULAR CALCIFICATION PREDICTS ATRIAL FIBRILLATION ON CHRONIC DIALYSIS PATIENTS

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Introduction and Aims: Valvular calcification has been considered a risk marker, associated to inflammation, cardiovascular events and mortality. The relationship of cardiac valve calcification with atrial fibrillation on chronic dialysis patients is still unknown. Our aim was to analyze the relationship between valvular cardiac calcification and the presentation of atrial fibrillation on the follow-up of chronic dialysis patients.
Methods: We conducted an analysis of 225 incident dialysis patients (hemodialysis or peritoneal dialysis) with sinus rhythm. Valvular calcification was assessed by Doppler-echocardiography and its association with atrial fibrillation in the course of follow-up until death, transplant, transfer out of our catchment area, or conclusion of the study was analyzed. Factors analyzed were: ECG, age, gender, smoking habit, diabetes, hypertension, previous ischemic stroke and ischemic coronary disease. Other factors measured in the 1st month of dialysis were: hemoglobin, urea, creatinine, lipids, calcium, phosphorus, parathyroid hormone, albumin, Troponin I, glycosylated hemoglobin and C-reactive protein.
Results: Of the enrolled patients, 103 (45.8%) had valvular calcification (aortic and /or mitral) at the start of dialysis. These patients were older (73.3±8.9 vs 55.2±16.3 yrs; p= 0.000) and more likely to have a history of diabetes (39,8% vs 18.9%, p= 0.001), ischemic coronary disease (12.6% vs 4.9%, p=0.038) and bundle branch block (14,6% vs 4.9%, p= 0.013). Left ventricle mass/body surface (gr/m2: 170.9± 49.5 vs 155.07±51.9; p= 0.025), left atrial dimension (mm: 42.18±7.13 vs 39.21±7.33; p= 0.003) and pulse pressure (62.6±22 vs 48.9±19; p=0.024) were greater and E/A ratio mitral filling flow lower (0.786±0.36 vs 0.977±0.45; p= 0.001). Levels of troponin I (0.28±1.2 vs 0.03±0.05; p=0.023) and glycosylated hemoglobin (4.85±1.31 vs 4.46 ±0.95; p=0.013) were higher and levels of creatinine (6.06±2.01 vs 7.49±2.38; p=0.000), albumin (3.38±0.52 vs 3.74±0.51; p=0.000) and phosphorus (4.87±1.56 vs 5.43±1.79; p=0.013) were lower. In the multivariate analyses, valvular calcification was independent predictor of atrial fibrillation presentation on the follow-up (OR: 5.23; 95% CI: 1.74-15.6; p= 0.003).
Conclusions: Valvular calcification at the commencement of dialysis predicts atrial fibrillation presentation.

FP465 CALCIUM SCORING (CASC) AS A LONG TERM PREDICTOR OF CARDIOVASCULAR MORTALITY IN A POPULATION OF DIALYSIS PATIENTS.

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Introduction and Aims: Chronic kidney disease is considered a proinflammatory state associated with high cardiovascular morbidity and mortality. The aim of the study was to evaluate factors influencing cardiovascular mortality in a group of dialysis patients, during a six year observation period.
Methods: The study group consisted of 67 patients (31 women, 36 men) with a mean age of 53 +/- 13 years, treated with peritoneal dialysis (PD) for a median period of 24 months (range 4 to 100 months). Calcium scoring (CaSc) was measured using multirow spiral computed tomography (MSCT). We assessed the following proinflammatory cytokines: interleukin-6 (IL-6), high sensitive tumor necrosis factor-alpha (hs TNF-a), hepatocyte growth factor (HGF). Level of acute-phase activation was represented by the hs C-reactive protein (hsCRP).
Results: During the six year observation period, 22 patients died (total mortality), where 17 patients died due to cardiovascular causes. Survival was 1-72 months (median 20 months, lower-upper quartile 6-45 months). Significant influence of microinflammation, as well as CaSc on cardiovascular mortality in dialysis patients were shown using univariate Cox regression (table 1). CaSc was shown to be a long term predictor of cardiovascular mortality in multiple regression model (table 2).
Conclusions: Increased values of proinflammatory factors like: IL-6, hs TNF-a, HGF and hs CRP could be risk factors for cardiovascular mortality in dialysis patients. CaSc is a long term predictor of cardiovascular mortality in the dialysis patient population and may become an essential non- invasive parameter in the evaluation of cardiovascular risk in this population.

FP465 Table 1. Univariate Cox regression models to predict cardiovascular mortality.

independent variable	HR	95% CI for HR	p
hs TNF-α	1.70	1.19-2.44	**0.004**
hsCRP	1.06	1.03-1.10	**0.0005**
HGF	2.51	1.28-4.93	**0.007**
IL-6	1.05	1.02-1.08	**0.001**
CaSc	1.0005	1.0002-1.0008	**0.003**

FP465 Table 2. Multiple Cox regression models to predict cardiovascular mortality.

independent variables	HR	95% CI for HR	p
hs TNF-α	1.56	1.3-2.36	0.36
CaSc	1.0003	1.0001-1.0006	**0.042**
hsCRP	1.07	1.12-9.29	**0.002**
CaSc	1.0005	1.0002-1.0008	**0.003**
HGF	2.88	1.38-6.01	**0.005**
CaSc	1.0005	1.0002-1.0008	**0.002**
IL-6	1.05	1.01-1.09	**0.007**
Ca Sc	1.0005	1.0002-1.0008	**0.004**

FP466 RADIAL ARTERY MICRO-CALCIFICATION IS ASSOCIATED WITH CORONARY ARTERY CALCIUM SCORE IN HEMODIALYSIS PATIENTS.

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Introduction and Aims: Coronary artery calcium score (CACS) is known as independent predictor of coronary artery disease (CAD) and overall mortality in hemodialysis (HD) patients as well as general population. The higher the score, the more CAD is present, the greater the risk. We have reported that radial artery micro-calcification (RAC) is closely related to early failure of radiocephalic arteriovenous fistula (RC-AVF) and aortic stiffness, which is risk factor of cardiovascular mortality in HD patients. This study was designed to evaluate relation of RAC and CACS in HD patients.
Methods: Twenty-two HD patients who received vascular access operation were included in this study. The RAC was diagnosed by pathologic examination of radial arterial specimen by von Kossa stain, which was acquired during the RC-AVF operation. All patients underwent a a multi- detector computed tomography (MDCT) imaging procedure and CACS was calculated. Moderate to high likelihood of CAD group defined as more than 100 of CACS, so the patients were classified into two groups, according to the CACS, as low (<100), in 10 patients, and high (>100), in 12 patients. We compared CACS between the patients with and without RAC.

FP466 Table 1.

	Total, n=22	RAC (+), n=11	RAC (-), n=11	p-value
Age (year)	60.3 ± 12.7	65.6 ± 9.9	55.1 ± 13.3	0.050
Sex (% male)	50.0 (n=11)	72.7 (n=8)	27.3 (n=3)	0.086
Diabetes (%)	68.2 (n=15)	100 (n=11)	36.4 (n=4)	0.004
CACS	209.9 ± 262.9	346.0 ± 277.7	73.7 ± 165.3	0.013
High CACS group (%) (CACS > 100)	54.5 (n=12)	90.9 (n=10)	18.2 (n=2)	0.002

Results: Mean age was 60.3 ± 12.7 years and the male gender was 11. The incidence of RAC was 54.5% (n=12). The mean CACS was 209.9 ± 262.9 (0-800) and high CACS group was 54.5%. Positive RAC group showed higher CACS (346.0 ± 277.7, vs 73.7 ± 165.3, p=0.013) and high incidence high CACS group (90.9% vs18.2%, p=0.002), compared to negative RAC group. Patients in the positive RAC group were significantly older (65.6 ± 9.9vs 55.1 ± 13.3, p=0.050), and had a higher prevalence of diabetes (100% vs 36.4%, p=0.004) than those in negative RAC group.
Conclusions: The present study suggests that RAC is closely associated with CACS in HD patients.

FP467 A NANOPARTICLE-BASED SERUM TEST MEASURING OVERALL CALCIFICATION INHIBITION

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Introduction and Aims: Accelerated vascular and soft tissue calcification is a major problem in patients with chronic kidney disease. As serum is supersaturated with regard to calcium and phosphate, inhibitors of calcification critically determine pathological calcification. An assay measuring the overall calcification inhibitory capacity in blood would be helpful to make informed therapy decisions.
Methods: We developed a novel nanoparticle-based serum test to quantify calcification-inhibitory properties of patient sera. The assay measures the formation of protein-mineral nanoparticles in real time.
Results: Exposure of serum towards high amounts of calcium and phosphate leads to the formation of primary calciprotein particles (CPPs). These spherical colloidal nanoparticles are mainly comprised of fetuin-A and albumin. Fetuin-A is a necessary constituent of primary CPPs, whereas albumin synergistically substitutes low fetuin-A concentrations. With time, primary CPPs undergo spontaneous transformation into elongate crystalline secondary CPPs which contain an extended mixture of plasma proteins. The time point of the spontaneous transition step reflects the combined effects of pro- and anti-calcific components present in a respective serum sample. Accordingly, the assay shows that fetuin-A, albumin and magnesium delay, whereas calcium and phosphate accelerate the transition step. The test is performed in 96-well format and requires 80 µl serum per well. The measurement time is 10 hours.
Applying our test, transition times were accelerated in sera from fetuin-A-deficient mice (n = 3, 96 ± 10 min.) when compared to wild-type mice (n = 3, 250 ± 65 min., p = 0.015). Likewise, transition times were accelerated in sera from hemodialysis patients (n = 20, 137 ± 45 min.) when compared to sera from healthy individuals (n = 20, 470 ± 110 min., p < 0.0001).
Conclusions: We have developed a test, which reflects the overall calcification inhibitory capacity of serum. Longitudinal association studies are now required to demonstrate the power of this novel assay in reflecting imminent and clinically relevant calcifications.

FP468 LANTHANUM CARBONATE DELAYS THE PROGRESSION OF CORONARY ARTERY CALCIFICATION COMPARED WITH CALCIUM-BASED PHOSPHATE BINDER IN PATIENTS ON HEMODIALYSIS.

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Introduction and Aims: Coronary artery calcification (CAC) is associated with future cardiovascular events and/or death of hemodialysis patients. We investigated whether the progression of CAC could be delayed by switching from a calcium-based phosphate binder to lanthanum carbonate in HD patients.
Methods: In a randomized intervention trial, the CAC score was evaluated at study entry and after 6 months in 52 HD patients using calcium carbonate as their phosphate binder. These patients were randomly divided into 2 groups, which were assigned to receive calcium carbonate (CC) or lanthanum carbonate (LC), and the CAC score was evaluated 6 months' treatment (12 month after study entry). Progression of CAC was assessed in relation to serum levels of calcium, phosphate, and intact parathyroid hormone.
Results: Forty-two patients completed the study (23 receiving CC and 19 receiving LC). Up to 6 months, there was an increase in CAC score in the CC and LC group by 37.3 % and 36.1 %, respectively. The change of CAC score from 6 to 12 months was significantly smaller in the LC group than the CC group (-288.9±1176.4 vs. 107.1±559.6, p=0.036), and the percent change was also significantly different (-6.4% vs. 41.2%, p=0.024). Serum calcium, phosphate, and intact parathyroid hormone levels were similar in both groups during the study period.
Conclusions: Lanthanum carbonate significantly delayed progression of CAC compared with calcium carbonate in HD patients.

FP469 DETERMINANTS OF VALVULAR CALCIFICATIONS IN PREVALENT HEMODIALYSIS PATIENTS

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Introduction and Aims: Valvular calcifications are important and highly prevalent complications in ESRD patients and are associated with exceedingly high cardiovascular mortality in this population. On the other hand, cardiac valvular calcification is a marker that reflects generalised atherosclerosis and calcification. Recent studies have described cinacalcet therapy as being associated with suppression of valvular calcifications. The aim of this study was to evaluate the determinants of valvular calcifications in a population of hemodialysis patients.
Methods: We conducted an observational study which included all stable patients attending our hemodialysis clinic. We tested the relationship between valvular calcifications, inflammation, mineral metabolism, magnesium, therapy with phosphate binders, statins and cinacalcet in a cohort of hemodialysis patients. Valvular calcifications (mitral and/or aortic) were determined by echocardiography. Statistical analysis was based on descriptive statistics and multiple linear regression.
Results: A total of 157 patients (68 females, 89 males, 20.4 % diabetic), with mean age of 64.4 years and medium time on dialysis of 61.7 months were included. In this population 30.6% of the patients presented valvular calcifications (21.7% had one valvular calcification; 8.9% presented with calcifications on both valves). This population presented mean values of the evaluated parameters such as follows: C-reactive protein = 11.1 ± 20.5 mg/L, CaxP = 37.2 ± 13.9 mg2/dL2, PTH = 444.1 ± 500.2 pg/mL, magnesium = 2.2 ± 0.3 mg/dL. Most patients were under therapy with a phosphorus binder (calcium-based in 36.3% and sevelamer in 32.5%). A minority (14.0%) were under cinacalcet therapy. Finally, statins were prescribed to 34.4% of patients. Using multiple linear regression we found a correlation between valvular calcifications and age (r = 3.061, p = 0.003), time on hemodialysis (r = 3.963, p = 0.001) and cinacalcet therapy (r = -2.536, p = 0.012).
Conclusions: In our population, the presence of valvular calcifications was directly associated with age and dialysis vintage, and inversely associated with cinacalcet therapy. Further studies evaluating clinical significance and its consequences on cardiovascular outcome are needed.

FP470 THE DIFFERENCES IN THE RISK FACTORS FOR PROGRESSIVE CALCIFICATION OF CORONARY ARTERY, AORTIC VALVE AND MITRAL ANNULUS

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Introduction and Aims: Excessive calcification of cardiovascular system, commonly observed in haemodialysis patients, is known to be an important risk factor for not only cardiovascular disease but also poor outcome. This abnormality is known to be associated with bone mineral disorders and hemodynamic stress. However, the calcified lesion in cardiovascular system does not always equally develop. The aim of this study was to investigate the differences in the risk factors for progressive calcification of coronary artery(CA), aortic valve (AV) and mitral annulus (MA).
Methods: In 39 patients (mean age 65.5+-12.1 yr, 36% women, duration of dialysis 12.6+-8.2 yrs) receiving regular haemodialysis treatment in our hospital, we evaluated calcium scoring (CS) (Agatston) in the CA, AV and MA at baseline and 2.5 years later using 64-row multidetector computed tomography (MDCT). We also measured serum lipids profiles, calcium, phosphorus, intact parathyroid hormone (iPTH), fetuin-A and matrix Gla protein (MGP), and assessed the differences in risk factors for CS and alteration in CS (delta CS) among three portions.
Results: Calcium score in CA, AV and MA showed significant correlations each other (CA vs. AV r=0.54, p=0.0005, CA vs. MA, r=0.35, p<0.05, AV vs. MA r=0.83, p<0.0001). Patients with coronary artery disease had significantly higher calcium score in CA (1240+-2156 vs. 4347+-4705, p<0.05), but not in AV and MA. Patients with secondary hyperparathyroidism (SHPT) had significantly higher calcium score in MA (200+-441 vs. 1547+- 2508, p<0.05), but not in CA and AV. There were no significant differences in calcium score in CA, AV and MA between patients with and without diabetes. Duration of dialysis correlated with CA-CS and MA-CS (r=0.40, p<0.05, r=0.45, p<0.01, respectively). In multivariate analysis, we found that age and SHPT were independently associated with CA-CS (t=2.54, p<0.05, t=2.78, p<0.01, respectively) and AV-CS (t=2.92, p<0.01, t=2.78, p<0.01, respectively). On the other hand, duration of dialysis and serum fetuin-A levels showed independent determinants of MA-CA (t=3.85, p<0.001, t=3.07, p<0.005, respectively). Furthermore, delta CA-CS was associated with diabetes and LDL-cholesterol (t=3.80, p<0.001, t=2.65, p<0.05, respectively), delta AV-CS with age and SHPT (t=2.73, p<0.05, t=2.58, p<0.05, respectively) and delta MA-CS with duration of dialysis and fetuin-A (t=2.77, p<0.05, t=2.78, p<0.05, respectively). MGP showed no significant relation.

Conclusions: In dialysis patients, both CA-CS and AV-CS are associated with aging and hyperparathyroidism, but impairment of glucose and lipid metabolism may play an important role in its progression. MA-CS probably relates to some different risk factors, which are dialysis vintage and higher fetuin-A levels. This result is not consistent with previous reports and warrants a larger prospective study.

FP471 THE RELATIONSHIP BETWEEN BONE MINERAL DENSITOMETRY AND VASCULAR CALCIFICATION IN PATIENTS WITH END-STAGE RENAL DISEASE

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Introduction and Aims: Vascular calcification (VC) and disturbed bone mineral metabolism (BMM) are commonly seen in patients with end-stage renal disease (ESRD). Fetuin-A has been found to be significantly low in ESRD patients. The aim of our study is to investigate the relation between coronary artery calcification, BMM and Fetuin-A in peritoneal dialysis (PD) and hemodialysis (HD) patients.
Methods: 46 PD (M/F=28/18) and 34 (M/F=20/14) HD patients are included in the study. Coronary artery calcification scoring is made by multi slice computed tomography. Patients are divided into 4 groups according to their CACS values as Group 1 (CACS: 0), Group 2 (CACS:1-99), Group 3 (CACS:100-399) and Group 4 (CACS: =400). Serum levels of Fetuin-A is measured. Bone mineral densitometry is measured by DEXA.
Results: Demographic, clinical, biochemical features, Fetuin-A levels and total CACS of patients were shown in Table 1. There was a statistically significant difference difference between CACS and femur T scores in PD and ESRD patients. Femur T scores have been found to be decreased when CACS are increased in PD patients (Table 2). We could not find any differences in PD and HD patients about CACS when we separated patients according to T scores greater or lower than -2. Osteopenic patients were found to be older and they had low Fetuin-A levels both in PD and HD groups (Table 3 and 4).

FP471 Table 1. Demographic, clinical, biochemical Fetuin-A levels and total CACS of patients.

Parameter	PD Patients (n=46) (mean±SD)	HD Patients (n=34) (mean±SD)	P value
Age (years)	50.4±15	47.7±12.3	0.48
BMI (kg/m^2)	26.9±5.0	26.6±5.4	0.61
SBP (mmHg)	134±28	145±28	0.13
DBP (mmHg)	84±17	89±17	0.24
Calcium (mg/dL)	**8.92±0.87**	**9.6±1.0**	**0.002**
Phosphorus (mg/dL)	**4.24±1.0**	**5.17±1.53**	**0.004**
PTH (pg/mL)	327±198	312±222	0.74
Albumin (g/dL)	**3.6±0.45**	**4.17±0.3**	**0.0001**
LDL	108.5±26.9	117.2±29.9	0.117
CRP	15.5±18.9	14.1±13.9	0.96
Fetuin A (ng/ml)	257±39.9	269±46.9	0.215
Total CACS	225.1±285.8	262.7±405.1	0.627

FP471 Table 2. Femur ve Lomber T values according to CACS groups in HD and PD Patients

CACS Groups	PD Patients		HD Patients	
	Femur T values (mean±SD)	Lomber T values (mean±SD)	Femur T values (mean±SD)	Lomber T values (mean±SD)
CACS Group 1	-0.793±1.54	-0.443±1.53	-0.973±1.28	-0.747±1.32
CACS Group 2	-0.923±1.37	-0.492±1.9	-0.36±1.12	-0.42±2.4
CACS Group 3	-0.091±1.65	-0.712±1.65	-0.077±1.14	-0.375±2.03
CACS Group 4	-2.06±1.55	-0.978±1.58	-0.992±1.49	-0.811±1.19
P value	0.04	0.14	0.42	0.99

FP471 Table 3. Serum Fetuin-A, age and CACS values according to T scores of PD patients

	Group 1 (t score ≤ -2) (n=13)	Group 2 (t score > -2) (n=33)	P value
Fetuin-A (ng/ml)	241,48±38,59	263,14±39,35	0,98
Age (years)	55,15±17,24	48,58±13,93	0,185
CACS	318,05±284,78	188,52±282,17	0,169

FP471 Table 4. Serum Fetuin-A, age and CACS values according to T scores of HD patients

	Group 1 (t score ≤ -2) (n=7)	Group 2 (t score > -2) (n=27)	P value
Fetuin-A (ng/ml)	267,97±55,89	269,27±45,59	0,94
Age (years)	52,29±9,28	46,56±12,89	0,206
CACS	246,89±453,41	266,87±400,94	0,91

Conclusions: There might be an important relationship between CACS and bone mineralization in ESRD patients.

FP472 THE RELATIONSHIP BETWEEN CARDIAC VALV? CALCIFICATION PRESENCE AND QT INTERVAL (ECG) PROLONGATION IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Hemodialysis (HD) patients may be at greater risk of cardiac arrhythmias and sudden death in post-HD period due to the prolongation of the QT interval on electrocardiograms (ECG). This study aimed to determine if cardiac valve calcification predicts post-HD recorded QT interval prolongation in long-term HD patients.
Methods: Baseline echocardiography was performed in 106 patients (49 male, mean age 51.8±24.3 years) on HD (mean duration of HD 81.7±58.1 months) to screen for calcification of the cardiac valves. Echocardiograms were graded as 0-2 for absence or presence of calcification of the mitral and aortic valve. The patients ware stratified according to the number of calcified valves in three groups: group I, those (n-32, 30.2%) without valvular calcification; group II, those (n-43, 40.6%) with one calcified valve (either mitral or aortic); group III, those (n-31, 29.2%) with calcification on both valves (mitral and aortic). Twelve-lead ECG were performed in all patients immediately after a single HD session to analyzed for QT intervals.
Results: A significantly longer QT and QTc intervals were observed in the group with one calcified valve (383.33±36.32 vs 359.31±38.54 ms, p=0.008 / 442.21±39.44 vs 423.72±40.26 ms, p=0.024), as well as in the group with both calcified valves (387.74±35.75 vs 359.31±38.54 ms, p=0.007 / 445.67±37.58 vs 423.72±40.26 ms, p=0.019) in comparison with group without valve calcification. There was not found significant differences in QT and QTc interval duration when compared the groups of the patients with one and with both calcified valves. Multivariate adjusted logistic regression analyses (with group of the patients without valvular calcification as the reference value) identified cardiac valve calcification presence as a factor independently and significantly associated with the QT [OR=1.128, CI (1.059-1.202), p=0.002 for the group with one calcified valve / OR=1.225, CI (1.103-1.361), p=0.001 for the group with both calcified valves] and QTc [OR=1.067, CI (1.008-1.124), p=0.005 for the group with one calcified valve / OR=1.137, CI (1.050-1.224), p=0.002 for the group with both calcified valves] interval prolongation in our HD patients.
Conclusions: Post-HD recorded QT / QTc interval is prolonged in HD patients with cardiac valve calcifications. The presence of valvular calcification may predispose hemodialysis patients to cardiac arrhythmias and sudden death.

FP473 DO CORONARY CALCIFICATIONS PREDICT CARDIOVASCULAR EVENTS AND MORTALITY IN ADVANCED CKD PATIENTS?

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Introduction and Aims: Patients with CKD have a high mortality, and cardiovascular disease is the leading cause of death. In these patients, coronary calcifications (CC) are more prevalent and more extensive. The main objective of this study is to analyse the predictive value of the presence of coronary calcifications

detected by multi-detector spiral computed tomography in the ocurrence of cardiovascular events (CVE) and in the overall mortality in CKD patients, for a 2 years period. The main independent variable will be the coronary calcium score (CCS). The secondary objectives will be: to evaluate the prevalence and severity of CC in CKD patients and to analyse the related factors with the developement of these calcifications, in particular the expression of the transcription factor Cbfa-1. The independent variable will be the expression of this transcription factor in circulating mononuclear cells.
Methods: The design of this study has 3 well-defined parts: Selection and follow-up of patients, the radiological and analytic studies, and the statistical analysis. Patients with CKD stages 4 and 5 who comply with inclusion criteria will be included.
Results: 165 patients with CKD, stages 4 and 5, 111 in hemodialysis (HD) and 55 in predialysis (PD) were included. There was 90 males and 76 females, diabetes prevalence was high (29 %), mean age was 64 ± 14 years and length of stay in HD was 27 (10 - 97) months. Follow-up time was 20 ± 8 months. CCS was 815 (152 - 1869) in HD and 255 (14 -855) in PD. CCS correlated with age ($p < 0.001$), tobacco ($p 0.03$), albumin ($p < 0.001$), triglycerides ($p < 0.02$) and CRP ($p < 0.02$). In the HD subgroup, body mass index (BMI) ($r = 0.28$, $p 0.01$) and diabetes ($r = 0.66$, $p<0.009$) also have a positive correlation with CCS, while in PD subgroup, cholesterol correlated too with CCS ($p < 0.03$). We measured Cbfa-1 content in circulating mononuclear cells in 88 patients in HD (0.64 ± 0.05) and in 12 patients in PD (0.59 ± 0.33). The Cbfa-1 in PD subgroup was associated with uric acid ($p 0.01$), tobacco ($p 0.04$) and CCS in left coronary artery ($p 0.01$) and posterior descending coronary artery ($p 0.01$). In HD subgroup, only highest levels of Cbfa-1 were associated with albumin ($p < 0.009$), length of stay on HD ($p < 0.06$) and CCS in circumflex coronary artery ($p < 0.05$) and right coronary artery ($p =0.04$). During the follow-up period, CVE happened in 40 % and global mortality in 21% (51% of this mortality could be attributed to CVE). The occurrence of cardiovascular mortality or CVE was associated with age ($p <0.001$), BMI ($p < 0.03$), previous CVE ($p <0.001$), diabetes ($p <0.001$), sedentary lifestyle ($p< 0.001$), albumin ($p <0.001$), CRP levels ($p < 0.002$), and total CCS ($p <0.001$). By Cox regression, CCS (HR 2.44) and CRP levels (HR 1.63) were independently associated with occurrence of cardiovascular mortality or CVE.
Conclusions: CC are very prevalent in our population and CCS are very severe, especially in HD patients. Age, tobacco, diabetes, BMI, albumin, triglycerides and CRP levels seem to influence the coronary calcification process. CC could influence the appearance of new CVE and cardiovascular mortality in these patients. However, it will be necessary to estimate if the analysis of these calcifications is a better marker of cardiovascular risk than other methods used to assess vascular calcifications. We found a narrow correlation between Cbfa-1 and both CCS and uric acid levels in PD patients. Nevertheless, we do not know yet the real role of the circulating Cbfa-1 in the coronary calcification process.

FP474 WARFARIN USE IS ASSOCIATED WITH HIGHER PREVALENCE VERTEBRAL FRACTURES, VASCULAR CALCIFICATIONS AND INCREASED MORTALITY IN CHRONIC KIDNEY DISEASE

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Introduction and Aims: In addition to bleeding, other risks have been associated with the use of warfarin, including an increased susceptibility to vascular calcifications and fractures caused by a reduction in the levels of vitamin K dependent carboxylated enzymes, matrix Gla-protein (MGP) and bone Gla-protein or osteocalcin (BGP), respectively. Indeed, warfarin acts as a vitamin K antagonist reducing Vitamin K levels. The Aim was to evaluate in hemodialysis patients the prevalence of Vertebral Fractures (VF), Vascular Calcifications (VC) and mortality in relation to warfarin use.
Methods: Multicenter, cross-sectional study in patients treated in 18 hospital based dialysis centers. We included 387 hemodialysis patients (11.9% on warfarin treatment). We evaluated VF with a computerized analysis, of scanned latero-lateral vertebral X-rays (T4 to L5). Reduction of >20% of vertebral body height was considered a VF, while reductions between 15% and 20% were considered borderline fractures (BF). VF severity was estimated as mild, moderate or severe (reduction: 20–25%, 25–40% or >40%, respectively). VC assessments were centralized. Witteman's method (Lancet, 1994) was used for blinded assessments in duplicate. VC were quantified by measuring the length of calcific deposits along the anterior and posterior wall of the aorta (mild 0.1-5 cm, moderate 5.1-10 cm and severe > 10 cm). They also evaluated the presence or absence of calcifications of the iliac arteries in the same radiograph (mild 0.1-3 cm, moderate 3.1-5 cm and severe > 5 cm). Any differences were resolved by consensus. Follow up 2.7±0.5 years.
Results: Bone markers were: Ca 9.15±0.68 mg/dl, P 4.8± 1.28 mg/dl, median ALP 83 U/L, median PTH 244, median BGP 175 mcg/L, median ucBGP 10.95 mcg/L, median MGP 19.36 nmol/L, median PCR 1.6 mg/L. We found that 55% of patients had VF and 30.9% of patients had BF. Prevalence of VC was 80.6% (mild 20.1%, moderate 30.8%, severe 29.7%) in the aorta and55,1% in the iliac arteries. VF were significantly associated with warfarin use in males (6.1% vs 14.4%, p=0.044) but not in females. Severe aortic calcifications appeared to be significantly related to age, male gender, hypertriglyceridemia, PPI treatment and also to warfarin treatment, the latter with an odd ratio of 3.04 (95% CI 1.52-6.07, p=0.0016). Also, severe iliac calcifications were significantly related to age, PTH and warfarin, the latter with an odd ratio of 3.30 (95% CI1.59-6.85, p=0.0013). Furthermore, during follow-up (2.7 ±0.5 years) overall mortality was19.9% (on 387 total patients), but significantly increased in warfarin treated patients (37%; Log rank test p=0.0009).
Conclusions: Hemodialysis patients treated with warfarin show a higher prevalence VF (in men), VC and increased mortality. Additional studies are warranted to explore the association among warfarin treatment, VF, VC and mortality.

FP475 SILENT MYOCARDIAL ISCHEMIA IN HEMODIALYSIS PATIENTS WITH CORONARY ARTERY DISEASE

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Introduction and Aims: The aim of this study was to evaluate clinical characteristics and cardiovascular prognosis of silent myocardial ischemia in hemodialysis patients with coronary artery disease (CAD).
Methods: Among 64 consecutive hemodialysis patients who underwent elective coronary angiography between July 2002 and March 2004, we selected 22 patients (14 male, 67 ± 9 years old, 14 (64%) diabetics, dialysis vintage 84 ± 68 months) who demonstrated both stress-induced myocardial ischemia and significant coronary artery stenosis. The presence or absence of chest pain was identified and all patients were followed until the end of 2009. The study endpoint was cardiovascular death.
Results: Myocardial ischemia was detected by positive stress electrocardiography and thallium-201 scintigraphy in 20 and 2 patients, respectively. Fourteen patients (64%) had stress-induced chest pain, while 8 patients (36%) did not.
A multiple logistic regression analysis identified a ratio of low-density lipoprotein cholesterol to high-density lipoprotein cholesterol as an independent predictor of chest pain (odds ratio per 1 unit increase: 4.7, 95% confidence interval 1.2-45.5, p=0.02). The prevalence of diabetes was not different between the patients with and without chest pain (64% and 63%, respectively).
Eighteen cardiovascular deaths (82%) were recorded during the follow-up period of 41 ± 28 months. Of the 18 patients, there were 5 sudden cardiac deaths, 4 (80%) of which occurred in the patients without chest pain. The absence of chest pain was not associated with cardiovascular death (p=0.62) but was marginally associated with sudden cardiac death (hazard ratio: 5.8, 95% confidence interval 0.9-113.5, p=0.07) in a Cox proportional hazard analysis.
Conclusions: Silent myocardial ischemia was detected in one-third of hemodialysis patients with stable CAD. This phenomenon might be associated with sudden cardiac death.

FP476 TRENDS IN THE INCIDENCE OF ATRIAL FIBRILLATION IN OLDER PATIENTS INITIATING DIALYSIS IN THE UNITED STATES

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Introduction and Aims: Atrial fibrillation (AF) is increasingly common in patients requiring long-term dialysis, especially among the elderly where 16.5% of patients had AF in 2006. Little is known, however, about the incidence of AF in older dialysis patients. We conducted a 15-year study to assess trends in the incidence of AF and associated mortality in older patients receiving long-term dialysis in the United States.
Methods: We used the US Renal Dialysis System to identify older patients (>67 years) who initiated dialysis from 1995-2007. Patients had to have 2 years of uninterrupted Medicare fee-for- service insurance prior to initiation of dialysis to be eligible (n = 339,413). Individuals with a prior medical claim for AF were excluded (n = 113,725) for a final study population of 225,688.
Individuals were followed from first dialysis to the occurrence of one of three outcomes: diagnosed AF (1 inpatient or 2 outpatient diagnoses), kidney transplantation, or death. Analyses were censored at 12/31/08. Time to event analysis was performed to assess time trends in incident AF. Death and transplantation were treated as competing risks and Cause Specific Hazards (CSH) and 95% confidence intervals (CI) were estimated. Analyses were adjusted for demographics and comorbidities.
Among those that developed newly-diagnosed AF, a second analysis was performed with time to death as the outcome of interest.
Results: 71,985 (32%) people developed AF before death, transplantation or censoring, for an event rate of 172 events per 1,000 person-years. Both unadjusted and adjusted analyses showed increasing incidence of diagnosed AF diagnoses until about 2002, at which point incidence rates remained stable. Men (vs. Women;HR = 0.98 [0.96,0.99]),

African Americans vs. Caucasians (HR = 0.70 [0.69,0.72]), and Hispanics vs. Non-Hispanics (HR = 0.72 [0.69,0.74]) were less likely to develop AF. While survival after incident AF increased significantly in more recent years, 1-year mortality after first diagnosis of AF remained high at 54%. By 2008 the CSH for death after AF compared to 1995 was 0.75 (0.69, 0.81). Among patients with AF, mortality did not differ by sex, race or ethnicity.
Conclusions: These results suggest that the increasing prevelance of AF in the elderly ESRD population can be attributable to both an increasing incidence of AF as well as longer survival of patients newly diagnosed with AF. In the absence of electrocardiographic data, we are unable to discern whether our observation reflects higher AF incidence or more aggressive coding of diagnosed AF over time. In light of the high incidence of AF in these vulnerable patients, future studies need to focus on potentially modifiable risk factors for incident AF in patients undergoing long-term dialysis.

FP477 RIGHT VENTRICULAR FUNCTION IN CKD STAGE 5 PATIENTS WITH END-STAGE RENAL DISEASE STARTING DIALYSIS THERAPY. A TISSUE DOPPLER IMAGING STUDY

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Introduction and Aims: Heart failure is highly prevalent in End Stage Renal Disease (ESRD) patients on long term hemodialysis . Detection of right ventricular (RV) dysfunction before starting dialysis may help to identify patients at a higher risk of developing heart failure. However, little data exists regarding RV function in predialysis patients.To assess RV function in predialysis patients using tissue Doppler imaging (TDI) derived myocardial performance index of RV (MPI-RV).
Methods: Echocardiography including pulsed TDI of lateral tricuspid annulus was performed in 41 patients with ESRD before starting dialysis therapy and 12 age and gender matched healthy controls. RV dysfunction was defined as MPI > 40; a value above the median MPI in controls.
Results: Compared to controls, ESRD patients had significantly higher blood pressure and lower haemoglobin level. MPI-RV was significantly impaired in ESRD patients compared to control (0.6 vs. 0.4, p< 0.001). RV dysfunction was identified in 23 ESRD patients (56%). ESRD patients had significantly lower e' velocity and e'/a' ratio as compared with controls. Pulmonary hypertension was detected in 15 (36.5%) patients. Among ESRD patients, no correlation was detected between MPI-RV and calculated mean pulmonary artery pressure (r=-0.13, p=0.47), pulmonary artery systolic pressure (r= -0.12, p=0.6), left ventricular ejection fraction (r=0.294, p=0.06), or MPI of left ventricle (r=0.3, p=0.065). ESRD patients with and without pulmonary hypertension had similar MPI-RV (0.6 vs.0.62, p = 0.32).
Conclusions: Subclinical RV dysfunction –as estimated by TDI derived MPI- is highly prevalent among ESRD patients even before starting dialysis therapy. Pulmonary hypertension is not significantly associated with RV dysfunction in these patients.

FP478 PREDICTION OF CARDIOVASCULAR EVENTS IN HEMODIALYSIS PATIENTS BY AMINOTERMINAL PROPEPTIDE OF TYPE III PROCOLLAGEN CIRCULATING LEVELS

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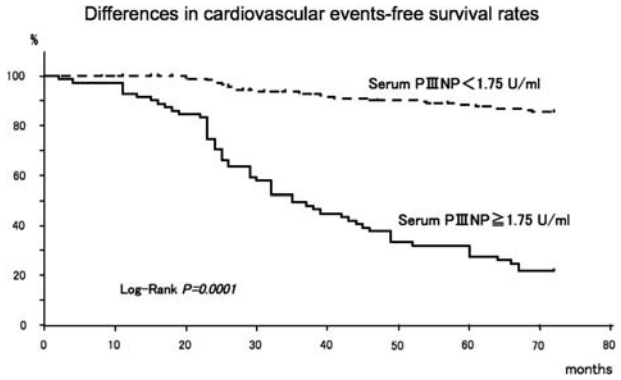
Introduction and Aims: Type III collagen abundantly exists in the cardiovascular system including the aorta and heart. The aminoterminal propeptide of type III procollagen (PIIINP) is an extension peptide of type III procollagen, which is cleaved off stoichiometrically during conversion from type III procollagen to type III collagen and liberated to serum. Elevated serum concentrations of PIIINP are considered a marker of higher collagen turnover and tissue fibrosis. In this study, we prospectively investigated whether serum levels of PIIINP can be a biomarker for predicting cardiovascular events in hemodialysis patients.
Methods: We measured serum PIIINP concentrations in 244 patients on maintenance hemodialysis (126 men and 118 women; mean age, 64 ± 11 years; dialysis duration, 11.5 ± 7.8 years) by immunoradiometric assay on February 2005. End point was cardiovascular events, and the patients were followed up through February 2011, until the end point was reached.
Results: During follow-up for 4.7 ± 1.8 years, cardiovascular events occurred in 78 (30.3%) of 244 patients: cardiac deaths (*n*=19: 14 sudden cardiac deaths, 3 acute myocardial infarction deaths, and 2 heart failure deaths), non-fatal acute myocardial infarction (*n*=1), obstructive coronary artery disease needing percutaneous coronary intervention (*n*=22), vasospastic angina identified by angiography (*n*=3), heart failure needing hospitalization (*n*=21), bradycardia needing pacemaker implantation (*n*=7: 5 sick sinus syndrome and 2 atrioventricular block), dissecting aortic aneurysm (*n*=2), aortic valvular stenosis needing valve replacement (*n*=1), peripheral artery disease needing bypass surgery (*n*=1) and leg amputation (*n*=1). Stepwise Cox hazard



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analysis associated the cardiovascular events with increased serum PIIINP concentration (1 U/ml; hazard ratio, 1.616, 95% CI, 1.449-1.804; P=0.0001). The mean serum PIIINP concentration of all subjects was 1.81 ± 1.22 U/ml, and the mean serum PIIINP concentrations were higher in patients with cardiovascular events than in those without (2.78 ± 1.73 U/ml versus 1.35 ± 0.40 U/ml. P<0.0001). When the patients were assigned to subgroups based on serum PIIINP cut-off value for cardiovascular events of 1.75 U/ml, cardiovascular events-free survival rates at 5 years were lower (P=0.0001) in the subgroup of serum PIIINP of 1.75 U/ml or more than in that of serum PIIINP below 1.75 U/ml (31.9% versus 88.2%) (FIgure).
Conclusions: Higher levels of circulating PIIINP may be associated with increased collagen turnover or fibrosis of the cardiovascular tissues, leading to sclerosis of the vascular systems and myocardial remodeling or overload. Serum PIIINP concentrations can be a new biomarker for predicting the cardiovascular events in hemodialysis patients.

FP479 ORAL NICORANDIL TO REDUCE SUDDEN CARDIAC DEATH OF HEMODIALYSIS PATIENTS WITH LEFT VENTRICULAR HYPERTROPHY

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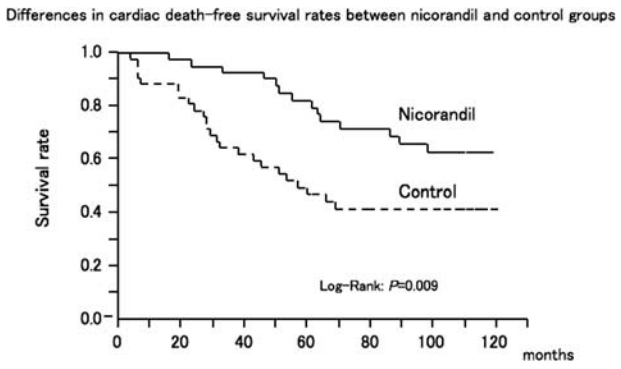
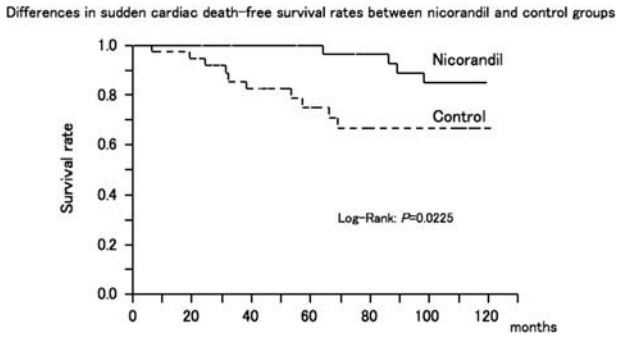
Introduction and Aims: Sudden cardiac death (SCD) is one of the main causes of death among hemodialysis patients. The hemodialysis patients appear to exhibit overactivity of the cardiac sympathetic nervous system, which may play a triggering role in the generation of ventricular dysrhythmias and SCD. Left ventricular hypertrophy (LVH) is a structural heart disorder most frequently found in hemodialysis patients, and one of the potent risk factors of serious cardiac events including SCD. We investigated the protective potential of oral administration of nicorandil for SCD in hemodialysis patients with LVH, focusing on the relation to the cardiac sympathetic activity.
Methods: Subjects were asymptomatic 84 propensity score-matched patients on maintenance hemodialysis (42 in the nicorandil [15 mg/d] group and 42 in the control group; 52 men and 32 women; mean age, 65 ± 12 years), who had LVH as determined by echocardiography and had undergone twenty-four-hour ambulatory



FP479 Differences in cardiac death-free survival rates between nicorandil and control groups



FP479 Differences in sudden cardiac death-free survival rates between nicorandil and control groups

electrocardiography between dialysis sessions to analyze heart rate variability. We calculated the ratio of the low-frequency component (LF, 0.04-0.15 Hz)/ high-frequency component (HF, 0.15-0.40 Hz) in the frequency –domain measures of the heart rate variability as a parameter of cardiac sympathetic activity.
Results: Over a follow-up of 6.1±3.1 years, we observed 38 cardiac deaths (14 SCD, 13 acute myocardial infarction [AMI] death and 11 heart failure [HF] death). Incidence of cardiac death was lower (P=0.016) in the nicorandil group (14/42; 33%) than in the control group (24/42; 57%). In stepwise Cox hazard analysis, cardiac death was positively associated with age or the LF/HF ratio, and inversely with left ventricular ejection fraction and administration of calcium channel blockers or nicorandil (Hazard ratio, 0.448; P=0.035). In Kaplan-Meier survival analyses, cardiac death-free survival rates were higher in the nicorandil group than in the control group (P=0.009). SCD-free survival rate was lower, and AMI-free survival rate tended to be lower in the nicorandil group than in the control group. However, HF-free survival rate did not differ between the two groups. The mean LF/HF ratios were lower in the nicorandil group than in the control group (1.1 ± 0.5 versus 1.8 ± 1.2, P=0.0008).
Conclusions: Oral administration of nicorandil could reduce cardiac deaths of hemodialysis patients with LVH mainly by inhibiting the occurrence of SCD. The inhibition of cardiac sympathetic activity by nicorandil may be one of the mechanisms of decreasing SCD among this population.

FP480 LOWER MAGNESIUM LEVELS PREDICT PULSE PRESSURE IN PREVALENT HEMODIALYSIS PATIENTS

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Introduction and Aims: It is well documented that large-artery stiffness is the main determinant of pulse pressure and that it has independent predictive value for total and cardiovascular mortality. Magnesium deficiency has been associated with increased risk for arterial stiffness in kidney transplant patients. The aim of this study was to identify determinants of pulse pressure (PP) in our population of hemodialysis patients and to assess if magnesium deficiency was associated with increased arterial stiffness.
Methods: We conducted an observational study which included all stable patients attending our hemodialysis clinic. Mean systolic and diastolic blood pressures, pre- and post-hemodialysis, of the ten treatments antedating blood sampling, were determined. PP was calculated as the difference between the mean systolic and mean diastolic values obtained. We tested the relationship between PP and inflammation, mineral metabolism, magnesium, therapy with phosphate binders and vitamin D in a cohort of hemodialysis patients. Descriptive statistics and a multiple linear regression model were used in the statistical analysis.
Results: A total of 162 patients (70 females, 92 males; 19.8% diabetic), with mean age of 64.1 years and mean time on dialysis of 58.7 months were included. This population presented mean values of the evaluated parameters such as follows: C-reactive protein = 10.8 ± 20.3 mg/L, CaxP = 37.4 ± 14.0 mg2/dL2, PTH = 442.8 ± 492.7 pg/mL, bicarbonate = 23.8 ± 2.6 mmol/L, magnesium = 2.2 ± 0.4 mg/dL and PP = 68.9 ± 15.8 mmHg. Almost half of the patients (46.3%) patients were treated with vitamin D, 35.8% were under treatment with calcium- based phosphate binders and 32.7% were under sevelamer. Using a multiple linear regression model we found a correlation between PP and age (r = 3.782, p = 0.001), diabetes (r = 2.714, p = 0.007) and magnesium levels (r = -2.596, p = 0.01).
Conclusions: In our population, diabetes, older age and lower magnesium levels predicted higher PP levels. Further studies are needed not only to better understand the relationship between magnesium plasma levels and PP but also to assess if magnesium correction in hemodialysis patients would reduce PP and consequently cardiovascular events.

FP481 SERUM MAGNESIUM CONCENTRATION RELATES TO INTRADIALYTIC HYPOTENSIVE EVENTS IN CHRONIC HEMODIALYSIS PATIENTS.

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Introduction and Aims: Serum magnesium (Mg^2+) concentration changes during hemodialysis (HD) treatment due to diffusive removal in the presence of dialysate Mg^2+ below that of serum. The magnitude of this gradient determines the diffusive forces involved and the extent to which serum Mg^2+ changes during HD. Changes in serum Mg^2+ may affect the occurrence of intradialytic hypotensive episodes (IDH) at different levels of dialysate calcium. (Elsharkawy, Hemodial Int 2006; Pakfetrat, Hemodial Int 2010). In this retrospective analysis we investigate the relationship of dialysate to serum Mg^2+ gradient (GMg^2+) with IDH.
Methods: We studied chronic HD patients treated in Renal Research Institute clinics in who serum Mg^2+ measurements were available in the period from 03/2011 to 12/ 2011. Systolic blood pressure (SBP) was measured every 30 minutes during treatments. A drop in SBP below 90 mm Hg or more than 20 mmHg within two measurements defined IDH. Logistic regression models with backward exclusion (P>0.1) adjusted for age, male gender, black race, pre HD SBP, diabetes, ultrafiltration rate, body mass index, albumin, GMg^2+, dialysate to serum sodium gradient (GNa+), difference post HD weight to target weight, dialysis vintage, dialysate calcium concentration and treatment time were employed to determine the relation between pre HD GMg^2+ and the occurrence of IDH.
Results: 502 chronic HD patients (age 61.1±15.6 years, vintage 4.0±4.0 years, 54 % male, 54 % blacks, 49 % diabetic patients, pre HD SBP 141.2±26.1, post HD SBP 135.4±25.8) were studied. Treatment time was 212.3±33.3 minutes, ultrafiltration volume was 2.6±1.1 L, GNa+ was -1.0±2.5, post HD weight was 78.0±21.7, difference between post HD weight and target weight was 1.4±9.7 kg, and dialysate Mg^2+ was 1.0 mEq/L. Mean GMg^2+ was -0.8±0.3 mEq/L. GMg^2+ was inversely related to the occurrence of IDH [Odds Ratio 0.34 (95% CI 0.15 to 0.77); P=0.01] (Table 1).
Conclusions: GMg^2+ and subsequently dynamic changes during HD is associated with IDH. Avoidance of low dialysate Mg^2+ may reduce the prevalence of IDH.

FP481 Table 1: Logistic Regression Model showing significant predictors of intradialytic hypotension after backward exclusion of parameters with P-values below 0.1. Excluded parameters were age, race, diabetes, body mass index, albumin, dialysate to serum sodium gradient, difference post HD weight to target weight, dialysis vintage, dialysate calcium concentration and treatment time.

	Odds Ratio	95% Confidence Interval	
		Lower limit	Upper Limit
Pre HD SBP [mmHg]	0.98	0.97	0.99
Diabetes [0/1]	0.62	0.938	2.43
Ultrafiltration rate [L/hour]	1.51	1.01	4.36
Dialysate to serum magnesium gradient [mEq/L]	0.34	0.15	0.77
Constant	0.62	n/a	

Hemodialysis (HD), systolic blood pressure (SBP).

FP482 EFFICACY OF DIGIT NUMBER OF NT-PROBNP FOR SCREENING OF CARDIOVASCULAR DISEASE IN NEW HEMODIALYSIS PATIENTS

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Introduction and Aims: K/DOQI guideline has recommended to make a screening for cardiac disease at the initiation of maintenance dialysis therapy. Simple and useful surrogate tools for identify cardiovascular disease and for assessment of prognosis are needed for new dialysis patients. The purpose of our study is to explore the efficacy of digit and absolute number of NT-proBNP for screening of cardiac disease at the initiation of dialysis therapy.
Methods: From January 2009 to April 2011, 71 new hemodialysis patients (68±14 years, 83% male, 48% diabetes) were enrolled into the final database for this study.

FP482 Table 1.

	Absolute NT-ProBNP			Digit NT-ProBNP		
	Cut-off	AUC (95%CI)	p	Cut-off	AUC (95%CI)	p
LVH	6301	0.602 (0.457-0.747)	0.167	4.5	0.596 (0.453-0.738)	0.196
LV dilatation	14480	0.685 (0.560-0.809)	0.008	4.5	0.644 (0.515-0.773)	0.039
EF <60%	10562	0.765 (0.618-0.911)	0.001	4.5	0.741 (0.593-0.889)	0.002
EF <50%	12893	0.872 (0.766-0.979)	0.003	4.5	0.820 (0.712-0.929)	0.01
CAD	6171	0.754 (0.619-0.890)	<0.001	4.5	0.710 (0.577-0.842)	0.004

LVH, leftventricular hypertrophy; EF, ejection fraction; CAD, coronary artery disease.

The usefulness of absolute Nt-ProBNP concentration and digit number of it for screening of cardiac disease were explored by using receiver operator characteristic curve analysis. Clinical information was recorded on all patients immediately prior to first HD session. Blood sample was collected just before the first HD session. NT-proBNP is determined by an electrochemiluminescence immunoassay on the Elecsys 2010 analyzer (Roche Diagnostics). All patients were performed echocardiogram and coronary angiography/pharmacologic-stress thallium-201 single photon emission computed tomography for screening of cardiovascular disease on the optimal body weight.
Results: Mean concentration of NT-proBNP was 15460±21426 pg/mL (median; 6576) at the just before the first dialysis session, and mean digit number of it was 4.3 ±0.6 (median; 4.4). As shown in Table, except of LVH, significant predictive ability of NT-proBNP were determined to each cardiovascular disease although those levels were showing wide variation from 6000 to 15000. On the other hand, best cutoff predictive values of digit number were 4.5, all same number to any cardiovascular disease.
Conclusions: Considering wide variation of NT-proBNP cutoff level (6000-15000 pg/mL) depending on each cardiac disease, digit number way could be a potential easier scale for first step risk stratification in new dialysis patients. Digit number of NT-proBNP 5 or more means potentially high risk for cardiovascular disease and 3 or less means low risk ESKD patients.

FP483 PLASMA LEVELS OF ADMA AND SDMA REMAIN STABLE IN INCIDENT PD PATIENTS DESPITE A DECLINING RESIDUAL RENAL FUNCTION: A PROSPECTIVE STUDY

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Introduction and Aims: Both low residual renal function (RRF) and high plasma levels of asymmetric dimethylarginine (ADMA) and symmetric dimethylarginine (SDMA) have been associated with increased cardiovascular risk in patients with CKD. ADMA and SDMA levels increase along the progression of kidney disease. This increase is attributed to a decreased glomerular filtration and decreased degradation by dimethylarginine dimethylaminohydrolase (DDAH). In patients with chronic renal disease DDAH is stated to contribute to >80% of the overall (plasma) clearance of ADMA but in patients with chronic renal disease, expression of DDAH in extrarenal tissues seems to be downregulated. The present prospective observational study was performed to test the hypothesis that ADMA levels increase along the loss of RRF in incident peritoneal dialysis (PD) patients.
Methods: Sixty-one incident PD patients (51,6± 17 years, male 58%) enrolled in an ongoing prospective observational study (NCT01306149) were included in the present analysis. At outpatient visits 1 to 5, sampling was performed for the calculation of urea nitrogen and creatinine clearances. ADMA was measured by HPLC. The linear mixed-model (LMM) approach was used to model time course of plasma ADMA and SDMA concentrations.
Results: At the start of PD therapy, mean age was 51,6± 17 years. The majority of patients was male (58%). Mean follow-up time was 320 days. Residual renal creatinine clearance at first visit was 54,7 L/wk/1,73m^2. Mean ADMA and SDMA plasma level amounted to 0.63±0.14 μM and 2.5±0.8 μM, respectively, at the first visit. ADMA levels were higher in diabetic patients and patients with cardiovascular history. In multivariate analyses ADMA measured at the first visit was positively associated with the presence of diabetes (p=0.003) and negatively with rkT/V (p=0.021). SDMA was negatively associated with age (p=0.0002) and rkT/V (p=0.00009). In the LMM, ADMA and SDMA levels remained stable over time (ADMA p=0.89; SDMA p=0.23). Residual renal creatinine clearance (p=0.0097) and rkT/V (p=0.011) declined and peritoneal clearance of creatinine (p= 0.0097) and ureum (p= 0.01) significantly increased with time and compensated at least partly for the loss of renal clearances.
Conclusions: Plasma levels of ADMA and SDMA remain stable in incident PD patients, despite a declining RRF. This suggests that peritoneal clearance (SDMA) and extrarenal degradation (ADMA) may compensate for the decreased glomerular filtration and renal metabolism by DDAH. Together with animal data, our findings challenge the thesis that renal failure *per se* is the cause of increasing plasma ADMA levels in CKD patients. The present study further refutes the hypothesis that increased plasma levels of ADMA and SDMA are in the causal pathway between low RRF and increased cardiovascular disease.

FP484 DYSLIPIDEMIA, CHOLESTEROL ESTERIFICATION AND HIGH DENSITY LIPOPROTEINS IN DIALYSIS PATIENTS

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Introduction and Aims: Chronic Renal Insufficiency (CRI) is associated with high cardiovascular (CV) mortality, beginning in the early stages but growing in advanced and particularly in dialysis. Dyslipidemia (DL) of CRI (namely low levels of high-density lipoproteins (HDL) and high levels of triglyceride-rich lipoproteins (VLDL, LDL), but also a complex disruption of the normal structure of lipoproteins) is reported to be an important CV risk factor, usually being reported more severe in Peritoneal Dialysis (PD) than Haemodialysis (HD) patients. Nevertheless data are, in all, scanty. Aim of our study was to describe lipids and lipoprotein profile in HD, PD and normal age matched controls (NC), analyzing the cholesterol esterification process measuring LCAT mass and activity and evaluating distribution of HDL subpopulations: the purpose has been to point out differences due to the two different dialysis methods.
Methods: We studied 21 HD patients, 22 PD patients (10 APD and 12 CAPD) from the same nephrology ward and 22 NC (blood donors). Clinical data about nephropathy, CV and metabolic diseases, and drug therapy were gathered. Plasma Total Cholesterol (TC), Triglycerides (TG), Phospholipids (PL), HDL-Cholesterol (HDL-C) and apolipoproteins (apo A-I, A-II, B) were determined by enzymatic and immunoturbidimetric assays (Integra 400 plus™ , Roche Diagnostics); non-esterified Cholesterol (FC) by colorimetric immunoenzymatic method. LDL-Cholesterol (LDL-C) was calculated by Friedewald formula. Cholesterol esterification rate (CER) was measured on the plasma sample after 1 hour incubation at 37 °C and LCAT Activity on an exogenous standardized substrate, as described by Murakami (1995); plasma LCAT mass and CEPT concentrations by immunoenzymatic assay. LpA-I and LpA-I:A-II plasma concentrations were obtained by the kit Hydragel LpA-I Particles™ (Sebia Italy). HDL has been separated by dimensions using poliacrilamide gel electrophoresis and by charge, measuring pre-b HDL, using bidimensional electrophoresis.
Results:
Conclusions: All dialysis patients showed lower HDL-C, ApoA-I and ApoA-II levels than controls; TG and VLDL-C were higher and TC, LDL-C, Apo-B were reduced. Unexpectedly the lipidic profile was better in PD than HD. LCAT mass and activity were reduced in HD patients and probably this induced a defect of Cholesterol esterification, modifying HDL subpopulations distribution, with increment of small HDL and reduction of the large ones, possibly altering their function; this was not evident in PD patients.

FP484 Table 1

	HD (n=21)	PD (n=22)	NC (n=22)	Kruskal-Wallis Test
TC (mg/dl)	157.5±48.6	172±42.3	211.2±38.2	p=0.0011
LDL-C (mg/dl)	86.8±33.7	102.8±37.2	130.1±34.3	p=0.0009
VLDL-C (mg/dl)	35.0±22.6	27.8±11.8	21.2±8.1	p=0.0259
HDL-C (mg/dl)	35.7±7.7	41.5±15.8	59.8±9.9	p<0.0001
TG (mg/dl)	175.0±113.2	138.8±59.1	105.8±40.8	p=0.0261
PL (mg/dl)	196.5±50.0	195.6±38.1	205.4±28.3	p=0.3424
ApoA-I (mg/dl)	94.3±16.1	106.3±26.2	135.1±14.4	p<0.0001
ApoA-II (mg/dl)	19.7±5.8	21.5±5.6	25.7±3.7	p=0.0005
Apo-B (mg/dl)	96.4±30.9	122.8±35.9	122.8±30.7	p=0.0164
FC/TC	0.31±0.04	0.28±0.03	0.27±0.02	p=0.0003
LCATmass (ug/ml)	4.42±0.81	4.43±0.95	5.23±0.75	p=0.0039
CER (nmol/ml/h)	36.7±13.5	35.4±9.6	36.3±6.1	p=0.6202
LCAT activity (nmol/ml/h)	31.0±6.8	35.5±10.4	38.3±9.3	p=0.0321
small HDL (%)	32.6±10.4	20.9±9.5	16.7±5.8	p<0.0001
Medium HDL (%)	17.5±3.7	18.2±9.3	18.2±3.3	p=0.4453
Large HDL (%)	49.9±10.7	60.9±15.7	65.2±7.8	p=0.0001

FP485 WHAT IS THE EFFECT OF A/V FISTULA FLOW ON RIGHT VENTRICULAR PERFORMANCE INDEX IN PATIENTS WITH ESRD; A THREE MONTH FOLLOW UP TISSUE DOPPLER ECHOCARDIOGRAPHIC STUDY?

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Introduction and Aims: No data exist regarding the direct impact of arteriovenous fistula (AVF) on right ventricular (RV) function in patients (pts) with end stage renal disease (ESRD). Myocardial performance index (MPI) is an independent predictor of mortality and adverse outcome. Our aim To study the relation between AVF flow volume (Qa) and changes in RV-MPI, in CKD patients stage 5D.
Methods: Thirty ESRD pts (mean age: 44 y, 17 male) who had their first AVF (60% forearm & 40% elbow/upper arm). All Pts had no prior cardiac disease, pulmonary hypertension or severe anemia. Before and 3 months after AVF, RV-MPI was calculated as the sum of isovolumic contraction and relaxation times divided by ejection time using pulsed tissue Doppler echocardiography within one hour of dialysis. Before AVF creation, Duplex scan was used to measure feeding artery (pre-FA) and receiving vein diameters. After 3 months, FA, receiving vein, and fistula diameters, velocities and resistivity indices were measured. Qa index was calculated as [FA cross-sectional area (cm2) x time averaged velocity (cm/sec) x 60] / body surface area. Change (?) in MPI was calculated by subtracting follow up value from baseline value. Taking median value as a cutoff, deteriorated RV function was defined as ? MPI > 0.015 and high AVF flow as Qa index > 950 ml/min/m2.
Results: Compared to pts with lower AVF flow, pts with high flow showed a trend toward increased ? RV-MPI (0.08 vs. -0.04, p=0.08). Among all clinical and AVF-related parameters, predictors of RV function deterioration are shown in table. ? RV-MPI showed positive correlations with Qa index (r=0.4, p=0.04), pre-FA (r=0.46, p=0.01) and fistula diameters (r=0.35, p=0.04). Qa index = 900 ml/min/m2 and Pre-FA = 2.5 mm can predict RV function deterioration with 73% & 73% sensitivity and 67% & 74% specificity respectively.
Conclusions: High AVF flow adversely affects right ventricular function as assessed by MPI. Qa index, AVF position, and pre-FA and fistula diameters are the most significant predictors of RV function deterioration.

FP485 Table 1

Variable	Δ RV-MPI > 0.015	Δ RV-MPI ≤ 0.015	p value
Qa index*, ml/min/m²	1079 (408- 3204)	691 (246 – 2224)	0.04
AVF elbow/upper arm position, no (%)	9 (60)	3 (20)	0.025
Pre-FA diameter*, mm	3.0 (1.2 -5.6)	2.1 (1.2 – 3.9)	0.013
Fistula diameter*, mm	4.0 (2.1- 5.9)	3.3 (1.4 -4.2)	0.03

*Data are presented as median (range).

FP486 PLASMA ADIPONECTIN LEVELS FOR PREDICTION OF CARDIOVASCULAR RISK AMONG HEMODIALYSIS PATIENTS

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Introduction and Aims: Background. Adiponectin (ADPN) is an endogenous insulin sensitizing and anti- inflammatory hormone, released by the adipose tissue. Because of its in vitro effects on endothelial cells, macrophages and vascular smooth muscle cells, ADPN is thought to have anti-atherogenic properties. Among human subjects, plasma ADPN concentrations are reduced among patients with atherosclerotic complications but are substantially increased among patients with advanced renal failure. The clinical and biochemical correlates of plasma ADPN levels were investigated and its predictive value with respect to survival rates and cardiovascular (CV) events in a cohort of hemodialysis (HD) patients.
Methods: We measured baseline ADPN in 55 hemodialysis patients, in addition to, 17 healthy subjects to serve as reference group. ADPN levels, were related to different clinical and biochemical cardiovascular risk factors such as, increased body mass index (BMI), serum triglycerides (TG), duration of HD, smoking, mean arterial blood pressure (MBP) and heart rate(HR), high density (HDL) cholesterol, low density (LDL) cholesterol, serum glucose, hemoglobulin and CRP levels in HD patients.
Results: Plasma ADPN levels were higher (P < 0.0001) among HD patients (15.06 ± 3.55 μg/ml) than among reference subjects (6.52 ± 1.09 μg/ml), were independent of age, and were higher among women (16.11 ± 3.10 μg/ml) than among men (13.97 ± 3.72 μg/ml). Plasma ADPN levels were inversely related to BMI, TG, and glucose levels. Furthermore, plasma ADPN levels were directly related to HDL cholesterol and Kt/V. Plasma ADPN levels were lower (P < 0.001) among patients who experienced new CV events (11.15 ± 2.22μg/ml) than among event free patients (16.6 ± 2.6 μg/ml).
Conclusion: Plasma ADPN levels were an inverse predictor of CV risk among HD patients.

FP487 DNA METHYLATION PROFILING REVEALS DYSREGULATION OF ATHEROSCLEROSIS-RELATED GENES IN DIALYSIS PATIENTS

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Introduction and Aims: The role of epigenetic dysregulation in human disease is increasingly appreciated. Only few studies focused on epigenetics in chronic kidney disease (CKD), virtually all of which assessed epigenetic dysregulation globally. We hypothesized that gene-specific epigenetic dysregulation in CKD exists, affecting genes pertinent to inflammation and atherosclerosis, two pathogenetic hallmarks of CKD.
Methods: Ten clinically stable dialysis patients undergoing standard hemodialysis therapy and ten healthy, age and sex matched controls were recruited for the study. DNA was purified from freshly isolated peripheral blood mononuclear cells (PBMCs) using the DNeasy Blood & Tissue Kit (Qiagen, Hilden, Germany). Genome-wide analysis of DNA methylation was performed by SMSDK (SuperTAG methylation-specific digital karyotyping) at GenXPro- GmbH, Frankfurt / Main, Germany, which uses 26 bp tags that are annotated to promotor databases. Additionally, gene ontology (GO) information was obtained from "www.GeneOntology.org" for annotated hits.
Results: Analysis of 27 043 436 tags revealed 4 288 genomic loci with differential DNA methylation (P < 10-10) between hemodialysis patients and control subjects. Annotation of these tags to promoter databases allowed us to identify 52 candidate genes associated with cardiovascular disease and 97 candidate genes associated with immune / infection diseases. These candidate genes could be classified to distinct proatherogenic processes including lipid metabolism and transport (e.g. HMGCR, SREBF1, LRP5, EPHX2, FDPS), cell proliferation and cell-cycle regulation (e.g. MIK67, TP53, ALOX12), angiogenesis (e.g. ANGPT2, ADAMTS10, FLT4) and inflammation (e.g. TNFSF10, LY96, IFNGR1, HSPA1A, IL12RB1).
Conclusions: In conclusion, we provide a comprehensive analysis of genome wide epigenetic alterations in CKD, identifying candidate genes associated with proatherogenic and inflammatory processes. These results may spur further research in the field of epigenetics in kidney disease, and point to new therapeutic strategies in CKD-associated atherosclerotic disease.

FP488 HYPER-BETA 2 MICROGLOBULINEMIA SEEMS TO BE A RISK FACTOR FOR VENTRICULAR ABNORMAL RELAXATION WITH NORMAL SYSTOLIC FUNCTION OF THE HEART IN HEMODIALYSIS PATIENTS.

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Introduction and Aims: Reportedly, congestive heart failure exists in 31% of hemodialysis (HD) patients at the time of initiation of dialysis therapy and occurs in 7% of HD patients in a year. Cardiac diastolic dysfunction with normal systolic function is an emerging risk factor for heart failure. From these points of view, we studied factors that are related to left ventricular abnormal relaxation (LVAR) in HD patients.
Methods: From 2010 to 2011, we performed a cross sectional study using 119 outpatients in our clinic, who underwent HD three times a week and Doppler echocardiography as a regular checkup. Eighty patients were included in this analysis (64.2 ± 10.1 y, 54 males, 25 diabetic, 39.5 months on HD [Median]) after 39 patients were excluded because of the following reasons: medical history of cardiac events (N=23)(percutaneous coronary intervention (9) / angina (2) / myocardial infarction (11) / aortic valve replacement (1)), ejection fraction (EF) less than 60% (N=20), and/or no blood test around the day of echocardiography (N=4). By Doppler echocardiography, early (E) and atrial (A) peak transmitral flow velocities, and deceleration time of early transmitral flow velocity (E-DT) were measured. LVAR was defined as the condition where E-DT and the ratio of E to A (E/A) are longer than 240 msec and less than 1.0, respectively. All the statistical analyses were done with JMP ver. 8 (SAS Institute Japan Ltd., Tokyo).
Results: EF, LAD (left atrial diameter), LVMI (left atrial volume index), E/A and E-DT were 73.5 ± 7.0, 39.0 ± 6.1, 182.8 ± 60.9, 0.82 ± 0.27 and 269.4 ± 70.3, respectively. Out of 80 patients with normal systolic function, 48 patients (60%) matched our definition of LVAR with normal systolic function. As compared with the non-LVAR (NL), LVAR (L) were older (66.1 ± 9.9 vs. 61.2 ± 9.9, p=0.0311) and

had higher values of serum beta-2 microglobulin (31.1 ± 7.4 vs. 27.9 ± 5.1mg/l, p=0.0400), lower albumin- adjusted calcium (9.5 ± 0.6 vs. 9.8 ± 0.5ml/dl, p=0.0314), and lower pre-dialysis arterial PO2 (99.2 ± 14.2 vs. 105.8 ± 12.3 mmHg, p=0.0358). There were no differences with regard to prevalence of diabetes, gender, hemodialysis vintage, serum albumin, serum phosphate, hemoglobin, LDL-cholesterol, HDL-cholesterol, intact-parathyroid hormone, arterial pH, arterial PCO2, arterial HCO3 -, brachial pulse wave velocities, pre-dialysis systolic blood pressure, pre-dialysis diastolic pressure, pre- dialysis pulse pressure, interdialysis weight gain, and other echographic parameters such as EF, LAD and LVMI. A logistic regression analysis using LVAR as the dependent variable showed beta-2 microglobulin and age were significant independent variables. Age-adjusted odd ratio of the highest quartile of beta-2 microglobulin (equal to or more than 33.225) was 6.602 [95%CI: 1.760 - 34.549]. A subanalysis using 52 patients who underwent echocardiography just after the dialysis session, who were expected to have no fluid overload, gave compatible results.
Conclusions: Hyper-beta 2 microglobulinemia seems to be a risk factor for ventricular abnomal relaxation with normal systolic function of the heart in hemodialysis patients. We speculate that serum beta-2 microglobulin level should be kept low in order to prevent diastolic dysfunction and subsequent heart failure.

FP489 ITALIAN SURVEY ON HEMORRHAGIC AND THROMBOEMOLIC RISK AND ORAL ANTICOAGULANT THERAPY IN A LARGE POPULATION OF HEMODALYSIS PATIENTS WITH ATRIAL FIBRILLATION.

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Introduction and Aims: Thromboembolic stroke (TS) is the most important atrial fibrillation (AF) complication and oral anticoagulant therapy (OAT) is thus usually recommended in AF patients to avoid it. However, even if AF is highly prevalent in HD patients, there is no agreement as to the risk/benefit of OAT in such a population, considering the increased bleeding risk associated to uremia and HD. Aim of our study is to quantify the thromboembolic and hemorrhagic risk in a large chronic HD patient population with AF whether undergoing treatment or not with OAT.
Methods: Data were collected by means of an electronic CRF from 1,529 patients treated in ten HD centers in Italy. CHADS2VASCs (Congestive heart failure, Hypertension, Age >75, Diabetes, Stroke/TIA, Vascular disease, Age 65–74, Sex category) and HASBLED (Hypertension, Abnormal renal and liver function, Stroke, Bleeding, Labile INR, Elderly, age >65 years, Drugs or alcohol) scores were used to evaluate thromboembolic and hemorrhagic risk.
Results: 18.8% of the study population (288 patients) [59.7% men, median age 75.9 (IQR 67.9-81.2) years and median HD duration 4.2 (IQR 1.8-8.1) years] had AF in a different form: 58 (20.1%) paroxysmal, 129 (44.8%) persistent, 101 (35.1%) permanent. The distribution of OAT or antiplatelet therapy was 119 (41.3%) AF patients received OAT, 110 (38.2%) salicylate, 32 (11.1%) ticlopidine, 8 (2.8%) clopidogrel, 35 (12.2%) low molecular weight heparin. Forty-five patients (15.6%) were taking neither OAT nor antiplatelet agents. Permanent AF was present in 53.8% of the patients. on OAT and in 21.9% of the patients not receiving OAT ($p<0.001$). Only 13 patients had a $CHADS_2VASCs$ score <2 (low risk) and no differences were found in the score between OAT and non-OAT subjects [4.2 (sd 1.6) vs 4.4 (sd 1.9)]. Mean HASBLED score was higher in patients taking OAT than in patients who were not taking OAT (4.2 ±1.2 vs 3.9 ±1.2, respectively $p<0.05$).
Conclusions: Our large survey shows that AF is present in 18% of chronic HD pts but less than half of them received OAT, even if there was a high thromboembolic risk. The hemorrhagic score risk is high in the whole HD population, but much higher in the OAT group. Our new prospective and longitudinal study, already in progress, will provide information as to the adequacy of the prescribed therapies in TS prevention and the utility of the common risk stratification scores also in HD pts.

FP490 POLYMORPHISMS OF ANGIOTESIN CONVERTING ENZYME AND MATRIX METALLOPROTEINASE 3 GENES IN HAEMODIALYSIS PATIENTS – ASSOCIATION WITH CARDIOVASCULAR MORBIDITY AND MORTALITY

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Introduction and Aims: Cardiovascular morbidity and mortality are the major concern in dialysis patients and many risk factors has been proposed to be involved in its pathogenesis. Apart from traditional and non-traditional risk factors, genetic susceptibility may be of importance including renin- angiotensin system (RAS) and matrix metalloproteinase 3 (MMP 3) polymorphism. The aim of this study was to analyse RAS and MMP 3 polymorphism in our group of haemodialysis patients and to correlate the findings with cardiovascular morbidity and mortality.
Methods: The study included 200 patients on regular haemodialysis, three time per week on polysulphone membrane for more than six months. Genetic analysis was performed by using polymerase chain reaction – restriction fragment lenght polymorphism method (PCR-RFLP).
Results: Out of 200 patients 73% had 5A/6A, 21% had 5A/5A and 6% had 6A/6A MMP 3 genotype respectively. I/D had 55%, D/D had 35% and I/I had 10% of our patients included ACE genotype. It was shown that patients with D allele genotype experienced significantly higher incidence of cerebrovascular accidents, left ventricular hypertrofy and peripheral vascular disease. The ACE polimorphism showed significant association with incidence of cerebrovascular accident and hiperlipoproteinaemia in our group of haemodialysis patients. The results of this study have shown correlation between 5A allele of MMP 3 gene and significantly higher risk for developing myocardial infarction, cerebrovascular accident and peripheral vascular disease. Less favourable genotype combination (5A allele for MMP3 and D allele for ACE) had higher incidence of developing cerebrovascular accident.
Conclusions: The ACE gene polymorphism is associated with development of cerebrovascular accidents and hyperlipoproteinaemia. We need longer follow-up since one-year mortality was not influenced by MMP3 and ACE polymorphisms.

FP491 "DE NOVO" CARDIOVASCULAR DISEASES ONSET DURING CHRONIC DIALYSIS: AN EPIDEMIOLOGYC STUDY

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Introduction and Aims: Cardiovascular disease is the leading cause of death in patients on chronic dialysis (CD). In addition, patients with ESRD have uremia-specific risk factors that can be responsible for the onset or progression of cardiovascular diseases. Our study aimed to evaluate incidence and factors associated with "de novo" cardiovascular diseases onset during CD.
Methods: Retrospective cohort study of 6,147 patients, who underwent CD in Lazio (Italy) in 2004-2010. We separately studied the onset of "de novo" cardiopathies (including both ischemic and congestive heart failure), of "de novo" cerebrovascular diseases and of "de novo" vasculopathies in 3,483 (56.7%) subjects. We performed multivariate logistic regression models to evaluate the factors associated with the onset of each pathology, focusing on the role of diabetes. Models were adjusted for CD start variables: age, gender, self-sufficiency, nephropathy, presence of several comorbidities, serum levels of haemoglobin, albumin, creatinine, calcium and phosphorus.
Results: We found a higher frequency of diabetes at CD start among patients with a cardiovascular disease compared with diseases-free ones (41% vs. 22%). We observed 23.3% new cases of at least 1 of 3 pathologies (cardiopathies 17%, cerebrovascular diseases 7%, vasculopathies 9%) during CD (median cohort follow-up 23 months). We found a higher probability of "de novo" cardiopathies (both ischemic and congestive heart failure) for patients with diabetes at start CD (OR=1.44; 95% CI:1.06-1.96) and no association with cerebrovascular diseases (OR=0.89; 95% CI:0.66-1.20) and vasculopathies (OR=1.22; 95%CI:0.95-1.57); however, in presence of cerebrovascular diseases diabetes is no more associated with cardiopathies onset (OR=1.01; 95%CI:0.59-1.73). We found a higher probability of cerebrovascular diseases for patients with vasculopathies at CD start (OR=1.35; 95%CI:1.02-1.80). We did not find association between cerebrovascular disease onset and presence at CD start of cardiopathies (OR=1.09; 95%CI:0.86-1.38) and diabetes (OR=1.17; 95% CI:0.79-1.74). We found a higher probability of vasculopathies onset in patients with diabetes at CD start (OR=1.39; 95%CI:0.97-1.99), but no association with cerebrovascular diseases (OR=0.90; 95%CI:0.65- 1.23) and cardiopathies (OR=1.09; 95%CI:0.88-1.36).
Conclusions: We observed that the presence of cardiopathies (both ischemic and congestive heart failure), cerebrovascular diseases, vasculopathies at CD start is not associated with a higher probability of the 2 other pathologies onset, except for cerebrovascular diseases in patients with vasculopathies. The presence of diabetes at CD start is associated with a higher probability of cardiopathies and vasculopathies, but not of cerebrovascular diseases. When we separately analysed the interaction between diabetes and each of the 3 pathologies, we only found the lack of association with cardiopathies onset in presence of cerebrovascular diseases. All these findings could suggest that patients did not have a higher probability of "de novo" pathology when already affected by another cardiovascular diseases and diabetes, perhaps as a consequence of therapies and a more attention in prevention. The importance to reduce the incidence of cardiovascular diseases in CD is a relevant issue given their role on CD mortality.

FP492 STRICT VOLUME CONTROL GUIDED BY BIOIMPEDANCE ANALYSIS AND THE EFFECT ON ARTERIAL STIFFNESS IN HEMODIALYSIS PATIENTS - A RANDOMIZED TRIAL

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Introduction and Aims: Chronic fluid overload is common in maintenance hemodialysis (HD) patients and is associated with severe cardiovascular complications, such as arterial hypertension, left ventricular hypertrophy, congestive heart failure, and arrhythmia. Therefore, a crucial target of HD is to achieve the so-called dry weight; however, the best way to assess fluid status and dry weight is still unclear. Dry weight is currently determined in most dialysis units on a clinical basis, and it is commonly defined as the lowest body weight a patient can tolerate without developing intra-dialytic or inter-dialytic hypotension or other symptoms of dehydration. One of the most promising methods that have emerged in recent years is bioelectrical impedance analysis (BIA), which estimates body composition, including hydration status, by measuring the body's resistance and reactance to electrical current. Our objective was to study the impact of strict volume control by using BIA vs clinical methods on arterial stiffness in a randomized trial.
Methods: We included 131 HD patients from a single center in a randomized prospective study, aiming to compare the long-term (36 months) effect of BIA-based versus clinical-based assessment of dry weight on pulse wave velocity (PWV). For the first 24 months (intervention period), in the "BIA" arm of the study the ultrafiltration was exclusively guided by BIA, compared to clinical methods only in the "clinical" arm. For the next 12 months (control period), in both arms of the study ultrafiltration and "dry weight" were guided by clinical methods only. The body composition was measured using the portable whole-body multi-frequency BIA device, Body Composition Monitor— BCM (Fresenius Medical Care, Bad Homburg, Germany). We evaluated the arterial stiffness by measuring the pulse wave velocity (PWV), 2 times during the "intervention" period and a 3rd time at the end of the control period, at 1 year intervals.
Results: For the first 24 months (intervention period), in the "clinical" group the mean PWV increased from 7.61 to 8.84 m/s ($p = 0.01$). In the "BIA" group PWV decreased from 8.23 to 6.69 m/s ($P < 0.001$). For the last 12 months of the study (control period), in both "BIA" and "clinical" arms we found a significant increase of PWV from previous values ($p < 0.05$).
Conclusions: Strict volume control in hemodialysis by using multi-frequency bioimpedance analysis had a significant impact on arterial stiffness when compared to using clinical criteria for assessing dry weight and guiding ultrafiltration. During the interventional period (24 months), PWV significantly decreased when using exclusively BIA for guiding ultrafiltration and increased in the "clinical" group. When reverting to only clinical methods (12 months control period), PWV increased significantly in both arms, suggesting that the initial intervention (strict BIA volume control) was responsible for the initial decrease in arterial stiffness.

FP493 CHANGES IN LEFT VENTRICULAR STRUCTURE AFTER PARICALCITOL THERAPY IN CHRONIC HEMODIALYSIS PATIENTS

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Introduction and Aims: Left ventricular hypertrophy (LVH) is prevalent in hemodialysis patients and is associated with increased cardiovascular morbidity and mortality. In recent years there has been a growing interest in the actions of vitamin D and its analogues beyond the effects of treatment of secondary hyperparathyroidism. Clinical and experimental studies suggest that treatment with vitamin D may improve survival and cardiac function in hemodialysis patients. The aim of the study was to analyze changes in cardiac structure and function of patients with secondary hyperparathyroidism at 6 and 12 months after treatment with paricalcitol.
Methods: We studied 44 stabilized chronic hemodialysis patients (66% male, mean age 57 ± 11.92 years, 43.2% diabetic, 95.5% hypertension) with moderate to severe secondary hyperparathyroidism (iPTH 300-800 pg/mL) treated with flexible doses of paricalcitol (mean dose 5.73 ± 2.26 mcg/week.). Before, at 6 and 12 months after paricalcitol treatment echocardiogram was performed and hemoglobin level, erythropoietin dose, blood pressure and parameters of bone-mineral metabolism were measured. Finally, we analized the evolution of patients treated with and without renin-angiotensin system inhibitors (RAS inhibitors).
Results: After 6 months of treatment left ventricular mass and left ventricular mass index decrease significantly (LVM: 283.3 ± 111.7 vs 249.24 ± 83.85 g, p= 0,010 - LVMI: 146.8 ± 48.8 vs 130.53 ± 39.4 g/m2, p= 0,014). At 12 months, we almost observed a decrease in left ventricular posterior wall (12.6 ± 2.5 vs 11.89 ± 2.1 mm, p= 0,045). When analyzing the group of patients not treated with RAS inhibitors, we found a significantly decrease in left ventricular diastolic diameter (**LVDD:** 50.4 ± 4.6 vs 45.6 ± 6.3 mm, p = 0.017), left ventricular systolic diameter (**LVSD:** 29.3 ± 4.3 vs 24.8 ± 4,1 mm, p = 0.021) and also in LVM (271.6 ± 86.4 vs 212.7 ± 60.9 g, p = 0.000) and **LVMI** (149.02 ± 36.6 vs 118.48 ± 28.1 g/m2, p = 0.000) after 12 months of treatment. In the group of patients treated with RAS inhibitors **LVSD** decrease significantly (31.9 ± 6.6 vs 28.6 ± 6.1 mm, p=0.004), observed no changes in other echocardiogram parameters. Analyzing cardiac remodeling we observed a significantly decrease of left ventricular concentric type (64,1% vs 42,9% p=0.001) and a decrease percentage of patients with left ventricular hypertrophy (65,9% vs 46,4% p=0.024).
Conclusions: Our study suggests that patients treated with Paricalcitol showed an improvement in left ventricular structure that begins to be evident at 6 months of treatment. Patients not treated with RAS inhibitors showed more evident changes of left ventricular structure, suggesting that the effects of paricalcitol at the cardiovascular level could be less evident when using RAS inhibitors.

FP494 CILOSTAZOL INCREASES HDL2 CHOLESTEROL LEVELS IN CHRONIC HEMODIALYSIS PATIENTS

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Introduction and Aims: Hemodialysis patients usually have lower plasma HDL cholesterol and higher triglycerides (TG) levels than healthy subjects. The antiplatelet agent cilostazol enhances macrophage reverse cholesterol transport. We established a single precipitation method for the measurement of HDL2 and HDL3 [J Lipid Res.49:1130-1136, 2008]. Using this simple assay, we examined the effect of cilostazol on HDL subspecies in hemodialysis patients.
Methods: Chronic hemodialysis patients with dyslipidemia were treated for 3 months with cilostazol at a dose of 100 mg/day. Plasma lipid profile and liver enzyme levels were assessed at baseline and then monthly during treatment. Nineteen patients with dyslipidemia were included (6 females and 13 males; mean age 64±11). Eleven patients had diabetes mellitus. Remnant-like particle (RLP)- cholesterol was measured by the homogenous method.
Results: Mean triglyceride (TG) levels (mg/dl) decreased during cilostazol treatment significantly from 163.3±85.0 to 136.6±59.0 ($p<0.01$). There was no significant change on low-density lipoprotein cholesterol (LDL-C) levels (mg/dl) from 91.2±28.3 to 85.0±24.6. There was also no significant change on small dense LDL-C levels (mg/dl) from 19.9±8.9 to 16.8±7.1. Mean high-density lipoprotein cholesterol (HDL-C) levels (mg/dl) increased significantly from 43.1±12.9 to 48.5±15.1 ($p<0.01$). Mean HDL2 cholesterol levels (mg/dl) increased from 27.9±10.6 to 34.8±11.2 ($p<0.01$). Mean HDL2-apolipoprotein (apo)A1 levels (mg/dl) increased from 78.7±12.2 to 83.5 ±18.8 ($p<0.05$). Mean HDL2-apoA2 levels (mg/dl) increased from 9.6±1.9 to 10.2 ±2.0 ($p<0.05$). There was no significant change on HDL3 cholesterol levels (mg/dl) from 10.9±2.6 to 9.8±3.6. Mean apo C3 levels (mg/dl) decreased from 13.2±4.0 to 12.0±2.8 ($p<0.05$) .
Conclusions: Cilostazol treatment increased HDL2 cholesterol, and may have restored the anti-atherogenic function of HDL particles in homodialysis patients. Cilostazol is an effective lipid-lowering agent for hemodialysis patients with dyslipidemia, because it may help to suppress development of atherosclerosis.

FP495 RELATIONSHIP BETWEEN ERYTHROPOIETIN RESISTANCE INDEX AND LEFT VENTRICULAR MASS AND FUNCTION AND CARDIOVASCULAR EVENTS IN PATIENTS ON CHRONIC HEMODIALYSIS

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Introduction and Aims: The response to EPO treatment varies considerably in individual patients on chronic hemodialysis. The erythropoietin resistance index (ERI) has been considered useful to assess the EPO resistance and can be easily calculated in the clinic. The aim of this study was to investigate the association between ERI and left ventricular mass (LVM) and function and to determine whether ERI was associated with cardiovascular events in patients on hemodialysis.
Methods: This study was designed prospectively. Clinical, laboratory, and echocardiographic variables were assessed in 72 patients on hemodialysis. The ERI

was determined as the weekly weight- adjusted dose of EPO (U/kg/week) divided by hemoglobin concentration (g/dl). Patients were divided into three groups by tertiles of ERI.
Results: Patients with higher tertiles of ERI had a higher LVM index and lower LV ejection fraction compared to those with lower tertiles of ERI (p = 0.019 and p = 0.030, respectively). The median follow-up period was 53 months. The Kaplan – Meier plot showed increased frequency of cardiovascular events in patients with higher tertiles of ERI, compared with those with lower tertiles of ERI (p = 0.011, log-rank test). The multivariate Cox proportional hazard models showed that the ERI was the significant independent predictor of cardiovascular events (HR 3.00, 95% CI, 1.04-8.62, p=0.042).
Conclusions: Our data show that ERI were related with LVM index, LV systolic function and cardiovascular events in patients with hemodialysis. By monitoring of ERI, early identification of the EPO resistance may be helpful to predict the cardiovascular risk in hemodialysis patients.

FP496 THE REDOX STATE OF SERUM ALBUMIN AND MORTALITY IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Increased oxidative stress may contribute to the excessive burden of cardiovascular disease in dialysis patients. Albumin comprises the largest thiol pool in plasma, and its redox state may be a good marker of oxidative stress of the HD patients. Oxidative modifications of human serum albumin (HSA).alter the biological properties of of HSA and may impact on its antioxidant potential. We prospectively followed a cohort of 248 HD for 3 years to examine the impact of oxidized form of serum albumin(non-mercaptoalbumin, HNA) on long-term survival of HD patients with normal serum albumin levels.
Methods: Measurement of the redox state of albumin was performed using the high performance liquid chromatography (HPLC). Cox proportional hazards regression analysis was used to identify independent predictors of all-cause and cardiovascular mortality.
Results: There was a statistically significant survival benefit in favor of patients who have higher BMI, lower HNA, higher ratio of HDL to cholesterol (HDL/Chol) and those without clinical history of CVD. During the 3-year follow-up period, 69 deaths (27.82%), including 25 CVD deaths (36.23%), were recorded. In crude analysis, each unit of increase in HNA was associated with increased CVD mortality, which persisted after adjustment for age, sex, dialysis vintage, diabetes, and baseline preexisting CVD.
Conclusions: This prospective study shows that increase serum concentration oxidized serum albumin (HNA) is a significant and independent risk factor for cardiovascular mortality in normoalbuminemic HD patients.

FP497 RENIN ANGIOTENSIN ALDOSTERONE SYSTEM BLOCHADE AND LEFT VENTRICULAR HYPERTROPHY IN MAINTENANCE HEMODIALYSIS PATIENTS

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Introduction and Aims: Left ventricular hypertrophy (LVH) is an independent and significant risk factor for morbidity and mortality in hemodialysis patients (pts). Blockade of rennin angiotensine aldosterone system (RAAS) by ACE inhibitors (ACEI) and sartans are widely used to diminish cardiac remodeling in such pts. However the results are controversial. Aldosterone by specifically activation of the mineral corticoid receptors (MR) in nonepithelial cells can induce cardiovascular damage by induction of cardiac fibrosis, which can be prevented by the administration of spironolactone. In anuric hemodialysis patients it is possible to blockade MR by spironolactone, without worrying about hyperkalemia development. The aim of study was to assess the additional effect of spironolactone on LVH in anuric hemodyalisis pts already receiving ACEI and sartans.
Methods: 71 anuric maintenance hemodialysis (HD) pts (age 50,74+9,44 years; mean+SEM) were randomized into the 2 groups: Group 1 received double-component therapy, including Lisinopril and Valsartan (n=35), and Group 2 in addition to Lisinopril and Valsartan received Spironolactone 25 mg daily (n=36). All patients underwent echocardiography before and thereafter 6 months of treatment period. Safety measurements of serum potassium were performed weekly.
Results: The basal parameters in both groups were consistent with left ventricular concentric hypertrophy: relative wall thickness (RWT) > 42, and left ventricular mass index (LVMI) > 95 g/m2 for women and > 115 g/m2 for men. After the 6-monts treatment period in Group 2: significantly decreased LVMI from 134.9 ± 12.94 to 132.2 ± 13.41 g/m2 (P <0.001), interventricular septum thickness (IVST) from 1.48 ± 0.23 to 1.44 ± 0.23 cm (P = 0.012), and left ventricular posterior wall thickness (LVPVT) from 1.43 ± 0.26 to 1,37 ± 0.26 cm (P = 0,008). However, RWT in this group increased from 0.58 ± 0.02 to 0.61 ± 0.02 (P <0.001). In contrast, in Group 1 significantly increased LVMI (from 144.9 ± 15.49 to 145.5 ± 15.13 g/m2; P <0.05) and LVPVT (from 1.35 ± 0.16 to 1.43 ± 0.16 cm; P<0.001). There were no changes in IVST and RWT (from 1.43 ± 0.18 to 1.48 ± 0.17 cm; P = 0.09, and from 0.57 ± 0.01 to 0.58 ± 0.03; P = 0.523, respectively). No cases of severe hyperkalemia developed during the entire treatment period in both groups.
Conclusions: We conclude that the addition of aldosterone antagonist spironolactone, to Lisinopril and Valsartan treatment in HD pts may have a significant positive effect on left ventricular remodeling.

FP498 EXERCISE IN END STAGE RENAL FAILURE: PATIENT PERCEIVED BARRIERS AND MOTIVATORS

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Introduction and Aims: The benefits of regular exercise for the end stage renal disease (ESRD) population undergoing haemodialysis are now well established. Exercise is recommended in national guidelines but uptake into the routine clinical service has been slow and effective strategies to enable its incorporation into clinical practice are required. The ESRD population encounter significant physical, psychological and social barriers to exercise participation, and an understanding of patient perceptions will be essential to underpin the design of feasible, patient centred physical activity interventions. We aimed to ascertain the common barriers and motivators to exercise participation in a unit-based haemodialyisis patient population.
Methods: With the permission of the authors, we employed the Dialysis Patient Perceived Exercise Barriers and Benefits Scale1 (DPEBBS). This validated questionnaire scores the importance of 24 potential barriers to and benefits of exercise participation, and also includes a free text section for explanation of any other factors the patient wishes to mention. The DPEBBS was completed by patients undergoing routine haemodialysis on a satellite unit as part of a service evaluation exercise. The questionnaire was distributed during routine dialysis sessions to all patients deemed clinically suitable for exercise participation, and consent was implied if participants filled out the questionnaire and returned it to the staff
Results: 58 patients completed the DPEBBS. Commonly identified barriers were general tiredness (69%), muscular fatigue (60%), the burden upon family members (53%), and body pain (45%). Although many patients understood the benefits of exercise (70%) a lack of knowledge about how to exercise (41%) remained a significant barrier. Commonly identified exercise benefits were preventing functional decline (94%), improving quality of life (89%), preventing muscle atrophy (89%) and keeping body weight at a steady level (89%). >80% agreed that exercise improved their optimism, self care abilities, mood and appetite. Thematic analysis of the free text comments revealed the wish to increase general fitness and sense of wellbeing, and a strong desire to exercise to increase positivity about life and self- perception, which was linked to feeling 'normal', weight loss and body image. Additional barriers included worries that exercise might induce other health problems or worsen ESRD/ dialysis-associated symptoms.
Conclusions: This survey provides a valuable insight into the perspectives of haemodialysis patients around exercise. Exercise was widely perceived to be beneficial, and the motivators identified can be utilised for physical activity promotion. Barriers to be addressed include fatigue management, lack of understanding of how to undertake exercise, and safety concerns.
Reference: [1]Zheng J et al Int J Nurs Stud 47:166-80,2010.

FP499 THE BEST CUT-OFF VALUE FOR DIAGNOSING OF ACUTE CORONARY SYNDROME AT EMERGENCY ROOM IN PATIENTS WITH END STAGE KIDNEY DISEASE

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Introduction and Aims: Acute coronary syndrome (ACS) is one of the leading causes of cardiovascular events in chronic dialysis patients. Troponin T (TnT), a marker for myocardial necrosis, is well known to be an essential tool for diagnosis of ACS in the general population. In end-stage kidney disease (ESKD) patients, an elevated level of TnT is an useful for predicting adverse outocome, however it remains unclear the efficacy of it for diagnosis of ACS. The purpose of this study is to search the best cut-off value of TnT for diagnosis of ACS in ESKD patients.
Methods: From January 2011 to Noveber 2011, 230 consecutive patients with chest symptom and/or acute dyspnea were visited emergency room and admiited in our

hospital. Among them, 56 patients who have suffered from CKD stage 5/5D, were enrolled into our database. Age and sex machted 26 CKD 5D patients without chest symptom were also put into our final database as a control. Finally 82 patients (72 ±13 years, 66% male, 50% diabetes) were examined for this study. The usefulness of TnT for diagnosing of ACS were explored by using receiver operator characteristic (ROC) curve analysis. Clinical information was recorded on all patients at emergency room. TnT is determined by semi-quantitative method (Roche diagnostics cobas h232, quantitative range 0.1-2.0 ng/mL) at emergency room on the blinded condition to physicians. The physicians could know just TnT concentration above or less 0.1 ng/mL which is standard cut off value for diagnosing of ACS in the general population.
Results: 15 patients were diagnosed as ACS clinically, then 25 patients were performed coronary angiography, and 11 patients were fixed as an ACS patients angiographically. Three ROC curves were dipicted to each 3 catgolized patients. The best cut-off values were 0.31 ng/mL (sensitivity; 53%, specificity: 89%) for clinical diagnosis, 0.17 ng/mL (sensitivity; 55%, specificity: 81%) for dicision making for CAG, and 0.31 ng/mL (sensitivity; 55%, specificity: 82%) for final diagnosis respectively.
Conclusions: It is well known that TnT level in ESKD patients has a tendency to be higher than the general population even though no suspicion of ACS. However, even in ESKD patients TnT would be a useful tool for diagnosing ACS. Based on our findings, 0.31 ng/mL is thought to be the best cut-off value, especially for ruling in.

FP500 REACTIVE OXYGEN METABOLITES (ROMS) ARE ASSOCIATED WITH CARDIOVASCULAR DISEASE AND NEW CARDIOVASCULAR EVENTS IN CHRONIC HEMODIALYSIS PATIENTS

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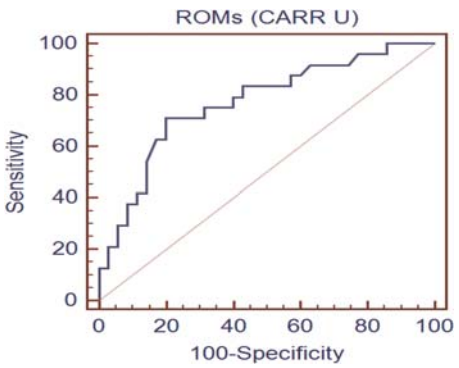
Introduction and Aims: Oxidative stress is significantly increased in patients on chronic hemodialysis (HD) patients. However the causal relationship between oxidative stress and CVD in HD patients has not yet firmly established. The purpose of this prospective study was to examine the potential relationship between ROMs and CVD as well as the influence of ROMs levels on the development of new cardiovascular events (CVE).
Methods: All prevalent HD patients referring to Hemodialysis Service of the Universitá Cattolica del Sacro Cuore of Rome, Italy in the period March 2004-March 2005 were considered eligible. Patients defined as having prevalent CVD included those with a documented history of myocardial infarction (MI), stroke, angina pectoris, coronary revascularization procedures, transient cerebral ischemia (TIA), peripheral artery surgery (not including the A-V fistula), carotid endoarterectomy, and peripheral vascular disease. Patients were followed for 72 months or until death. During the follow-up, new CVE (myocardial infarction, stroke, angina pectoris, coronary revascularization procedures, transient cerebral ischemia, peripheral artery surgery, carotid endoarterectomy, and peripheral vascular disease) were recorded. The oxidative status was evaluated by measuring hydroperoxides (ROOH) serum levels (ROMs test; Diacron srl, Grosseto, Italy). Plasma levels of total thiols (SH) was obtained using the SHp test (Diacron International, Grosseto, Italy). Glutathione Peroxidase (GPx) activity was measured on whole blood samples using the Ransel Kit (Randox Laboratories td). Glutathione plasma levels were measured by HPLC with fluorescent detection.
Results: The levels of ROMs presented a median value of 270 (238.2-303.2) CARR U (interquartile range). We created a ROC curve (ROMs levels vs CVD) and we identified a cut-off point of 273 CARR U. The multiple regression analysis showed that age, creatinine and C-reactive protein were independent factors associated with ROMs. Thirty five (46.1%) had prevalent CVD at the moment of the inclusion in the study. Patients with CVD were significantly older and had lower creatinine and haemoglobin levels and higher troponin T and total cholesterol concentrations. ROMs were significantly higher in patients with CVD than in those without. The multiple logistic regression analysis showed that ROMs levels and CVD were independently associated together with age and C-reactive protein. Twenty six patients developed CV events during the follow up. Of these, 7 were in the group with ROMs levels < 273 CARR U and 19 in the group with ROMs levels =273 CARR U. The Receiver operating characteristic (ROC) curve for ROMs levels (CARR U) and new CVE is shown in the Figure. The logistic regression analysis showed that both age and ROMs levels were associated with CVD events in the follow up. Interestingly, limiting the analysis to patients with age =60, the ROMs levels only were associated with CVD in the follow-up (OR: 1.02, 95% CI 1.00-1.05, p=0.045).
Conclusions: ROMs are independently associated with prevalent CVD and new CVE in chronic HD patients.



FP500

FP501 EFFECT OF LOW DOSE ASPIRIN ON PREVENTION OF FOOT ULCERS IN HEMODIALYSIS PATIENTS WITH DIABETES : A RETROSPECTIVE COHORT STUDY

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Introduction and Aims: Peripheral arterial disease is frequent in hemodialysis patients with diabetes. Peripheral arterial disease is a major risk factor for foot ulcers and lower extremity amputation, remarkably reduced quality of life. However, the prevention of foot ulcers is uncertain. The aim of this study was to evaluate the association between occurrence of foot ulcers and low dose aspirin use.
Methods: We conducted a retrospective cohort study of fifty-nine hemodialysis patients with diabetes, two dialysis centers between April 2010 and October 2011. Exclusion criteria were the history of extremity amputation and uses of other antithrombogenic drugs. Group A (n = 34) received low dose aspirin, whereas group B (n = 25) received no low dose aspirin. The primary outcome measure was occurrence of foot ulcers in need of surgical attention, and the secondary outcome measure was a new gastrointestinal bleeding event during the study period. Cox regression models were used to examine whether low dose aspirin use was associated with the risk of foot ulcers in need of surgical attention and a gastrointestinal bleeding event.
Results: Low dose aspirin use was significantly related to a lower risk of foot ulcers in need of surgical attention [Hazard ratio = 0.15 ; 95% confidence interval, 0.03 to 0.70, p=0.02]. The occurrence of a new gastrointestinal bleeding event during the study period was not associated with low dose aspirin use [Hazard ratio = 1.10 ; 95% confidence interval, 0.19 to 6.60, p=0.92].
Conclusions: These results suggest that low dose aspirin use may prevent the occurrence of foot ulcers in hemodialysis patients with diabetes.

FP502 POOR PATIENT SURVIVAL AFTER EARLY DIALYSIS INITIATION MAY BE EXPLAINED BY ADVANCED AGE

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Introduction and Aims: Some studies postulated that early dialysis start may increase mortality. To examine this issue we measured survival associated with Modification of Diet in Renal Disease eGFR and age at dialysis initiation in our centre, with sequential adjustment for a number of covariates.
Methods: We studied the following variables at dialysis initiation: eGFR, age, gender, diabetes mellitus, serum albumin, hemoglobin, date of dialysis initiation (1995-1999, 2000-2004 and 2005-2009), history of ischemic heart disease and stroke.
Results: Over the last 15 years 428 patients initiated dialysis therapy in our reference area. Mean age at dialysis start was 63±13 years and 65% were male. The three years survival rate was significantly increasing within the different periods 63% 1995-1999, 69% 2000- 2004, and 77% en 2005-2009 (p=0.003). Causes of death were heart disease (25%), infections (24.5%), neoplasms (10.5%), and stroke (8.6%). The mean eGFR at dialysis start was 8.16 mL/min/1.73. In the univariate analisis, increased eGFR, age, period of dialysis initiation 1995-99 and 2000-2004, diabetes and history of ischemic heart disease were associated with increased mortality in end-stage renal disease (ESRD) patients (p<0.05). Patients that started dialysis program with eGFR >8.16 mL/min were older than patients with eGFR <8.16 (66 vs 61 years, p<0.001). In the multivariate Cox model (without including age), eGFR, period of dialysis initiation, serum albumin levels and history of ischemic heart disease were associated with mortality (Table). The association between mortality and eGFR was lost when the model was adjusted by age (Table).
Conclusions: In conclusion, history of ischemic heart disease, serum albumin levels and dialysis start before 2005 were risk factors for mortality in ESRD patients. Older age is usually associated with early dialysis initiation, so age adjustment is needed to perform studies aimed to calculate the effect of eGFR at dialysis initiation on survival.

FP502 Table 1.

Model without AGE included			Adjusted by age		
Variables included in the model	Relative risk	p	*Variables included in the model*	Relative risk	p
eGFR (ml/min/1.73)	1,05	0,004	**eGFR (ml/min/1.73)**	1,12	0,364
Period 1995-1999 (2005-2009=1)	2,16	<0,001	**Period 1995-1999 (2005-2009=1)**	2,39	<0,001
Period 2000-2004 (2005-2009=1)	1,63	0,029	**Period 2000-2004 (2005-2009=1)**	1,67	0,024
Albumin (g/l)	0,76	0,022	**Albumin (g/l)**	0,65	0,001
Ischemic heart disease	1,92	<0,001	**Ischemic heart disease**	1,58	0,005
			Age (years)	1,07	<0,001

FP503 ANALYSIS OF QT PROLONGATION IN ESRD PATIENTS DURING HEMODIALYSIS TREATMENT

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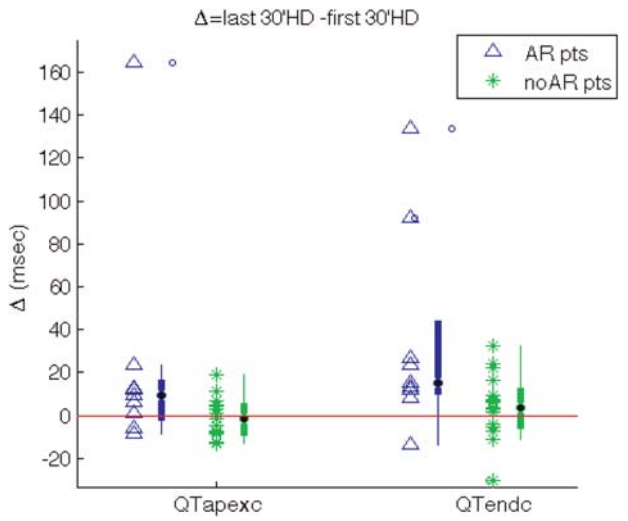
Introduction and Aims: The relationship between prolonged QT and arrhythmias is well known. HD treatment produces an alteration of electrolyte balance. Changes in ventricular repolarization duration associated with HD largely depend on the concentrations of Ca2+ and K+ in the dialysis bath. The objective of this study is to verify the association of QT prolongation in ESRD patients during HD with the appearance of cardiac arrhythmias from a beat-to-beat analysis.
Methods: 26 patients from San Bortolo Hospital, Vicenza, were enrolled in the study. A 3-lead 24h ECG Holter (Cardioline, Italy) was performed during the midweek HD session. The patients were retrospectively divided in two groups. While none of the pts had significant arrhythmias during the first 30 minutes of HD, 9 patients concluded the treatment with significant arrhythmias (AR group); 17 pts did not present arrhythmic events in the 24hr (noAR group). A beat-to-beat QT duration was assessed by an automatic algorithm. The corrected values of QTapex and QTend were compared (QTc=QT/vRR), where QTapex is the time interval between the start of Q wave and the peak of T wave and QTend is the time between the start of the Q wave and the end of the T wave.
Results: Patients in the AR group showed a significant increase of QTend during the treatment (first 30' of HD: 428.6±38.2 ms; last 30' of HD: 463.0±38.7 ms, paired Wilcoxon signed test p- value=0.027). No significant trends were observed in noAR group (first 30' of HD: 436.6±20.3 ms; last 30' of HD 441.1±20.0). The variation DQTend and DQTapex, estimated as the difference between the average values measured during the last 30' of HD and the average values estimated during the first 30', were significantly different between the two groups. They resulted higher and positive in AR group (DQTapex AR group: 23.64±53.60ms; noAR group: -1.19±8.93 ms; DQTend AR group: 34.37±47.01ms; noAR group: 4.56±14.62ms; both Wilcoxon rank sum test p-value<0.05). Figure 1. A linear regression was performed for each patient on QT values averaged every 5 minutes of HD. A significant increasing trend was found in AR group.
Conclusions: The lengthening of QT induced by HD treatment was an indicator of arrhythmic events, which occurred later during the HD session. The monitoring of beat-to-beat QT duration could help to prevent the insurgence of arrhythmic events. Further studies in a larger population are needed to understand the effects of HD treatment in pts at higher risk to develop arrhythmias during the treatment.



FP503 Figure 1: Boxplots of variations and values of ΔQTend and ΔQTapex for each patient.

FP504 BETA 2-MICROGLOBULIN IS A PREDICTOR OF LEFT VENTRICULAR MASS INDEX IN HEMODIALYSIS PATIENTS.

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Introduction and Aims: Left ventricular mass index (LVMi) is a strong predictor of cardiovascular morbidity and mortality in hemodialysis (HD) patients. The aim of this study is to identify modifiable predictors of LVMi in HD patients.
Methods: This cross-sectional study included baseline data of 330 HD patients from 15 dialysis centres in the Netherlands (n=14) and Canada (n=1), who were enrolled in the COnvective TRansport STudy (CONTRAST). Clinical characteristics and standard laboratory tests were used for this analysis. M-mode echocardiography was performed on an inter-dialysis day and LVMi was calculated. Predictors of LVMi were analysed by multivariable linear regression. To improve the fit of the model LVMi was logarithmically transformed (logLVMi), residuals were checked for normality.
Results: The patients had a median age of 64 years (range 23 – 94), 203 were male (61%) and the median dialysis vintage was 2.00 (range 0,08 – 16,42) years. The median LVMi was 123 g/m2 (range 41 – 357) or logLVMi 2.08 ± 0.14 g/m2. Multivariable linear regression analysis showed that male sex (β=0.055, p=0.002), use of a renine angiontensin (RAS) inhibitor (β=0.043, p=0.011), and beta 2-microglobulin (β=0.002, p=0.02) were significantly and independently related to logLVMi. A significant inverse relationship was found between logLVMi and dialysis vintage (β=-0.01, p=0.006) and creatinine (β=-0.0001, p=0.007).
Conclusions: Male sex, use of RAS inhibitor, dialysis vintage, creatinine and beta 2-microglobulin were found to be significantly and independently related to LVMi in our population of HD patients. The positive correlation with RAS inhibitor use is unexpected and could be explained by prescription bias in this observational study. The positive correlation between beta 2-microglobulin and LVMi suggests that middle molecular weight molecules might contribute to the pathogenesis of LVMi. Since LVMi is a powerful predictor of cardiovascular morbidity and mortality, therapies that lower middle molecular weight molecules may decrease LVMi and thereby the incidence of clinical events.

FP505 THE ACTIVATION OF MTOR PATHWAY INDUCED BY INFLAMMATION ACCELERATES THE PROGRESSION OF ATHEROSCLEROSIS IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Our previous studies *in vivo* and *in vitro* demonstrated that inflammation accelerated the progression of atherosclerosis via the dysregulation of low lipoprotein receptor (LDLr) pathway, which was inhibited by Rapamycin, an inhibitor of mammalian target of Rapamycin (mTOR). The study was to investigate whether inflammation exacerbates lipid accumulation in the tissues of radial arteries in hemodialysis patients and its underlying mechanisms.
Methods: Thirty-one hemodialysis patients receiving arteriovenostomy were divided into two groups by the plasma level of C-reactive protein: Control (n=16), inflamed group (n=15). Hematoxylin- eosin staining and Oil Red O staining were used to check foam cell formation and lipid droplets accumulation using the tissues surgically removed from radial artery. Immunohistochemistry and immunofluorescent staining were used to check protein expressions related with intracellular cholesterol trafficking.

Results: There was significant lipid accumulation in the radial artery of inflamed group compared to control, which was correlated with the increased protein expressions of LDLr, sterol regulatory element binding protein-2 (SREBP-2), and SREBP cleavage-activating protein (SCAP). Confocal microscopy observation showed that inflammation enhanced the translocation of SCAP escorting SREBP-2 from the endoplasmic reticulum to the Golgi, thereby activating LDLr gene transcription. Further analysis showed that dysregulation of LDLr pathway induced by inflammation was associated with the increased protein expression of mTOR, especially with the enhanced co-expression of mTOR and SREBP-2.
Conclusions: Inflammation accelerated the progression of atherosclerosis in hemodialysis patients through the disruption of LDLr pathway, which could be partly through the activation of mTOR pathway.

FP506 CLINICAL RESEARCH OF RELATIONSHIP BETWEEN CAROTID INTIMA-MEDIA THICKNESS AND CARDIOVASCULAR RISK FACTORS IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Cardiovascular disease is the leading cause of mortality in hemodialysis patients with a cardiovascular risk 10 to 20 times higher than in general population. It is known that accelerated atherosclerosis and vascular calcifications contribute to the risk excess. This study aimes to evaluate the degree of plaque burden and the correlation between carotid intima- media thickness (cIMT) assessed by ultrasonography with both traditional and novel cardiovascular risk factors in hemodialysis patients.
Methods: We enrolled 75 patients with end stage renal failure (35F and 40M) aged 56.3 +/- 14.1 years being on maintenance hemodialysis for 42.1 +/- 58.0 months. Carotid arteries were evaluated at 0.5cm, 1cm, 1.5cm and 2cm distance from bifurcation on both sides. We considered the mean cIMT as the average of the 8 determinations. Biochemical tests where performed before the midweek hemodialysis session for Hb, total cholesterol, LDL, HDL, Ca, P, iPTH, CRP and uric acid levels. Demographic data, blood pressure, BMI, smoking, history of diabetes mellitus and duration of hemodialysis period were investigated as well.
Results: During the 18 months follow-up period 6 patients died (8%), the majority from cardiovascular disease (66.7%). One third (37.3%) of the patients had carotid atheroma plaques, most of which were calcified (19 out of 28). The mean cIMT was 9.5 +/- 4mm and it associated with age, hypertension, diabetes mellitus and CRP. Logistic regression analysis revealed a significant correlation between calcified atheroma plaque and dyslipidemia, male gender, duration of hemodialysis, hyperuricemia, Ca x P> 55 and iPTH. The study of the risk factors showed that cIMT, CRP, P, CaXP and iPTH were death predictors in our population.
Conclusions: Our findings suggest cIMT could be useful to identify vulnerable subjects but only combined analysis of traditional and uremia related risk factors can identify the cardiovascular risk profile in this population. Further study is recommended to evaluate the prediction impact of each risk factor in patients with different stages of kidney disease compared to control subjects.

FP507 PRO-INFLAMMATORY AND PRO-COAGULANT CHARACTERISTICS OF PLATELET DERIVED MICROVESICLES IN HAEMODIALYSIS PATIENTS

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Introduction and Aims: Haemodialysis (HD) patients are at a high risk of cardiovascular (CV) mortality, although the reasons for this are not fully explained by traditional risk factors. Cell derived microvesicles (MVs) are protein bearing vesicles of <1μm diameter, known to be elevated in chronic kidney disease, inflammation, thrombogenesis and CV disease. P-selectin, a cell adhesion molecule, and the humoral complement C3 are two proteins implicated in CV events due to their pro- inflammatory and pro-coagulant abilities. As of yet, P-selectin and C3 have not been documented on HD patient's MVs. This study hypothesises that haemodialysis patients display P-selectin and C3 positive MVs.
Methods: Platelet MVs were generated from healthy controls to optimise methods for subsequent use in characterising HD patient samples. Briefly, platelets were stimulated with calcium ionophore A23187 (10μM) and MVs were then isolated using graduated centrifugation. Multiple techniques were used to elicit the size, structure, count and characteristics of resuspended MVs including: negative staining electron microscopy (EM): counting using NanoSight® nanoparticle tracking analysis (NTA): flow cytometry with fluorochrome labelled annexin-V and CD41 antibodies and: western blotting using anti-P-selectin and anti-C3c antibodies. MVs were then isolated from the plasma of HD patients (n=5) for quantification and characterisation with each sample run in duplicate.
Results: The presence of platelet MVs was verified in patient samples using the above techniques. EM confirmed the size and bilayer characteristic of MVs. NTA showed the mean number of MVs gated between 0.1-1μm as $0.13 \times 108 \pm 272$ particles/ml. Flow cytometry confirmed the presence of platelet derived MVs by positive labelling with both the MV specific annexin-V and platelet specific CD41 fluorochromes. Western blotting characterised the surface proteins present, clearly identifying P-selectin (140kDa) and both the a and β units of C3 (110kDa and 75kDa respectively) against appropriate controls.
Conclusions: This study has identified P-selectin and C3 positive microparticles in haemodialysis patients. P-selectin and C3 play a role in the development of cardiovascular disease due to their pro- inflammatory/-coagulant nature. Our results could indicate a novel mechanism for the identification and modification of CV risk in HD patients.

FP508 HYPERPHOSPHATAEMIA AND MICROVESICLE FORMATION: A NOVEL MECHANISM FOR CARDIOVASCULAR RISK IN CHRONIC KIDNEY DISEASE

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Introduction and Aims: Cardiovascular disease (CVD) is the leading cause of death in patients with advanced renal disease. Microvesicles (MVs) are membrane-derived vesicles ranging from 100-1000nm released into the circulation following cell activation and apoptosis. They are elevated in uraemic patients and are associated with increased cardiovascular (CV) risk. Hyperphosphataemia is common in advanced renal disease and is also associated with increased CV risk. Elevated inorganic phosphate [Pi] is reported to stimulate apoptosis and generation of reactive oxygen species (ROS) in cultured human vascular endothelial cell line Ea.Hy926 (Di Marco GS *et al* Am J Physiol 294, F1381-7; 2008). We hypothesise that in uraemia formation of MVs is driven partly by hyperphosphataemia through apoptotic damage to the endothelium and circulating platelets.
Methods: Immortalised human endothelial Ea.Hy 926 cells were incubated for up to 48h with standard (1mM) and high (2.5mM) phosphate concentrations. Intracellular Pi was assayed using a selective colorimetric approach based on generation of phosphomolybdate complexes. Microvesicle formation, phosphate-induced cell apoptosis and ROS generation were measured using flow cytometry and NanoSight® nanoparticle tracking analysis (NTA).
Results: Intracellular Pi levels were higher in endothelial cells (ECs) incubated in 2.5mM phosphate solution (13.9 + 1.7 nmol/mg protein vs 8.2 + 1.3 in standard Ea. Hy cultures, Mean + SEM, P=0.003). This observation was time dependent with maximal response at 48h (P=0.003). After 24h incubation with the higher extracellular phosphate, Annexin V flow cytometry detected a 50 + 29% increase in phosphate-induced apoptosis in these cells accompanied by a 44 + 13% increase (P=0.021) in release of sedimentable protein-containing particles into the medium. NTA showed that higher extracellular phosphate was associated with an increase in the release of 100-200nm MVs from ECs, within 90 minutes. However, no significant increase was observed in ROS production detected by dihydroethidine staining.
Conclusions: In human vascular endothelial cells, elevated phosphate is associated with: higher intracellular Pi concentration; elevation in apoptosis; and increased release of cell-derived vesicles into the medium. These data suggest that such vesicles are a novel marker for phosphate-induced toxicity in endothelium which may be of value in assessing cardiovascular risk in hyperphosphataemic patients.

FP509 PARATHYROID HORMONE INDUCES ENDOTHELIAL-TO-MESENCHYMAL TRANSITION IN HUMAN AORTIC ENDOTHELIAL CELLS

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Introduction and Aims: Secondary hyperparathyroidism is a common complication of chronic renal failure, which is closely correlated with the development of cardiovascular morbidity and mortality in uremia. However, the potential mechanism has yet to be clarified. Recent studies have demonstrated that endothelial dysfunction mediated by endothelial-to-mesenchymal transition (EndMT) plays a significant role in cardiovascular injury. Thus, the purpose of this study was to investigate the effects of PTH on the endothelial-to-mesenchymal transition (EndMT) in human aortic endothelial cells.
Methods: Primary human aortic endothelial cells (HAECs) were treated with PTH 1-34 (10-9 to 10-7 mol/L). Pathological changes were examined by fluorescence microscopy for co-expression of endothelial cell marker (CD31) and fibroblast markers, such as fibroblast-specific protein 1 (FSP1) and a-smooth muscle actin

(SMA). The expressions of CD31, FSP1 and a-SMA were detected by real-time PCR and western blot. Ultra structural changes of cells were observed by electron microscope.
Results: Quantitative real-time PCR analysis revealed that exposure of HAECs to PTH 1-34 at concentrations of 10-9, 10-8 or 10-7 mol/L increased the mRNA levels of FSP1 and a-SMA in dose-dependent manners (P<0.05), which was consistent with the changes of FSP1 and a- SMA expression detected by Western blot. In contrast, the expression of CD31 was decreased in mRNA and protein levels after incubation with PTH 1-34, which were also in dose dependent manners (P<0.05). Moreover, double staining of the HAECs treated with PTH 1-34 at 10-7mol/L indicated a co-localization of CD31 and FSP1, and a loss of CD31 staining. Meanwhile, morphology analysis showed some cells acquired spindle-shaped morphologies after PTH 1-34 incubation. Compared with control group, endothelial cells with PTH 1-34 treatment exhibited a more dilated endoplasmic reticulum and vacuolization in mitochondrion in transmission electron microscope analysis.
Conclusions: These results demonstrated a novel insight that PTH might directly mediate vascular disease through induce the endothelial-mesenchymal transition.

FP510 ALFACALCIDOL AND PARICALCITOL HAVE SIMILAR EFFECTS ON LEFT VENTRICULAR HYPERTROPHY

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Introduction and Aims: Left ventricular hypertrophy (LVH) is high prevalent in chronic hemodialysis patients (pts) and is associated with increased cardiovascular morbidity and mortality. Recent studies showed a slowing in LVH progression with vitamin D receptor activators (VDRA). Aim of the study was to compare the impact of two different VDRA on LVH in hemodialysis pts.
Methods: Forty (40) chronic HD pts (M/F: 24/16, mean age: 61,6±9,8 years, mean HD-duration: 71,9±66,7 months) were enrolled in our study. Exclusion criteria were pts < 18 years, severe coronary artery disease and valvulopathy. During the study time of 16 weeks blood pressure, haemoglobin levels and dry weight remained stable. After a washout period of 8 weeks, the mean iPTH level was 604,40±99,41 pg/ml, pts were randomly divided in two groups. Group A consisted of 20 pts (mean iPTH 594,77±102,43 pg/ml) received i.v. alfacalcidol at each HDsession. Group B (mean iPTH 614,03±97,08 pg/ml) received Paricalcitol. Doses of both VDRA were given according the K/DOQI guidelines. No statistically differences regarding the iPTH levels were between the two groups. Pts underwent an echocardiography examination at baseline and after 16 weeks in accordance with the American Society of Echocardiography. LVMI was calculated by Devereux's formula considering in men>125g/m2 and in female >110g/m2 as LVH. Serum calcium, phosphorus and iPTH were continuously measured during the study.
Results: After 16 weeks of therapy the iPTH levels decreased significantly in the two groups. In group A(alfacalcidol) from 594,77±102,43 41 pg/ml to 235,07±60,48 pg/ml, ?iPTH:60,4%, in group B(Paricalcitol) 614,03±97,0841 pg/ml to 207,23±35,53 pg/ml, ?iPTH:66,1%,p<0.001 respectively. After the echocardiography examination all pts had increased LVMI 263,15±36,02 g/m2. In detail in group A the LVMI was 259,38±43,68 g/m2 and decreased after alfacalcidol therapy to 240,26±35,82 g/m2,? LVMI:7,2%. In group B the LVMI decreed after Paricalcitol from 266,92±35,51 to238,47±39,21 g/m2, ?LVMI:10.3%. The changes of LVMI in both groups were statistically no significant. No correlation was found between the iPTH levels and the LVMI. No significant changes were observed in the calcium and phosphate levels.
Conclusions: Paricalcitol and alfacalcidol showed the same tendency to regress left ventricular hypertrophy in chronic hemodialysis patients.

FP511 THE RELATIONSHIP BETWEEN TNF-RELATED APOPTOSIS INDUCING LIGAND CONCENTRATION AND INFLAMMATORY MARKERS.

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Introduction and Aims: TRAIL (TNF-related apoptosis-inducing ligand) is a member of TNF superfamily. Recent studies have provided a new function of TRAIL on vascular cells, such that TRAIL can promote endothelial cell (EC) and VSMCs migration and proliferation and it has been detected in normal and diseased atherosclerotic tissue. Its expression levels are higher in vulnerable plaques than in stable one. Chronic kidney disease is associated with accelerated atherosclerosis and exacerbated but ineffective inflammatory response.Aim of the study was to investigate the relationship between soluble TRAIL (sTRAIL) and selected markers of inflammation in patients on maintenance hemodialysis.

FP511 Table 1.

sTRAIL			
Parameter	r (Pearson's)	r^2	p
hs CRP	-0.1431	0.0205	<0.2177
IL-6	-0.2752	0.0757	<0.0483
IL-8	-0.3046	0.0928	<0.0155

Methods: Studied group: 76 patients (36 female and 40 male) of average age 60±12 years on maintenance hemodialysis (25±5 months). sTRAIL, IL-6, and IL-8 were determined by ELISA and hsCRP using immune-nephelometry methods.
Results: The mean values of sTRAIL was 959.6±204.0 pg/mL, hsCRP 11.5±18.8 mg/L, IL-6: 6.4±8.7 pg/mL and IL-8: 20.0±15.7 pg/mL. The obtained correlations between sTRAIL and tested parameters were given in table 1.

FP512 BENEFITS OF AN ENDURANCE TRAINING PROGRAM IN PATIENTS ON HEMODIALYSIS: A CASE-CONTROL STUDY

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Introduction and Aims: Patients on hemodialysis (HD) have a decreased physical and functional capacity. Prevention of dependency takes a greater reliance in these patients in order to avoid deterioration in quality of life.There is growing evidence about the safety and benefits of exercise training for patients on HD.Despite these results, exercise programs on hemodialysis are not comonplace. The purpose of this study was to analize the effect of an intradialysis endurance exercise training program on muscular strenght and functional capacity in our HD patients.
Methods: A 6 months single-center prospective study.HD patients were non-randomly assigned into an excercise training (ET) or control group (C). ET included a complet resistance physical fitness using balls, weights and elastic bands in the first two hours of every HD session. C receieved standard HD care. All subjects were evaluated at baseline and at the end of the study using the following data:1.- Biochemical parameters. 2.-Anthropometric data: Basic measurements and biceps and quadriceps muscle tone. Maximum length quadriceps strength (MLQS) and "hand- grip (HG) dominant arm.3.- Functional capacity tests:"Sit to stand to sit" (STS10) and "six- minutes walking test" (6MWT).
Results: 63 HD patients.23 patients exluded (21% high comorbidities).40 patients included data: 55% men.Mean age 68.4 years and 61.6 months on HD. The main etiologies of ESRD were the HBP (28%) and DM (23%). 16 patients were assigned to ET and 24 on C group.There were no differences beetwen groups at baseline characteristics. At the end of the study, 6MWT significally improves in ET group (20%, 293.1 vs 368 m,p<0.001) and lowered in CO group (10%, 350 vs 315 m, p<0.004).In ET, remaining functional test showed a whole improvement (MLQS 15.6 ±10.7 vs 17.7±12.5 kg, HG 22.1±13.2 vs 24.1±15.8 kg, STS10 32.1±18.5 vs 28.7±20.6 sec) at the end of the study, while in C group a global decrease was reported (MLQS 20.9±9.3 vs 16.2±8.4 kg, HG 25.1±10.3 vs 24.1±11.1 kg, STS10 31.5±17.9 vs 36.4 ±19.8 sec), though significant differences were not found. Biochemical parameters and anthropometric data did not change at the end of the study.
Conclusions: 1.-An intradialysis endurance exercise training program improved muscular strenght and functional capacity in our HD patients.2.- These results supports the benefits of exercise training for HD patients.3.- Neprhologist should consider exercise training as a standard practice of the HD patients care.

FP513 SEASONAL AND WEEKLY VARIABILITY OF HOME BLOOD PRESSURE EVALUATED WITH TELEMEDECINE SYSTEM USING CELLULAR PHONE IN HEMODIALYSIS PATIENTS.

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Introduction and Aims: In general population, there are weekly and seasonal variability of blood pressure (BP) which is supposed to be the risk of cardiovascular disease. Home BP is well correlated to the cardiovascular risk compared to office BP. But sometime we can not get precise home BP data because of patient's bias. We already developed a telemedicine system using a cellular phone to monitor precise home BP without patient's bias (J of Hypertension. 25: 2352-2358, 2007). The aims of this study are to determine whether home BP in hemodialysis patients make weekly variability and whether home BP and plasma catecholamine make seasonal variations, collecting BP data via our telemedicine system

Methods: Twelve patients (6 male, 6 female) hemodialyzed in our hospital were recruited. All patients were asked to measure their BP at least twice a day in a sitting position, once in the morning after urination before breakfast and medication and once in the evening just before going to bed. Data from Nov. 2006 to Aug. 2010 were analyzed. If the dialysis were performed 3 times a week (Mon, Wed, Fri), Monday was defined as 1st day. If the dialysis were performed on Tue. Thurs. and Sat., Tuesday was defined as 1st day. Plasma samples for measurement of catecholamine were collected before dialysis in each season.
Results: Weekly home BP variability in the morning, 1st day 162±18 / 77±11 mmHg, 2nd day 147±18 / 73±10, 3rd day 156±17 / 76±10, 4th day 146±19 / 73±9, 5th day 155±18 / 76±11, 6th day 148±18 / 74±10, 7th day 155±17 / 76±10. Systolic home BPs in 1st, 3rd and 5th days were significantly elevated compared with 2nd, 4th and 6th days. Morning home BP significantly elevated gradually from 6th, 7th and to 1st day. Seasonal changes in home BP in the morning, spring 149±15 / 73±11 mmHg, summer 147±18 / 73±11, autumn 155±22 / 78±11, winter 158±19 / 76±12. Systolic BP in winter was significantly elevated compared to spring and summer. The noradrenalin concentrations are as follows; spring 358±152 pg/mL, summer 345±242, autumn 600±487, and winter 539±231. The noradrenalin concentration in winter was significantly higher than those in spring and summer.
Conclusions: In home BP evaluated by our telemedicine system of hemodialysis patients, there are weekly variability probably due to volume status and seasonal variability along with sympathetic nerve activity.

FP514 PULMONARY CONGESTION AND PHYSICAL FUNCTIONING IN CKD-5 HD PATIENTS

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Introduction and Aims: Decline in physical function is commonly observed in patients with kidney failure on dialysis (CKD-5D). Whether lung congestion, a predictable consequence of cardiomyopathy and fluid overload, may contribute to the low physical functioning of CKD-5D patients has not been investigated.
Methods: In 288 hemodialysis patients (HD) we investigated the cross-sectional association between the physical functioning scale of the KDQOL-SF-™ and an ultrasonographic (US) measure of lung water recently validated in dialysis patients. The relationship between physical functioning and lung water was also analyzed taking into account the level of dyspnoea as measured by the New York Heart Association (NYHA) classification currently applied to grade the severity of heart failure.
Results: Pre-dialysis US evidence of moderate to severe lung congestion was observed in 166 (58%) patients. On univariate analysis physical functioning was significantly and inversely associated with lung water in the entire group of 288 patients (r=-0.19 P<0.001), as well as in the sub-group of 66 asymptomatic (i.e NYHA class I) patients (r=-0.18 P=0.002). Age (r =- 0.40 P<0.001) and previous cardiovascular events (r=-0.22 P=0.002) were also inversely associated to physical functioning, while serum albumin(r=0.24 P<0.001) was directly associated with the same parameter. NYHA class correlated strongly and inversely with physical functioning (r=-0.46 p<0.001). In multiple regression analysis adjusted for all the univariate predictors, both NYHA class and lung water maintained their independent association with physical functioning.
Conclusions: Symptomatic and asymptomatic lung congestion is a relevant factor in the poor physical functioning of patients on HD. The association of pulmonary congestion with physical functioning is independent of NYHA suggesting that this measurement may have prognostic value complementary to that of NYHA categorization in dialysis patients.

FP515 INCIDENCE AND MORTALITY RISK FACTORS ASSOCIATED WITH NON-OCCLUSIVE MESENTERIC ISCHAEMIA IN PATIENTS UNDERGOING HEMODIALYSIS

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Introduction and Aims: Non-occlusive mesenteric ischaemia (NOMI) is an emergent pathology in haemodialysis (HD) patients. Although it is associated with a poor outcome, it has not been studied enough. The aim of this study was to analyze the incidence, characteristics, risk factors and prognosis of NOMI in HD patients.
Methods: A retrospective study was conducted between 2003 and 2011 in HD patients. During follow- up time, all cases were registered, and demographic, clinical, biochemical and HD parameters were collected. Then, analysis was performed between this group and a control one (n=100). Risk factors associated with the NOMI development and prognosis were studied and survival curves were established between both groups.
Results: There were fifty-seven episodes of NOMI in 44 patients (mean age 72.9±8.9 years; 56% male). Thirty percent were diabetic. The incidence of NOMI was 2.29 episodes/100- patients/year. Cardiovascular risk factors were present in 72% of the patients. The patients with NOMI had leukocytosis (16945±4672/μL), mild acidosis (bicarbonate 22.6±4.3 mEq/L), even though the episodes were posthaemodialysis, and serum lactate (2.6±1.8 mg/dL), LDH (441±649 UI/L) and CPR (21.4±15.5 mg/dL) increase. The caecum was the most frequently (42%) affected segment, followed by diffuse bowel involvement. Nineteen patients (33%) were surgically treated. Twenty six patients (59%) did not survive the acute episode of NOMI. Caecum damage was the only protective factor related with mortality in the univariate and multivariate analysis (RR 0.16; p=0.009). The incidence of NOMI was related to age (RR 1,11; p<0,001), diabetes mellitus (RR 2,61; p=0,037) and duration of dialysis (RR 1,01; p=0,006), when compared with the control group. Those patients who survived the acute episode (41%) were compared with the control group (47%), showing a higher mortality at 5- year follow-up (Log Rank 26.48; p<0.001).
Conclusions: NOMI is associated with age, diabetes mellitus and long time undergoing haemodialysis. Caecum damage is the most frequent location, but is related with better prognosis. Mortality is very high both in the acute episode and long-term.

FP516 COGNITIVE DYSFUNCTION AND WHITE MATTER LESIONS IN MAINTENANCE HAEMODIALYSIS PATIENTS

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Introduction and Aims: White matter lesions (WML), a form of small-vessel cerebrovascular disease, and cognitive dysfunction (CD) are common in dialysis patients. Given the proposed role of microvascular disease on cognitive function, we hypothesized that prevalent WML would be associated with CD in maintenance haemodialysis (HD) patients. No studies have explored the relationship between WML and CD in these patients.
Methods: We studied 67 maintenance HD patients, aged 40-65 years, without known cerebrovascular disease. Cognitive function was assessed using a battery of validated cognitive test, measuring several cognitive domains (attention and processing speed, executive function, language, memory). CD was defined as performance = 1.5 standard desviations less than normative values on 1 or more cognitive domains. Subjects were classified as having no, mild, moderate or severe CD. All patients underwent brain magnetic resonance imaging and subcortical and periventricular WML were evaluated by using semiquantitative measures. Patients were classified into 2 groups depending on the presence or absence of WML. Carotid ultrasonography was also performed to evaluate the presence of carotid plaques and stenosis.
Results: Mean age of patients were 54 years; 10 (15%) were diabetic, 15 (22.5%) had cardiovascular disease, and median dialysis therapy was 78 months. WML were present in 54% of patients (more frequently subcortical), and global CD in 82% of patients (36% mild-moderate and 46% had severe CD). Factors associated with global CD were age, educational level, C- reactive protein, lower predialysis and postdialysis diastolic blood pressure, and presence of carotid plaques. Severe CD was related to the presence of WML (p=0.036). Evaluating individual cognitive test performance, WML patients had worse scores on the cognitive test results than patients without WML. Multivariate regression analysis showed educational level (OR 39.7, IC 95% [1.8-872]) and presence of carotid plaques(OR 14.36, IC 95% [1.5-135]), to be independently associated with CD.
Conclusions: CD and WML are common in maintenance HD patients. WML may contribute to severe CD. The presence of WML is also associated with worse cognitive performance on several cognitive domains. Our data support the hypothesis that WML are related to CD in this population.

FP517 UREMIC FOOT: THE EMERGENT ROLE OF VITAMIN K-ANTAGONISTS

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Introduction and Aims: Foot ulceration (FU) and lower limb amputation, that we also define "uremic foot syndrome", is a common complication affecting Hemodialyzed patients (HDpts). Its prevalence is 4 times higher in HDpts than in diabetic non HDpts, because it is due to the inflammation and vascular calcifications in addition to diabetes. New insights in vascular calcifications recognize the role of vitamin K (Vit-K) to activate Matrix-Gla protein, a potent calcification inhibitor. In vitro and in vivo studies reveal a diffuse metastatic calcification during Vit-K

deficiency and pts assuming Vit-K Antagonists (Vit-K Ant) present excessive calcification in coronary arteries and aortic valve. HDpts are at higher risk for Vit-K deficiency and for Vit-K Ant therapy, because of cardiovascular and systemic diseases. The aim of our study is to evaluate the correlation between the Vit-K Ant therapy and the uremic foot among HDpts attending our Centre.
Methods: 313 prevalent and incident HDpts from January 2005 to March 2011, mean follow-up 34±24 months; age 67.2±14.9 years, 240 (65.2%) male, 102 (32.6%) diabetic, 134 (42.8%) with ischemic heart disease. Previous surgical revascularization or percutaneous transluminal angioplasty (PTA), smoldering peripheral artery disease (sPAD) (intermittens claudicatio, non critical ischemia at the Doppler ultrasonography), ischemic chronic FU and lower limb amputation were considered.
Results: The prevalence of sPAD is 53% (166 pts), FU 32.3% (101 pts), amputation 9.3% (29 pts), previous surgical revascularization 8% (25 pts) and PTA 11.8% (37pts). At the end of the follow up 144 (45.7%) pts died, 22.4% for ischemic heart disease, 16.4% for complications of PAD, 16.1% for not otherwise specified cachessia, 14.2% for neoplasiae, 6.2% for infections and 3.8% for others.73 pts assume Vit-K Ant, 36 (49.3%) for cardiac causes (arrhythmia or valve disease), 18 (24.6%) for permanent venous central catheter permeability, 13 (17.8%) for previous venous tromboembolism, and 6 (8.2%) for systemic diseases.HDpts assuming Vit-K Ant are older (70.7±10.5 vs. 66.4±15.3 years, p=0.012), and show more ischemic heart disease (58.9 vs. 37.9%), surgical revascularization (16.4 vs. 5.4%), FU (60.3 vs. 23.7%) and amputation (15 vs. 7.5%) (p<0.001). The prevalence of diabetes (35.6 vs. 31.6%) and the PTH values (270±170 vs. 217±153 pg/ml) are not different. They have also less chance to undergo kidney transplantation (1.4 vs. 16.3%) and higher risk of death (60.3 vs. 42.2%) (p<0.0001).
Conclusions: Our study demonstrate that the "uremic foot" is a common complication among HDpts, associated with higher mortality, morbidity and direct and indirect costs. The Vit-K Ant may be a potent additional risk factor for uremic foot. Additional studies are need to evaluate the role of Vit-K Ant in peripheral vascular calcifications and other anticoagulation drugs may be considered for pts with end stage renal disease.

FP518 VITAMIN E-COATED POLYSULFONE MEMBRANE IMPROVED RED BLOOD CELL ANTIOXIDANT STATUS : A PROSPECTIVE MULTICENTER STUDY

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Introduction and Aims: Prevention of oxidative stress linked to bio-incompatibility-induced inflammation might be completed by anti-oxidant supplementation and can be achieved either by oral or intravenous supplementation (vitamin E, vitamin C, selenium) or by vitamin E-coated based dialyzers. The aim of this prospective multicenter study was to evaluate the short term effects of a vitamin E coated membrane with polysulfone (PS) structure (ViE®) on biocompatibility (inflammation and oxidative stress) performances and anemia in hemodialysis (HD) patients.
Methods: 43 end stage renal disease patients (23 men /20 women, median age = 65 [31-82] years) undergoing maintenance HD in five French dialysis facilities were included in this study. After a 3 months wash-out period with a high flux synthetic dialyzer, all patients were switched, the day of inclusion, to vit E PS dialyzer. Sampling were performed at baseline (month 0, corresponding to the end of the wash out period) and then after 1, 2 and 3 months of treatment. We used the Wilcoxon signed rank test to compare two dependent measures and the Friedman test for three or more dependent measures. We also used a linear mixed model to analyze the 3-month change on EPO resistance index (ERI). The model included time and center as an adjusted variable.
Results: Use of vitamin E coated membrane for 3 months was not associated to any change in inflammatory parameters (CRP p=0.77, IL-6 p=0.13), MDA, LDL oxidizability, plasma vit E, plasma vit C, plasma GSH-Px activity and myeloperoxydase. By contrast, Vitamin E-coated polysulfone dialyzer resulted in a progressive increase in red blood cell (RBC) vitamin E concentration (from 0.58 to 0.92 µg/mL) which is closed to normal values by the second month and in RBC superoxide dismutase activity (from 1.06 to 1.13 U/mgHb) by the third month. Also, a concomitant progressive significant decrease in AOPP concentration at 2 months was observed (from 40.3 to 37.7 µM), suggesting an associated diminution in oxidative stress. Finally, performing multivariate-adjusted random-effect model, a significant decrease of ERI over the time was found (p=0.01).
Conclusions: This prospective study showed that use of the new vit E-PS dialyzer increases the erythrocyte anti-oxidative defence and significantly decreases the erythropoietin resistance index. Beneficial effects of this dialyzer obtained with Vit PS are all the more encouraging for HD patients by its potential ability to reduce EPO dose.

FP519 P WAVE DURATION, ATRIAL DIMENSION AND ATRIAL FIBRILLATION IN HEMODIALYSIS PATIENTS.

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Introduction and Aims: Atrial fibrillation (AF) is a frequent complication of hemodialysis (HD) sessions and it is highly prevalent in chronic HD population. Structural and electrical atrial remodelling , in particular intra-atrial conduction velocity slowing, play an important role in AF onset. High resolution P wave recording is a recognised method to asses intra-atrial conduction velocity, but few clinical studies have investigated the relation between P wave duration and AF onset in HD patients. Aim of our study was to measure P wave duration, in different groups of HD patients with and without history of AF.
Methods: Forty-one patients were enrolled. In a first group 18 patients were studied within the first six months from starting HD therapy (HD1) and 18+3 months later (group HD2). Two other groups were performed including patients with no history of AF and long dialytic age (HD3, n=11) and patients with normal sinus rhythm, but history of paroxysmal or persistent AF (HDAF, n=12). In all patient P wave high resolution registrations and plasma values of Na+, K+, Ca++ e HCO3- were obtained before and after a middle-week HD session and an echocardiogram was performed to measure antero-posterior atrial diameter.
Results: Patients of group HD3 were older than HD1 (71+13 vs 59+16 years, p<0.05) and HD2 (60+16 years, p<0.05), but had similar age of HDAF group (69+7 years). Dialytic age was greater in group HD3 in comparison with all other groups [135.1 +67.8 vs 4.3+1.8 (HD1), 22.2+3.3 (HD2), 72.9+45.5 (HDAF) months, p<0.01], and in HDAF group in comparison to groups HD1 e HD2 (p<0.01). P wave duration pre-HD was prolonged in HDAF group in comparison to all other groups [153 +17vs132+10 (HD1),141+12(HD2),142+8 (HD3) msec; p<0.05]. P wave was shorter in group HD1 as compared to all other groups (p<0.05). The HD session induced a significant increase of P wave duration in all patients (p<0.001), which was inversely correlated to modifications of plasma K+ concentration (R=0.74, p<0.001). In HD1 group atrial diameter was smaller than in HD3 ((41+3 vs 44+3 mm, p<0.05) and HDAF (46+6 mm, <0.05) groups , while it was not different between HD1 and HD2 (42,3+3 mm) groups. Both pre and post HD P wave duration correlate significantly to left atrial dimensions (R=0.36 e 0.41, respectively, p<0.05).
Conclusions: The high incidence of AF onset HD session related may be partially explained by the observed intra-dialytic decrease in atrial conduction velocity, which correlates with intra- dialytic changes in plasma potassium concentration. After 18 months of HD therapy intra- atrial conduction velocity was reduced in spite of any atrial diameter modifications. Atrial diameters were not different in patients with long dialytic age without or with previous AF episodes (HD3 and HDAF group, respectively), while P wave duration was greater in HDAF. These findings suggest that high prevalence of AF in HD population is more correlated to intra-atrial conduction (P wave) duration than atrial dimension increase.

FP520 ROLE OF PRE-TRANSPLANT ECHOCARDIOGRAPHY IN PREDICTING OUTCOME IN PATIENTS WAITING FOR KIDNEY TRANSPLANTATION

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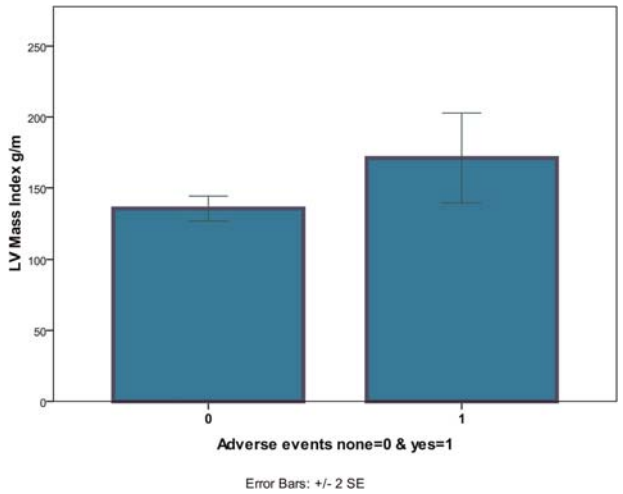
Introduction and Aims: Patients on kidney transplantation wait list suffer from significant morbidity and mortality. A significant proportion of these patients undergo echocardiographic examination to establish suitability for transplantation. However the role of echocardiography for pre-transplant work up in predicting cardiovascular events is not clear. This study aimed to investigate the role of pre-transplant echocardiogram in predicting adverse outcomes including cardiovascular events and death.
Methods: Data were collected retrospectively in 126 patients from the kidney transplant waitlist from the St George's and Guy's Hospitals in London. The study excluded patients with significant heart valve disease and heart failure. The mean age of the population was 54±11 years with 60% [76/126] males. Majority of the patients 89% [112/126] were hypertensive while 21% [26/126] suffered from diabetes. Smoking history was unknown in a 45 patients. The left ventricular mass was calculated using the Penn Formula, and indexed for height. Patients were followed from the day of work up echocardiogram till transplantation, death or mid- 2010. Data were analysed using IBM SPSS 19 comparing continuous variables with t test and categorical variables chi square test.

Results: At baseline the mean left ventricular mass index [LVMI] was 139±35 g/m, and left atrial diameter was 3.9±0.6 cm. Eleven patients suffered from adverse events; 2 patients died, 4 patients had coronary events, 3 had cerebrovascular events and 2 suffered from peripheral vascular events. Patients who suffered from adverse events had significantly higher LVMI compared to patients without adverse events [171±52 vs. 135±43 g/m; p=0.013]; see figure 1. The left atrial diameter was also higher in patients with adverse events compared to patients without [4.3±0.8 vs. 3.8±0.5 cm; p=0.012]. The patients with adverse events were older [61±9 vs. 53±11; p=0.02] and more often suffered from diabetes [6/10 vs. 20/116; p=0.005].
Conclusions: The results demonstrate that left ventricular thickening and dilatation of the left atrium are indicators of poor prognosis in patients on kidney transplantation waiting list and thereby suggest that pre-transplant echocardiography may be more useful than just for the assessment for suitability for transplantation.



FP520 Figure 1: The difference of LV Mass index between patients without and with adverse events

FP521 CHANGES IN RELAXIN'S SERUM LEVELS DURING ACETATE-FREE BIOFILTRATION: WHAT MEANINGS?

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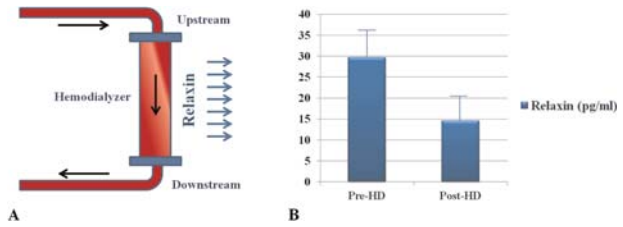
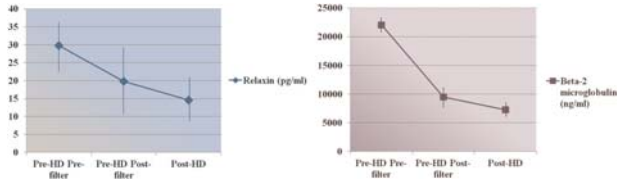
Introduction and Aims: Relaxin is a 6 kDa-peptidic-hormone made up of 53 aminoacids and characterized by two separate polypeptide chains (A-B) cross-linked by three disulfide bonds. It is best known for its physiological role in the renal and systemic haemodynamic changes which occur during pregnancy. Many data show that this factor can also be involved in the pathophysiology of arterial hypertension and heart failure, in the molecular pathways underlying fibrosis and cancer, in angiogenesis and bone remodeling. In particular, relaxin induces vasodilatation and its circulating levels are significantly lower in patients with arterial hypertension; moreover, it exerts a protective effect on cardiovascular system and its administration seems to be effective in patients with heart failure. The aim of the present study has been to evaluate the relaxin behavior during hemodialysis (HD) session and the potential effects of its intradialytic variability.
Methods: We enrolled a cohort of 28 patients (13 women, 15 men; mean age, 62.7 ± 14 years; dialysis vintage in months, 36 [10-284]; residual GFR 2.3 ± 0.6 ml/min) receiving dialytic treatment in 3-hour sessions, three times a week, employing the AFB technique. Blood samples were obtained from upstream of the hemodialyzer (Nephral® ST 400) at the beginning and at the end of the HD session, and from downstream of the dialyzer at the beginning. The samples were stored at -80 °C until assay. Relaxin's levels were assessed employing the commercial available Human Relaxin-2 Immunoassay kit (Quantikine®, R&D Systems, Inc.). All values were normalized to volume; to do this, we measured hematocrit employing a micro-hematocrit centrifuge. The statistical analysis was performed using MedCalc software (ver. 8.0; MedCalc Software, Mariakerke, Belgium). P<0.05 was considered significant.
Results: During HD session, relaxin is removed from blood in the passage through the filter. Its serum levels has shown to change significantly between the start and the end of the treatment (from 29.73 ± 6.63 to 14.57 ± 5.99 pg/ml, p<0.0001) (Fig. 1). In particular, relaxin shows the same trend of beta2-microglobulin (Fig. 2), the most extensively studied low molecular weight protein in end-stage renal disease, regarded as uremic toxin especially because of its association with ongoing inflammation and adverse cardiovascular outcomes in HD patients.
Conclusions: The drop we observed in relaxin's serum concentrations during HD session could play a key role in the pathogenesis of some cardiovascular complications which may occur in HD patients. Although these preliminary data require further studies, they allow us to hypothesize that relaxin could take part in the physiological adaptations of vascular tone to volume removal in relation to patients' plasma refilling ability. Similarly, abnormalities in its serum levels may affect the vascular response to the hemodynamics changes induced by HD, and then play a pathogenetic role in some intradialytic complications, such as hypo- or hypertensive episodes, especially in subjects with underlying cardiovascular disease.



FP521 Figure 1: A) Schematic representation of relaxin's behavior during blood's passage in the hemodialyzer. B) Relaxin's serum levels decrease significantly between the start (Pre-HD) and the end (Post-HD) of HD session (from 29.73 ± 6.63 to 14.57 ± 5.99 pg/ml, $p<0.0001$).



FP521 Figure 2: Relaxin shows the same trend of beta-2 microglobulin during HD session.

FP522 RISK OF SUDDEN CARDIAC DEATH IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Sudden cardiac death (SCD) is the leading cause of death among chronic hemodialysis patients (CKD). The aim of our study was to determine in which degree the dialysis is implicated in arrhythmias development in CKD.
Methods: Continuous 24-hour Holter monitoring were carried out in 37 CKD and in a control group (C) composed by 32 patients with cardiovascular morbidity but without renal failure. We studied atrial and ventricular arrhythmia in several times: the dialysis session (HD), 4-hour post dialysis period (early-HD) and the next 16 hours (late-HD). Temporal parameter (Standard Deviation of the NN intervals SDNN) of heart rate variability was calculated from these recordings.
Results: The included patients had cardiovascular morbidity (HTA in 91,9 of CKD vs 100% of C, p = 0,15; left ventricular hypertrophy in 73 vs 68.8%, p = 0,4; diabetes in 37,8 vs 18,8%, p = 0,07, hypercholesterolemia in 67,6 vs 75%, p = 0,3). Ectopic atrial premature contractions were uniformly distributed in the different periods of the Holter (p = 0,01, Spearman correlation). 13.5% of CKD (which 40% only during the HD, 20% during the HD and the late-HD, 20% during the early and the late-HD and 20% only during the late-HD) and 3.12% of C displayed atrial fibrillation (AF) (p = 0.2). Ventricular premature contractions (VPC) were frequent (81% in CKD *vs* 77% in C, p = 0,48). Ventricular tachycardia was observed in 5% of CKD (which 100% in the HD) vs 6% of C, p = 0,64. Only CKD developed torsade de pointes (3% of CKD during the late-HD period). Polymorphic VPC were described in 32% of CKD and 3% of C, p = 0,002. These polymorphic VPC were equally distributed in each period of the Holter (p = 0,01, Spearman correlation). A fallen SDNN less than 80 msec was found in 54% of CKD vs 26% of C, p= 0,036). There was not correlation between AF (p = 0,64), ventricular arrhythmia (p = 0,40) and low SDNN in our study.
Conclusions: CKD developed as many atrial and ventricular arrhythmia as high cardiovascular comorbidity C except for torsade de pointes and polymorphic VPC. This difference would be explained by uremic myocardial fibrosis. Dialysis could provoke arrhythmia because of fast hydro electrolyte shifts. Cardiac autonomic functions were significantly altered in CKD, which is related with an increased risk of sudden death.

FP523 AUTONOMIC NERVOUS DYSFUNCTION AND INFLAMMATION IN HAEMODIALYSIS PATIENTS

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Introduction and Aims: Alterations in autonomic nervous function are common in haemodialysis patients. Several studies showed sympathetic overactivation while the functional status of parasympathetic activation is less clear. Sympathetic as well as parasympathetic activation may influence immunocompetent cells and contribute to the regulation of inflammatory responses. Since chronic inflammation is found in the majority of dialysis patients, we intended to confirm a role of the autonomous dysregulation for inflammation in these individuals.
Methods: Thirty chronic haemodialysis patients (among them 15 with diabetes mellitus) and 15 healthy individuals were studied for heart rate variability using Fourier analysis of 5 min ECG recordings (technically best segment out of 20 min) according to the protocol of the CARLA study. Patients with atrial fibrillation or a cardiac pacemaker could not be enrolled. Heart rate variability was estimated using the standard deviation of the R-R distance (SDNN) and the percentage of pairs of adjacent RR intervals differing by more than 50 ms (pNN50). Sympathetic and parasympathetic activity was estimated using derived parameters from the ECG analysis (high- and low-frequency variation of RR distances, HF and LF). Inflammation was detected as serum CRP, IL-6 concentrations as well as circulating monocyte CD14/CD16 subpopulation numbers. Immunocompetent cells were characterized by their expression of the nicotinic acetylcholine receptor.
Results: The study enrolled rather old (66.8 ± 9.4 years) patients who were on dialysis for 4.9 ± 3.1 years (range, 1-11 years). Patients differed from healthy control individuals in terms of age (controls, 54.5 ± 7.4 years, $p<0.05$ vs. patients) and heart rate variability (SDNN, controls 40.7 ± 20.2 ms, patients 23.4 ± 24.7 ms; $p<0.01$ by Kruskal-Wallis-test). This finding was not restricted to patients with diabetes mellitus although diabetes is an important cause of autonomous dysfunction (SDNN, diabetics 20.9 ± 19.6 ms, non-diabetics 25.7 ± 29.2 ms). The low frequency (LF) and high frequency (HF) variations of RR distance were reduced to 1/3 of those found in healthy individuals. These parameters are thought to reflect the parasympathetic (HF) branch of autonomous regulation and the relative intensity of parasympathetic to sympathetic activity (LF/HF ratio). Since LF and HF variations were reduced by the same magnitude, the LF/HF ratio did not differ from healthy controls. Patients suffered from chronic inflammation (CRP, patients 11.2 ± 11.5 mg/l, controls 1.8± 1.3 mg/l, $p<0.01$) and expanded proinflammatory monocyte subpopulations (CD14/CD16 positive cells, patients 47 ± 25 /µl, controls 28 ± 19 /µl, $p<0.01$). Parameters of ECG analysis did not correlate with inflammatory markers. Nevertheless, monocyte acetylcholine receptor expression was enhanced in patients indicating potentially elevated responsiveness of this cell type to parasympathetic regulation.
Conclusions: Long-term haemodialysis patients have strongly impaired heart rate variability. Assessment of frequency domain parameters from ECG analysis did not confirm the expectation of an autonomic dysbalance biased to the sympathetic branch. Chronic inflammation is not directly related to autonomous dysfunction, although monocytes express the acetylcholine receptor at enhanced density making them potentially more sensitive to parasympathetic effects.

FP524 HEPCIDIN-25 IS RELATED TO CARDIOVASCULAR EVENTS IN CHRONIC HEMODIALYSIS PATIENTS.

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Introduction and Aims: Hepcidin-25 is a key regulator of iron homeostasis and may be involved in iron accumulation in macrophages in atherosclerotic plaques. In hemodialysis (HD) patients, hepcidin-25 levels are increased. Therefore, it is conceivable that hepcidin is associated with all-cause mortality and/or fatal and non-fatal cardiovascular (CV) events in this patient group. The aim of the current analysis is to investigate the relation between hepcidin-25 and all-cause mortality and fatal and non-fatal CV events in chronic HD patients.
Methods: Data from 405 chronic HD patients included in the CONTRAST study (NCT00205556) were studied (62% men, age 63.7 ± 13.9 [mean ± SD]). The median follow-up was 2.5 (0.1-6.6) years. Hepcidin was measured with mass spectrometry. The relations between hepcidin-25 and all-cause mortality or fatal and non-fatal CV events were investigated with multivariate Cox proportional hazard models, adjusted for determinants of mortality, CV events and hepcidin (i.e. age, sex, race, diabetes, history of CV disease, treatment frequency, prescription of calciumblockers, RAS inhibitors and statins, eGFR, dialyzer type, dialysis spKt/V_{urea}, hemoglobin, albumin, ferritin, hsCRP and soluble transferrin receptor).
Results: Median (interquartile range) hepcidin-25 level was 13.8 (6.6-22.5) nmol/L. During follow-up, 158 (39%) patients died from any cause and 131 (32%) had a CV event (including death from a cardiac event and "sudden death"). Hepcidin-25 was not associated with all cause mortality (HR 0.99 per 10 nmol/L, 95% CI 0.85-1.16; p=0.97). However, it was significantly related to fatal and non-fatal CV events (HR 1.19 per 10 nmol/L, 95% CI 1.02-1.39, p=0.02). Additional adjustment for the dose of erythropoiesis stimulating agents did not change the results.
Conclusions: Hepcidin-25 was significantly associated with fatal and non-fatal CV events after adjustment for various covariates including markers of inflammation and iron stores. These findings may implicate that hepcidin plays a critical role in the pathogenesis of CV disease in chronic HD patients.

FP525 INCIDENCE OF CARDIOVASCULAR DISEASE (CVD) IN CHRONIC KIDNEY DISEASE SUBJECTS (PRE-DIALYSIS): THE ROLE OF PLASMA HIGH SENSITIVITY C-REACTIVE PROTEIN (HS-CRP), HOMOCYSTEINE (HCY), CAROTID INTIMA MEDIA THICKNESS (CIMT) AND LEFT VENTRICULAR HYPERTROPHY (LVH).

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Introduction and Aims: Ischemic heart disease (IHD) and stroke are the two most common causes of death worldwide. CKD is a poorly recognized but important risk factor for CVD. The increased cardiovascular risk begins quite early in renal insufficiency. There are very few studies done in India on the incidence of CVD in pre-dialysis CKD subjects. This study aimed at the role of Hs-CRP, plasma Homocysteine, CIMT and LVH in CKD patients (pre-dialysis) and their correlation with the incidence of CVD.
Methods: This prospective study of 77 patients with pre-dialysis CKD was carried out in Bhabha Atomic Research Centre Hospital from August 2008 to October 2011. The subjects were assessed by taking thorough history, clinical examination and metabolic, haematological parameters, Hs-CRP, Homocysteine, CIMT, LVH. Stress test and/or MIBI scan were subjected to coronary angiography if indicated. Statistical analysis was performed with software SPSS version15.0.
Results: The study included 47 males and 30 females with mean age of 60.80 ± 18.5 years. The most common aetiology of CKD was diabetic nephropathy in 30 subjects (39 %). 62 subjects (80%) subjects had GFR < 60ml/min. 24 subjects (31.16%) were diagnosed to have CVD, 17 subjects (22.1%) using various tests (like TMT, nuclear perfusion imaging and CAG as indicated) and 16 subjects (20.8%) had cardiovascular events (CVE) during the study period. CVE included unstable angina, myocardial infarction, arrhythmia, congestive heart failure, ischemic stroke and haemorrhagic stroke. Positive test results were associated with age, (p: 0.006), Glycosylated Haemoglobin (p: 0.04), Glomerular Filtration Rate (p: 0.047), Proteinuria (p: 0.006), High Sensitivity C-Reactive Protein (p: 0.001), Plasma Homocysteine (p: 0.002), carotid plaque (p: 0.046) and Left Ventricular Hypertrophy (p: 0.04). CVE were associated with age (p:0.006), Glycosylated Haemoglobin (p:0.043), Haemoglobin (p:0.015), Serum Albumin (p:0.036), Glomerular Filtration Rate (p:0.014), Proteinuria (p:0.004), High Sensitivity C-Reactive Protein (p:0.001), Plasma Homocysteine (p:0.023), Carotid Intima Media Thickness (p:0.034) and carotid plaque (p:0.00).
Conclusions: Diabetic nephropathy was associated with increased incidence of CVD. CVD was more commonly associated with GFR = 60 ml/min, Increased levels of Hs-CRP (> 3 mg/dl), and plasma Hcy levels (> 20 meq/dl) were associated with CVD. Other parameters like Hba1c > 6 gm%, hypoalbuminemia (serum albumin < 3.5 mg/dl), aanaemia (Hb < 10 gm %) and overt proteinuria (> 300 mg/24 hrs.) were associated with the CVD. Increased CIMT and presence of plaque were associated with CVD in pre-dialysis CKD patients.

FP526 NONINVASIVE DETECTION OF CORONARY ARTERY STENOSIS WITH MULTIDETECTOR ROW COMPUTED TOMOGRAPHY IN CHRONIC KIDNEY DISEASE PATIENTS AT THE INITIATION OF RENAL REPLACEMENT THERAPY

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Introduction and Aims: Cardiovascular disease accounts for more than 50 % of deaths among patients with chronic kidney disease (CKD). The prevalence of coronary artery stenosis (CAS) at the initiation of renal replacement therapy (RRT) in patients with CKD has not been fully elucidated. A precise diagnose of CAS needs coronary angiography. However, the inconvenience and economic deliberations of the method have strengthened the search for a non-invasive alternative.

Methods: We analyzed 87 consecutive patients (57 male, 30 female; mean age 57.5 ±13.5 years; range 24-80 years) with asymptomatic CKD who underwent multidetector row computed tomography (MDCT) at the initiation of dialysis. We excluded patients with a history of angina and/or acute myocardial infarction. The definition of stenosis in this study was lesions with >50% stenosis by MDCT. Fasting blood samples were collected to examine serum total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, lipoprotein (a), free fatty acid, plasma fibrinogen. The purpose of the present study was to evaluate the prevalence of coronary artery stenosis in asymptomatic stage 5 CKD patients at the initiation of RRT by MDCT and the relationship between findings of MDCT and clinical factors to estimate an efficiency of MDCT for assessing significant stenosis of coronary arteries in asymptomatic stage 5 CKD patients.
Results: Fifty (57.4 %) patients had diabetes, and 80 patients (91.9 %) had hypertension. The causes of end-stage renal disease were diabetes (n = 46), hypertension (n = 22), glomerulonephritis (n = 14), and other/unknown (n = 5). Forty-five patients (51.8 %) were started on HD, and 42 patients (48.2 %) received continuous ambulatory peritoneal dialysis (CAPD). The mean value of coronary artery calcium (CAC) score was 98.5 ± 205.1 in the present study, ranging from 0 to 784.6. Significant coronary artery stenosis was seen in 29 (33.3 %) of 87 asymptomatic CKD patients on MDCT. Of these 29 patients, 18 (62.0 %) had single-vessel disease, five (17.2 %) had two-vessel disease, and six (20.8 %) had triple-vessel disease. The presence of CAS was positively correlated with age (p = 0.002), the presence of diabetes (p = 0.045), CAC score (p = 0.003), free fatty acid (p = 0.045). Several clinical markers, including total cholesterol, LDL cholesterol, HDL cholesterol, and fibrinogen did not show a significant difference between the groups with and without CAS. Multiple regression analysis revealed that CAC score using MDCT were independent risk factors for CAS in asymptomatic CKD patients at the initiation of dialysis.
Conclusions: This study provided that nearly 30% of asymptomatic CKD patients have significant coronary artery stenosis at the initiation of RRT. Also, our results showed that assessment of coronary artery calcium score using MDCT may be predictive for detecting the presence of coronary artery disease in CKD patients at the initiation of RRT.

FP527 IMPAIRMENT IN ENDOTHELIAL PROGENITOR CELLS MOBILIZATION AS A COMPONENT OF MALNUTRITION INFLAMMATION COMPLEX SYNDROME: WHICH ROLE FOR DIALYSIS MODALITIES?

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Introduction and Aims: The number of circulating endothelial progenitor cells (EPCs) is decreased in chronic kidney disease (CKD), such impairment being an independent risk factor for cardiovascular events when patients are on dialysis. In this study, we explored the relationship between EPC number and T cells activation alongside with markers of inflammation and malnutrition in a population of dialysis patients.
Methods: Twenty CKD stage 5D patients were enrolled in this prospective and randomized study in two parallel arms, conventional haemodialysis (HD) versus on line haemodiafiltration (HDF). EPCs number and T cell activation were analysed at baseline and monthly during a four- month period of follow up.
Results: Parameters associated with T cells activation (CD38bright expression) and inflammation (interleukin-6, C reactive protein, and beta2-microglobulin) were frequently elevated in CKD 5D patients whereas parameters related to nutritional status were frequently sited below the normal values (transthyretin, transferrin concentrations and lymphocyte count). CD38bright and HLA-DR+ expression among CD8 memory T cells were negatively associated with both CD34+ (r= -0.70; p=0.0006) and CD34+ CD133+ (r= - 0.62; p=0.004) cell numbers. Conversely, a positive correlation was observed between both CD34+ and CD34+ CD133+ cells with transferrin (r= 0.75; p= 0.0001 and r= 0.47; p=0.04 respectively). The concentration of transthyretin was also positively associated with the number of CD34+ CD133+ EPCs (r= 0.51; p=0.02). No significant association was found between dialysis modality and evolution of the EPCs number.
Conclusions: Chronic T cell activation and malnutrition which are involved in amplification loops seem to adversely influence EPCs number in CKD 5D patients. Attempt to reduce chronic T cell activation and to improve nutritional status of these patients may improve EPCs mobilization.

FP528 CARDIOPROTECTIVE DRUGS PROLONG HEART FAILURE SURVIVAL IN LONG-TERM HEMODIALYSIS PATIENTS

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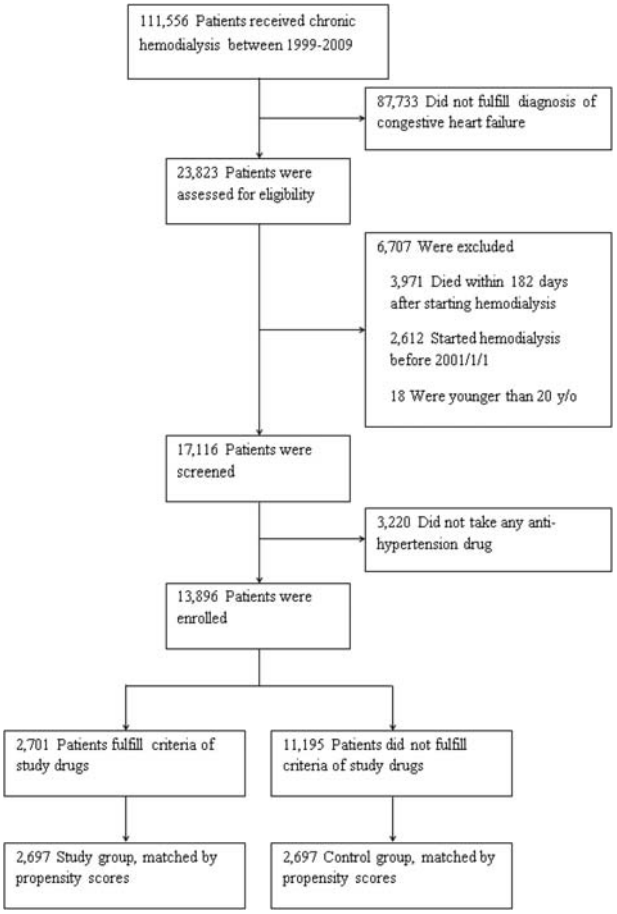
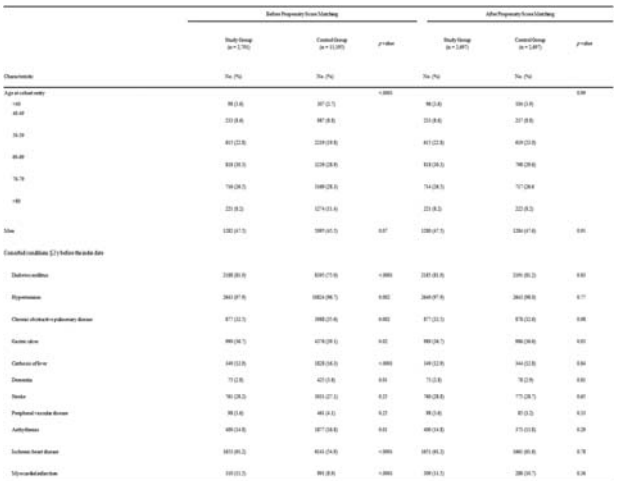
Introduction and Aims: Heart failure appears to be one of the most frequent complications of hemodialysis patients. The benefits of angiotensin-converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARB), and beta blockers in these patients are uncertain.
Methods: We examined patients with end-stage renal disease (ESRD) and heart failure, covering the years 1999 to 2009 obtained from the Taiwan National Health Insurance claims database. Study group was defined as patients who taking bisoprolol, carvedilol, metoprolol succinate, ACEI, or ARB for more than six months



FP528 Figure 1: Enrollment of Study Participants.

FP528 Table 1. Baseline Characteristics of the Study Patients, According to Treatment Group.



in the first year after their starting hemodialysis. We used propensity score matching, Kaplan–Meier method, and Cox proportional hazards regression models to analyze the association of study drugs with mortality over a follow-up of up to 3 years.
Results: We included 2,697 patients in study group and obtained 2,697 control patients after a 1:1 non- repeated propensity score match. All-cause mortality was estimated. There were 560 deaths (10.4%) in study group, lower than 804 deaths (14.95%) in control group (log rank, p< 0.0001). Among study patients, the survival rates of 12, 24, and 36 months of study group in this cohort were higher than control group (96.3%, 84.3% and 73.9%, vs. 88.0%, 73.8% and 65.1%, respectively). In multivariable-adjusted analyses, there were significant associations among drugs use of study group and survival (HR 0.6 [95% CI 0.54 to 0.67, p< 0.0001]).
Conclusions: Our findings suggest long-term benefits of bisoprolol, carvedilol, metoprolol succinate, ACEI, or ARB was associated with reductions in mortality on ESRD patients with heart failure.

FP529 ACUTE MYOCARDIAL INFARCTION IN INCIDENT DIALYSIS PATIENTS

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Introduction: Acute myocardial infarction (AMI) in dialysis patients is associated with high mortality. However, its incidence, type and clinical characteristic are not well established. AIMS: To estimate the incidence, characteristics and short and long-term prognosis of AMI in incident dialysis patients.
Methods: We study the patients who started dialysis between January/99 and December/07 and identified those suffering from AMI on the follow-up. Previous diagnoses of documented coronary artery disease (CAD), ischaemic stroke and peripheral vascular disease were recorded. We studied the association of AMI with the following variables: age, gender, diabetes, arterial hypertension, smoking, cholesterol and triglyceride levels, hematocrit values, urea, creatinine, serum calcium, phosphorus, PTH and albumin levels and the presence of previous atherosclerotic events. The patients were followed until death, transplantation, lost of following or end of the study in December/10.
Results: There were 576 incident dialysis patients (age 64.6±16 yrs; 56% males; 24.7% diabetics; 88% hemodialysis and 12% peritoneal dialysis). 34 patients (5.9%) had a history of CAD (29 AMI and 5 abnormal coronary angiography). During a follow-up of 1931 patient-yrs, 40 (6.9%) patients had AMI; the incidence was 2.13/100 p-yrs. In patients without prior CAD the incidence was 1.84/100 p-yrs and in those with prior CAD was 7.53/100 p-yrs. 15 patients (37.5%) presented with ST-segment elevation AMI and 25 (62.5%) with non ST-segment elevation. Incidence of ST-segment elevation AMI was 0.79/100 p-yrs and non-ST-segment elevation AMI was 1.33/100 p-yrs. In 22.5% of patients who had AMI, the event occurred within three months and 37.5% within one year after the initiation of dialysis. Multivariate analyse identified the following independent predictors of AMI: older age (OR: 1.037 (IC 95:1.009-1.067), P=0.011], previous CAD [OR: 3.35 (IC 95:1.48-7.16), P=0.004] and the presence of diabetic end-stage renal disease [OR: 2.96 (IC 95:1.49-5.86) P=0.002]. In-hospital mortality was 30% of patients, 45% at 1 month, 72.5% at 1 year and 82.5% of patients at 2 year. 80% of patients undergoing coronary angiography had more than 1 vessel lesions.
Conclusions: Incidence of AMI in incident dialysis patients is very elevated. In patients with previous coronary disease the incidence is three times higher. Mortality is very high and multivessel disease is very frequent.

FP530 SAFETY AND EFFICACY OF BETA BLOCKERS IN HAEMODIALYSIS

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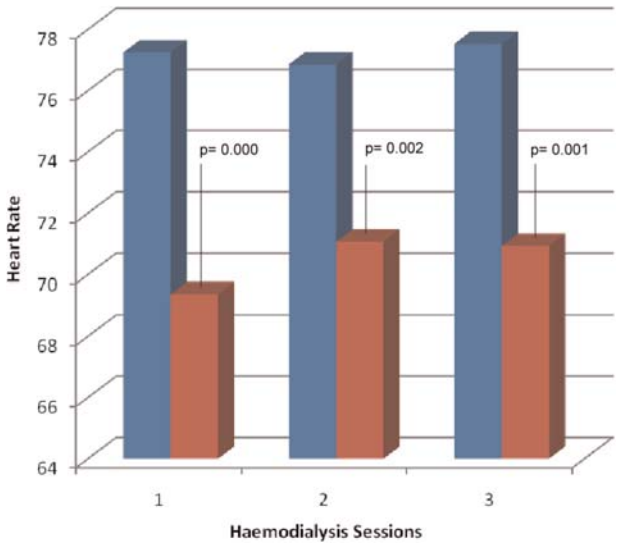
Introduction and Aims: Pre-dialysis tachycardia has been associated with increased mortality in haemodialysis patients. Carvedilol use has been shown to improve morbidity and mortality in haemodialysis patients with heart failure. However the value of Beta-blockade [BB] in dialysis patients without heart failure remains unclear. Beta blockers although seem attractive agents to reduce sympathetic overactivity and cardiovascular mortality they have been largely underused in the dialysis population due to safety concerns about adverse effects such as bradycardia and hyperkalaemia. This study examined the safety profile and the efficacy of beta blocker use in lowering heart rate in a cohort of haemodialysis patients in South London.
Methods: Data were collected on 262 patients undergoing maintenance haemodialysis. Baseline clinical characteristics are summarised in Table 1. Systolic Blood Pressures (SBP) and heart rates (HR) were recorded before dialysis in three consecutive sessions starting from the first day of the week. Statistics were performed using SPSS 17. For comparison continuous data two sample t-tests and pair sample t test, and for categorical data Chi square and were used.
Results: 77 patients were on beta blockers. Thirty-nine (50%) patients were on Metoprolol, 23 (29%) on Bisoprolol, 8 (10%) on Carvedilol and 7 patients (9%) on Atenolol. 80% of the patients on beta blockers were taking less than one fourth of the maximum dose. Hyperkalaemia defined as K> 6.0meq/L was present in only a few patients. There was no difference in hyperkalaemia between patients on beta blockers (6%) compared to patients not on beta blockers (5%) (p= 0.468). Bradycardia defined as heart rate < 50 beats per minute, was present in 3% of patients on beta blockers and 2.6% of patients not on beta blockers, with no difference between the two groups (p= 0.577). Beta blocker use was associated with a statistically significant decrease in the heart rate for the first, second and third recording of the week (p= 0.000, p 0.002 and p 0.001 respectively) (Figure 1). Systolic blood pressure after the large inter- dialytic interval was elevated compared with both the second and the third recording of the week for all patients. (Mean SBP 145.7 mmHg, SD 22.6 compared to Mean SBP 141.5 mmHg, SD 23.1, and mean SBP 141.7 mmHg, SD 24.1 respectively, p=0.006) There was no significant heart rate variability between the three sessions of the week in all patients.
Conclusions: Beta Blocker use is associated with a decrease in heart rate in all three pre dialysis recordings of the week. Use of beta blockers is not associated with significantly increased hyperkalaemia or bradycardia. Heart rate does not exhibit variability after the large interdialytic interval and thus any pre-dialysis recording of the week can be used to guide treatment. Thus the study suggests beta blockers are safe and effective in haemodialysis patients.



FP530 Figure 1: Comparison of heart rate with and without beta blockers before the first, second and third haemodialysis of the week (red and blue columns correspond to mean pre-dialysis heart rates on patients on and off beta blockers respectively).

FP530 Table 1 Clinical Characteristics

Age	65.5 ±15
Diabetes Mellitus	86 patients (33.3%)
Ethnicity	58 (22%) Asian 78 (30%) Black 106 (41%) Caucasians
CRP	22.8±40 mg/L
Hb	10.4±1.5 g/dl
Dialysis Vintage	33.9±24.6 months
On Beta blocker	77 (29%)
Dose of beta blocker (percentage of maximum dose) = 25% 25-50% 50-100%	 79% 18% 2%

FP531 VARIABILITY IN ESA DOSING AND NOT IN HAEMOGLOBIN LEVELS IS A STRONG PREDICTOR OF DEATH RISK IN HAEMODIALYSIS PATIENTS

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Introduction and Aims: Variability in haemoglobin (Hgb) levels has been associated with an increased mortality risk in haemodialysis patients. However variability in Hgb levels has been also associated with coexistent comorbidities. Furthermore some studies have pointed to ESA dose as a potential risk factor. So, it is not clear what is the true contribution of Hgb variability to the higher mortality. Finally, to date no study has evaluated the impact of variability in ESA dosing on death risk. Aim of our study was to determine if variability in Hb levels and/or ESA dosing were independent risk factors among haemodialysis patients.
Methods: Four hundred and twenty-two haemodialysis patients (m 254) from 7 Dialysis Centres in Tuscany were selected because of ESA therapy lasting at least for sex months. HD vintage was 84 ± 90 months. Baseline pts clinical characteristics are shown in Tab 1. Other variables were on average inside current guidelines Biochemical blood tests and data about comorbidities and ESA dose were collected monthly during 1 year. Hgb variability was calculated as standard deviation (SD) and as ratio of SD/average Hgb value. Primary outcome was all-cause and cardiovascular mortality tracked in the following twelve months of follow-up after twelve months of follow-up. We fit Cox model of one-year mortality with and without adjustment for number of comorbidities and other variables. Impact of Hgb variability and ESA dosing parameters on subsequent mortality risk was evaluated. Statistical analysis was performed by SPSS package.
Results: The number of comorbidities was associated with ESA dose variability, age, CRP, but not with haemoglobin variability. Haemoglobin variability, when adjusted for comorbities, age, CRPand ESA dose variability, was not associated with any increase in death risk. In the multivariate Cox model (Tab 2) age, CRP and ESA dose variability and number of comorbidities were the only independent risk factors for mortality.
Conclusions: According to our study, after adjustment for concurrent comorbidities no evidence supports an association between haemoglobin level variability and mortality risk. *Per contra*, ESA dose variability is strongly and independently associated with mortality in haemodialysis patients.This is a novel finding that calls for properly designed studies aimed at evaluating the impact of different ESA dose adjustment strategies on mortality in haemodialysis patients.

FP531 Table 1 Baseline pts clinical characteristics

	average	SD
Age (years)	67.1	13.0
Crp (mg/dl)	1.43	5.1
Hgb (g/dl)	11.4	0.86
Bmi	25.1	4.7
ESA dose (U/W)	8820	2214

FP531 Table 1. Multivariate adjusted COX model of mortality

Variable		HR (95% IC)		P
Age	1.07	1.03	1.12	.001
CRP	1.05	1.02	1.08	.000
ESA per 1 SD	.098	0.96	.099	.000
Comorbidities (N°)	.22	.087	.580	.002

FP532 AGE AND GENDER PREDICT OPG LEVEL AND OPG/SRANKL RATIO IN MAINTENANCE HEMODIALYSED PATIENTS.

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Introduction and Aims: Cardiovascular disease (CVD) is a major cause of death among end stage renal disease patients. Gender and older age belong to its classical risk factors. OPG/RANK/sRANKL (Osteoprotegerin/ Receptor Activator of Nuclear Factor ?B/ soluble Receptor Activator of Nuclear Factor ?B Ligand) axis is a system connecting bone and vascular remodeling. OPG is a well-known bone protector which additionally prevents vascular calcifications. However, elevated OPG levels predict cardiovascular events in HD patients. OPG/sRANKL ratio is a determinant of skeletal integrity apparently also vascular stability.
Methods: We aimed to evaluate the concentrations of OPG, sRANKL and OPG/sRANKL ratio in 21 chronically hemodialysed (HD) patients (10 females) and 16 healthy volunteers (10 females) and to relate them to gender, age as well as other clinical and laboratory parameters. All examined women were postmenopausal (>50 yrs.).
Results: Overall OPG and OPG/sRANKL ratio were significantly higher in HD patients than controls (p<10-5) whereas sRANKL was similar in both groups. Adjusted to gender, in controls OPG were higher in women (p=0.03), whereas sRANKL did not differ between man and female. In HD group OPG and sRANKL were higher in women (p=0.04, p=0.02 respectively) whereas OPG/sRANKL ratio was similar in both gender. Female patients compared to healthy women revealed 44% higher OPG concentration (p<10-4) and 46% higher OPG/sRANKL ratio (p=0.004). Comparison of male patients and controls revealed 39% higher level of OPG (p= 0.001) and 25% higher OPG/sRANKL ratio (p=0.003) in HD group. (Table) In controls and HD females patients there was no straight correlation between OPG and age. Interestingly, OPG and OPG/sRANKL ratio positively correlated with age in male HD patients (p=0.001 and p=0.011, respectively). Contrary, the association between OPG/sRANKL ratio and age was negative in HD women. In female HD group OPG and OPG/sRANKL ratio were independently and inversely predicted by total cholesterol level. In male HD group the main predictor of OPG and OPG/sRANKL ratio was age.
Conclusions: Higher OPG levels in HD women, comparing to age-matched HD men has not been described so far. Although its significance is unknown, it may indicate the difference in regulatory mechanisms of OPG/RANKL axis in men and women. A negative association between age and OPG/sRANKL ratio in female HD group warrants in-depth study and thorough understanding of this complex mechanism.

FP532 Table 1.

	OPG (pmol/l)		sRANKL (pmol/l)		OPG/sRANKL ratio	
	HD	*Control*	*HD*	*Control*	*HD*	*Control*
up	11.1 [A] (4.9–19.1)	4,3 (2,8-8,7)	143,8 (83–361)	170,14 (60,41- 372,8)	0,091 (0,027-0,173)	0,032 [A] (0,009-0,073)
en	11,43 [B] (10,37-19,1)	5,0 [C] (3,6-8,7)	158,1 [B] (89,7-361,1)	167,8 (82,7-237,3)	0,071 (0,029-0,159)	0,033 [C] (0,024-0,058)
n	9,2 (4,86-19,1)	3,6 [D] (2,8-4,9)	110 (83,04-197,6)	174,2 (60,4-372,7)	0,095 (0,027-0,173)	0,024 [D] (0,009-0,073)0

Abbreviations:
[A]HD vs control p < 10-5; B Women vs Men p < 0.05; c Women vs Women p = 0.004;
[D]Men vs Men p = 0.003

FP533 EVALUATION OF LUNG WATER BY ULTRASOUND AND ITS RELATION WITH CARDIAC PARAMETERS AND BIOIMPEDANCE-DERIVED BODY WATER IN HAEMODIALYSIS PATIENTS

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Introduction and Aims: Volume overload is a leading risk factor for death and cardiovascular events in patients maintained on chronic dialysis. Extra-vascular lung water (ELW), a fundamental component of body fluids volume, represents the water content of the lung interstitium - dependent on total body water (TBW) and the filling pressure of the left ventricle. Chest ultrasound (US) recently emerged as a reliable, simple and inexpensive technique for assessing ELW. In the presence of excessive ELW, the sub-pleural thickened interlobular septa, a low impedance

structure surrounded by air, generates hyper-echoic reverberation artefacts defined as "lung comets" (USLC). USLC could be a new approach for quantifying pulmonary congestion and hydration status in dialysis patients.
Methods: The aim of our study was to establish the relation between USLC, hydration status evaluated by multifrequency bioimpedance (body composition monitoring – BCM) and different echocardiograpic parameters in dialysis patients and to investigate the effect of a single dialysis session on ELW. The number of USLC and BCM derived parameters (total body water – TBW, extracellular water – ECW and intracellular water – ICW) were evaluated before and 30' after the midweek dialysis session. An echocardiographic and BCM evaluation was performed at the same time in all patients.
Results: Our study included 63 HD patients (47.6% men, 9,5% DM, mean age 57.1 ±13.9 years and mean HD vintage 77.7 months). USLC decreased from a median of 11 pre-HD to a median of 4 post-HD (P<0.001). The pre – post HD USLC difference was related to the UF volume (r=0,27, p=0,33), but not with differences in IBW or ECW (as measured by BCM), or any of the echocardiographic parameters. There was also a significant association between USLC (pre- and post-HD) and the bioimpedance quantitative determination of the deviation in hydration status from normal ranges* (overhydration) pre- and post-HD (r=0,27 pre-HD and r=0,4 post-HD respectively and p<0,05 for both), but not with any of the other bioimpedance derived body composition parameters (TBW, ECW, ICW) measured at the same time or with pre/post-HD BP. The only echocardiographic parameter related to the number of USLC measured either pre- or post-HD was the left atrium diameter (r=0,37 pre-HD and r=0,42 post-HD respectively, p<0,007 for both).
Conclusions: Lung water decreases following dialysis. And is closely related to LA dimensions.The amount of lung water appears to be predicted by bioimpedance-derived overhydration but not by ECW or ICW. Further analyses are required to determine the usefulness of indirectly assessing lung water by US, in HD populations.
* Wabel P. *et al*. Towards improved cardiovascular management: the necessity of combining blood pressure and fluid overload. *Nephrol Dial Transplant* 2008; 9: 2965–2971.

FP534 THE EVALUATION OF ARTERIAL STIFFNESS AND VOLUME STATUS IN CHRONIC KIDNEY DISEASE PATIENTS

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Introduction and Aims: Arterial stiffness has an independent predictive value for cardiovascular events in several populations, including patients with uncomplicated essential hypertension and type II diabetes. There is limited information regarding the prognostic value of arterial stiffness in patients with mild to moderate renal disease. As markers of arterial stiffness; Pulse wave velocity (PWV) and Augmentation index (AIx) are non-invazive methods using to determine the level of vascular injury. In this study, we aimed to study PWV, AI x and volume status of the stage 3 – 5 CKD and CAPD patients comparing with healthy controls.
Methods: Sixty six stage 3 – 5 CKD patients (without cardiovascular disease), 21 CAPD patients (treated with CAPD at least 3 months) and 34 healthy controls were included into the study. PWV and AIx were evaluated by the same operator after 15 minutes rest period (Mobil-O- Graph®). Volume status of the patients were evaluated by bioimpedance spectroscopy (BIS) for detection of hypervolemia. Body composition analysis using the BIS technique [50 frequencies (Body Composition Monitor: Fresenius Medical Care, Bad Homburg, Germany)] were performed.
Results: Median PWV values was 7,5 m/sn in stage 3 – 5 CKD patients, 6,2 m/sn in CAPD group, 5,9 m/sn in healthy controls. PWV values were significantly increased in stage 3 – 5 CKD patients than CAPD and healthy controls (p=0,002). PWV values were not different between CAPD patients and healthy controls. Normalized AIx values (according to heart rate of 75/min) were not different among three groups (p=0,287). Extracellular fluid excess was +1,26 L in stage 3 – 5 CKD patients, +1,21 L in CAPD patients compared with healthy controls. Overhydration (OH) was more prevalent in in stage 3 – 5 CKD and CAPD patients (p<0,001). PWV was positively correlated with OH in stage 3 – 5 CKD patients (p=0,004). PWV was negatively correlated with total protein (p<0,001), albumin (p<0,001) and calcium values (p<0,001) PWV was weakly correlated with OH in CAPD patients. (p=0,021).
Conclusions: PWV were find to be increased in stage 3 – 5 CKD patients. OH may possibly be a contrubuting factor in this increment of PWV.

FP535 CIRCULATING SCLEROSTIN AND DICKKOPF-1 (DKK1) IN PRE-DIALYSIS CHRONIC KIDNEY DISEASE (CKD) : RELATIONSHIP WITH BONE DENSITY AND ARTERIAL STIFFNESS

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Introduction and Aims: Vascular calcification (VC) and CKD-MBD are common findings in patients with CKD and are major causes of morbidity and mortality. Recent evidence over the last decade suggests a molecular link between the dysregulation in bone metabolism and the process of VC, although the mechanistic pathways involved are not completely understood. Evidence derived mainly from animal models also suggests that the **Wnt signalling pathway** may be implicated in the pathogenesis of VC. Msx2-expressing cells promote vascular calcification, via the activation of Wnt signals. Canonical Wnts signal via the heterodimeric LDL receptor –related proteins, LRP5 and LRP6 to stimulate osteogenic gene expression via nuclear β- catenin-dependent transcription. We theorised that a common regulatory pathway may involve the soluble Wnt signalling inhibitors, sclerostin and DKK1. The aim of the study was to investigate **for the first time** the possible link between circulating concentrations of DKK1 and sclerostin with BMD and arterial stiffness in pre-dialysis CKD.
Methods: Seventy-seven ambulant pre-dialysis patients, free from known bone pathology and with no history of any bone-related therapies (48 M, 29 F) aged (mean [SD]) 57 years with CKD stages 3B and 4 were recruited into this cross-sectional study over 9 months. Serum iPTH was measured by Roche 2010 electrochemiluminescence immunoassay (ECLIA). 25- hydroxyvitamin D (25 (OH) vitamin D) and 1,25 Di-OH Vitamin D by Radioimmunoassay (RIA). Sclerostin and DKK-1 was measured using commercially-available ELISAs. Arterial stiffness (SIDVP) and DEXA-derived bone mineral densities (femoral neck (FN) and lumbar spine (LS)) were also measured.
Results: In univariate analyses, serum sclerostin correlated positively with age (r = 0.47, p < 0.0001). Sclerostin was significantly higher in men compared to women (M : 50.5[30], F : 34 [15.8] pmol/L, p =0.015). Following correction for age and gender, sclerostin was negatively correlated with eGFR. We found that sclerostin was positively associated with BMD at the FN (p= 0.004) and LS (p=0.0001). In contrast, DKK1 was inversely associated with BMD at the FN (p=0.038). In univariate analyses of the study population, a significant inverse correlation was observed between SIDVP and DKK-1 (r = - 0.287, p = 0.013). SIDVP correlated significantly with age (r = 0.276, p = 0.017), systolic BP (r = 0.242, p = 0.038), diastolic BP (r = 0.270, p = 0.021) and total cholesterol (r = 0.227, p < 0.05). Following correction for age, gender, e GFR, diastolic blood pressure, total cholesterol, triglycerides, CRP, HDL, DKK1 remained a significant negative predictor of SI DVP (p=0.027).
Conclusions: This study demonstrates that sclerostin is positively associated with BMD at the hip and lumbar spine in CKD stage 3B and 4, confirming a similar finding shown recently in haemodialysis patients. In contrast, we observed for the first time a negative association between DKK1 and BMD at the femoral neck. Further, DKK1 was negatively associated with SI DVP . Thus we have shown that the recently-reported positive relationship between circulating sclerostin with age and bone mass is also seen in patients with pre-dialysis CKD (this being reported **for the first time**). Circulating sclerostin is higher in men and is affected by renal clearance. In contrast, DKK1 was negatively associated with bone mass and arterial stiffness, suggesting an important role for this Wnt inhibitor in CKD-MBD.

FP536 ABI TO EVALUATE PERIPHERAL ARTERIAL DAMAGE IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Peripheral arterial disease in uremic patients may present in the form of occlusions or mediacalcinosis of arteries of the legs. Different means have been used to assess the prevalence of these conditions, including questionnaires for leg pain, history of previous diagnosis or interventions for peripheral arterial disease or palpation of arterial pulses in the feet. We have used ankle-brakial pressure index (ABI), a very effective and reliable means to assess arterial integrity in the legs, to evaluate the prevalence of occlusions and/or mediacalcinosis in leg arteries in a random sample of patients of our dialysis centre.
Methods: A cross-sectional study was conducted in our hemodialysis center in March 2011. Systolic pressures were measured in 100 consecutive haemodialysis patients on anterior and posterior artery in the ankle on both feet using a hand held Doppler device. ABI was calculated for each artery. ABI < 0.9 is accepted as evidence for arterial occlusions and ABI > 1.3 for mediacalcinosis.
Results: Occlusion of at least one leg artery was found in 36% of patients while mediacalcinosis in 69% of them. Mean number of arteries affected for patients positive for lesions was 1.7 for occlusions and 2.2 for mediacalcinosis. Patients with occlusions had much more time in Chronic Renal Disease compared with those without occlusions. The prevalence of occlusions doubled after 10 years of CRD. There was no statistical difference between groups for the time in Haemodialysis. No correlation resulted between mediacalcinosis and the time in CRD or HD. The seric concentrations of PTH, calcium, phosphorus or their product had no effect on the prevalence of occlusions or mediacalcinosis. Age and sex were not statistically different in the group of patients with or without either type of arterial lesions. High Blood Pressure had no effect on the prevalence of occlusions or mediacalcinosis. There was a small number of diabetics and current smokers in the cohort for any statistical correlation.
Conclusions: Chronic renal disease is a great contributor and marker for occlusions and mediacalcinosis. ABI is a very good, simple to do and cheap mean to assess these changes in the arteries.

FP537 **A RANDOMIZED TRIAL OF BIOIMPEDANCE VS. CLINICAL METHODS FOR EVALUATING "DRY WEIGHT" IN HEMODIALYSIS AND THE EFFECT ON HYDRATION STATUS, BLOOD PRESSURE AND MORTALITY**

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Introduction and Aims: Chronic fluid overload is common in maintenance hemodialysis (HD) patients and is associated with severe cardiovascular complications, such as arterial hypertension, left ventricular hypertrophy, congestive heart failure, and arrhythmia. Therefore, a crucial target of HD is to achieve the so-called dry weight; however, the best way to assess fluid status and dry weight is still unclear. Dry weight is currently determined in most dialysis units on a clinical basis, and it is commonly defined as the lowest body weight a patient can tolerate without developing intra-dialytic or inter-dialytic hypotension or other symptoms of dehydration. One of the most promising methods that have emerged in recent years is bioelectrical impedance analysis (BIA), which estimates body composition, including hydration status, by measuring the body's resistance and reactance to electrical current. Our objective was to compare in a randomized trial BIA vs. clinical methods in evaluating "dry weight" and the effect on blood pressure (BP), volume control and mortality.

Methods: We randomized 131 HD patients from a single center in two groups: the "BIA" group, where the dry weight was determined exclusively by bioimpendace analysis and the "clinical" group, where only clinical methods were used. Body composition was measured using the portable whole-body multi-frequency BIA device, Body Composition Monitor— BCM (Fresenius Medical Care, Bad Homburg, Germany). In both "BIA" group and "clinical" group hydration status and "dry weight" were determined every 3 months by bioimpedance analysis, buy only in the "BIA" group measurements were disclosed and used to guide ultrafiltration. During the follow-up period of 2,5 years, we evaluated pre-dialysis BP, hydration status and mortality. Hydration status was evaluated as "relative fluid overload" (RFO), the procentage of extracelular water from the total body water, as measured by bioimpedance analysis.

Results: In the interventional arm of the study, the "BIA" group, we found that BP decreased gradually during the first 6 months, from 145 mmHg to 135 mmHg, and remained constant for the rest of the follow-up period. In the "clinical" group, the BP was overall higher ($p = 0.03$), with no significant trend. "Relative fluid overload", as a marker of fluid overload, was overall lower in the "BIA" group compared to the "clinical" group ($p= 0.004$). At the end of the follow-up period there was a significant difference in mortality (Log-Rank test, $p=0.009$). Mean survival rate was 29.2 months in the "BIA" group and 27.7 months in the "clinical" group.

Conclusions: Multi-frequency bioimpedance analysis is better than clinical methods in achieving and maintaining the "ideal weight" in HD patients. After randomization, the "BIA" group showed significantly better volume control, evaluated by the RFO. In the "BIA" group BP control was better compared to the "clinical" group. After a 2.5 year follow-up, our randomized trial showed a significant difference in mortality, in favor of the "BIA" group, possible explained by the better volume control and the better BP control.