

Cardiovascular complications of CKD 2

SaP234 THE ASSOCIATION OF CIRCULATING CARDIAC BIOMARKERS WITH THE FREQUENCY AND SEVERITY OF LEFT VENTRICULAR REGIONAL WALL MOTION ABNORMALITIES

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Introduction and Aims: Haemodialysis (HD) patients who develop myocardial dysfunction have a poor prognosis. Recurrent sub clinical myocardial ischaemia is an important risk factor in the development of heart failure in non dialysis patients. We have previously demonstrated that sub clinical myocardial ischaemia develops during HD. HD patients prone to episodes of intradialytic hypotension (IDH) have higher levels of circulating cardiac troponin T (cTnT) than non IDH-prone dialysis patients. HD patients with an elevated cTnT also have an increased incidence of mortality from all causes. We sought to examine whether increased cTnT levels were associated with the development, frequency and severity of left ventricular (LV) regional wall motion abnormalities (RWMAs).

Methods: We studied 38 prevalent HD patients and took blood samples for cTnT immediately prior to (baseline), immediately after the end of (post) and 48hours after HD treatment. At the same treatment session, serial echocardiography with quantitative analysis was performed pre-dialysis, at peak stress and during recovery. This was used to assess the development of wall motion abnormalities over 10 regions of the left ventricle. A motion abnormality was defined as a reduction in movement of >20% from baseline and >2 RWMAs were significant. Severity was scored as a composite of the number of RWMA and the magnitude of reduction in motion.

Results: Circulating plasma cTnT levels did not correlate with left ventricular mass index (LVMI) (P=0.37). Increased LVMI was not associated with the development of RWMAs (P=0.25). Patients who developed RWMAs during HD had a higher baseline cTnT (0.028±0.006 vs. 0.1±0.017, P=0.017). However, there was no correlation between levels of cTnT and the severity of stunning as evidenced by numbers of RWMAs (P=0.3) or the magnitude of reduction (P=0.31). There was also no significant rise in the post (P=0.49) and 48 hour (P=0.48) cTnT levels from baseline in those patients who developed left ventricular RWMAs.

Conclusions: The development of left ventricular RWMAs is associated with an elevated cTnT. However, plasma cTnT levels do not forecast the number of RWMAs that develop or their severity. Circulating biomarkers of myocardial injury may be of use to identify patients experiencing dialysis induced myocardial stunning. However, the degree of elevation appears to correlate poorly with the severity of the functional insult.

SaP235 A NOVEL HIGHLY EFFICIENT BIO-ASSAY TO MONITOR MICROBIOLOGICAL PURITY OF DIALYSIS FLUIDS

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Introduction and Aims: Microbial contamination of the dialysis fluid has a pro-inflammatory potential. The increased application of high-flux hemodialysis and on-line hemodiafiltration has made the need for ultrapure dialysis water even more stringent. Classical test methods for bacteriological contamination, such as bacteriological cultures or the Limulus Amebocyte Lysate (LAL)-test, fail to detect a substantial number of contaminants with intact lipopolysaccharide (LPS) as the only exception.

Methods: We developed a novel bio-assay for dialysis water contaminants using a monocytic THP-1 cell line. After a 24h rest period, calcitriol (10nM)-differentiated (72h) THP-1 cells, were incubated overnight (24h), in the presence of dialysis fluid samples (1/1) or samples containing potential activating microbiological agents. Secretion of IL-1β (pg/ml) was detected in the cell culture supernatant as a parameter of biological activity of the dialysis fluid. To validate the sensitivity of this test method to various types

of contaminants, response to peptidoglycan (PGN), short bacterial DNA fragments and LPS fragments was compared to the response observed with the LAL-test.

Results: The presence of peptidoglycan (0.1; 1; 5; 10; 50; 100; 500; 1000; 5000 ng/ml) induced IL-1β secretion from 5 ng/ml on (P<0.05) whereas the classical LAL-test remained unresponsive. Likewise, addition of short bacterial DNA fragments (2006 stimu; 1μM and K3; 10μM) caused a significant IL-1β induction but no LAL-response. LPS fragments (MW<5kD) from *P. aeruginosa* induced no LAL-response, per se, but showed a marked biological activity. Intact LPS induced a significant IL-1β secretion versus control in a dose dependent manner from a concentration of 0.01 ng/ml on. A comparable evaluation with a biological test based on whole blood emanated in more scattered and/or less sensitive results.

Conclusions: The present data show that this novel bio-assay detects bacteriological derivatives which cannot be found by the classical screening methods. Application of this assay is useful to reveal contaminants which otherwise go undetected aiming at the timely prevention of biofilm formation in the dialysis circuit and micro-inflammation in the hemodialysis patient.

SaP236 ASSOCIATION BETWEEN TUMOR NECROSIS FACTOR ALPHA (TNF) GENE POLYMORPHISM AND CARDIOVASCULAR MORTALITY IN END-STAGE RENAL DISEASE PATIENTS

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Introduction and Aims: Whereas circulating levels of pro-inflammatory cytokines such as IL-6 are known to be closely associated with protein-energy wasting, cardiovascular disease (CVD) and premature mortality in ESRD patients (pts), such associations are not usually found with circulating TNF, which could be due to the more local nature and shorter half-life of this cytokine and many other factors. The TNF -308G/A gene polymorphism has been reported to be associated with increased production of TNF. However, the impact of this genetic polymorphism on CVD risk factors including body composition, and mortality has not previously been studied in ESRD pts.

Methods: A total of 229 ESRD (87 women, 5412 years) pts starting dialysis therapy were genotyped for the TNF -308G/A gene polymorphism, and relations with CVD mortality, body composition, inflammatory markers including adipocytokines and various risk factors for CVD were analyzed. Pts were followed for a median of 57 months (range 1-130 months).

Results: Sixty (26%) pts had the TNF -308G/A A allele. The circulating levels of TNF and other cytokines did not differ from the levels in non-A carriers. When analyzing the TNF genotype groups, systolic blood pressure was however higher in the A allele carriers compared with non-A carriers (p=0.049) and the body fat mass/body weight ratio was lower in the A allele carriers (P=0.046) compared with the others. Furthermore, TNF -308G/A A-carriers had higher levels of troponin T (cTnT) (p=0.01) and also showed a higher CVD mortality during follow-up (Kaplan-Meier; Log-rank 6.38, p=0.012). After adjustment for age, DM and inflammation (CRP>10mg/L), wasting and presence of clinical CVD, the A allele of TNF -308G/A was still significantly associated with a higher CVD mortality.

Conclusions: ESRD pts with the A allele of -308TNF, which is thought to result in an increased transcription of TNF, was associated with hypertension, lower fat body mass/weight ratio and higher serum cTnT levels as well as with a significantly increased risk of cardiovascular death following initiation of dialysis.

SaP237 PERSISTENT ELEVATION OF INFLAMMATION MARKER C-REACTIVE PROTEIN IS ASSOCIATED WITH ATHEROSCLEROSIS AND LEFT VENTRICULAR HYPERTROPHY IN CHRONIC HEMODIALYSIS PATIENTS: 2 YEAR FOLLOW-UP STUDY

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Introduction and Aims: Cardiovascular disease is the main cause of mortality in hemodialysis patients. The precise cause of this accelerated mortality is still unclear. Recently, emerging evidence suggests that beside the traditional risk factors, inflammation may have a role in the development of cardiovascular disease. In addition, left ventricular hypertrophy (LVH) and carotid intima media thickness (CIMT) was described as independent risk factors for cardiovascular morbidity and mortality in this population too. The aim of this study is to evaluate relation between inflammation and CIMT and LVMI in patients with end stage renal disease undergo hemodialysis.

Methods: Seventy-four HD patients without diabetes and history of cardiovascular disease were recruited in the two-years study. Forty-five patients (20 female, 25 male, mean age; 52.6±14.1 years; mean time on HD 52±44 months) completed the study. CIMT and LVMI were determined baseline, end of first and second years. Changing in CIMT and LVMI were calculated from these measurements at end of two year (Δ CIMT and Δ LVMI). Biochemical parameters (creatinin, BUN, glucose, electrolytes, albumin, hemoglobin, lipid levels) were measured at the beginning of the study and at four-week intervals; inflammatory markers (homocysteine, fibrinogen, C reactive protein (CRP), erythrocyte sedimentation rate (ESR), lipoprotein-a) and iPTH were determined at the initiation and at three-month intervals during two-years. Mean values of biochemical parameters were calculated yearly for each patient. Patients were stratified into two groups according to mean serum CRP levels: low levels (<1 mg/dL; group I = 26 patients), high levels (>1 mg/dL; group II = 19 patients).

Results: No difference was observed in traditional risk factors and measurements of CIMT and LVMI between groups at the beginning of study. In group-II, the mean value for CIMT and LVMI (0,67±0,15 mm; 91,6±34,2 g/m², respectively) were significantly lower than measurements at two-years (0,78±0,21 mm; 110,9±37,5 g/m², respectively p<0,05). In group-I patients had similar values of CIMT and LVMI at the beginning and end of two years (0,65±0,15 vs. 0,68±0,17 mm/93,5±24,4 vs. 99,0±35 g/m² respectively p>0,05). Incidence of patients with progressed CIMT and LVMI was higher in patients' group-II than in patients' group-I (n=16, 85% vs. n=3, 23% respectively, p<0,05). During two-years, systolic and diastolic blood pressure, Kt/V, interdialytic weight gain, hemoglobin levels, CRP, ESR, lipoprotein-a and lipid levels did not show significant variation and difference between groups.

Conclusions: Our study showed inflammatory state of hemodialysis patients might have an impact on the CIMT and LVMI progression thereby cardiovascular disease in this population. CRP, the prototype marker of inflammation may be also important prognostic indicator for atherosclerosis and left ventricular dysfunction in patients with ESRD.

SaP238 A COMPARISON OF THREE DIFFERENT THERAPEUTIC OPTIONS IN PREVENTION OF INTRADIALYTIC HYPOTENSION

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Introduction and Aims: In spite of all hemodialysis technology advances and despite of all pharmacological and other preventive interventions, intradialytic hypotension (IDH) remains very frequent complication of hemodialysis (HD) treatment. Most authors report the presence of IDH in 15-30% of all HD treatments. Among technical devices, most promising is ultrafiltration (UF) control by Blood Volume Monitor (BVM) along with zero temperature balance by BTM-Blood Temperature Monitor. (BVM and BTM are trade marks of Fresenius, Bad Homburg, Germany). Among

medications, positive effects are reported with administration of midodrine (alpha-1 adrenergic receptor agonist) or sertraline (serotonin reuptake inhibitor). Those three therapeutic options have not been compared directly in the same group of patients. The aim of this paper was to show our results of comparison of the efficacy of each that protective-therapeutic maneuver in the prevention of IDH.

Methods: Ten (6 female, 4 male) chronic (7,3±4,5 years) HD patients (mean age 59,0±20,5 years; range: 28-82) which were prone to IDH (IDH in more than 40% of HD treatments), after first (monitoring) phase (9 standard HD treatments, during 3 weeks) underwent three therapeutic phases in random order in a blinded fashion: B-phase (biofeedback, controlled UF rate by BVM, with zero temperature balance achieved by BVM), M-phase (midodrine, 10 mg per os, 30 min. prior to HD, during 3 weeks), S-phase (sertraline, 50 mg p.o. daily, during 3 weeks). In every phase, for each patient, blood pressure and pulse were measured in the same time periods of HD, and the number of episodes of IDH was noted.

During the study, all patients had their usual dialysis conditions, and they were asked not to change significantly their usual interdialysis weight gain, medications and life habits.

Results: In the first phase, during 3 weeks and 90 HD treatments, 80 IDH episodes were registered, or 0,89±0,23 episodes per treatment. Individual critical Relative Blood Volume (crit.RBV) was determined for each patient. Mean value of all crit.RBV was 81,1±3,9% (range 74-87%). In the second part of the study, during B-phase: 27 IDH episodes (0,30±0,25 episodes IDH per treatment), during M-phase: 57 IDH episodes (0,64±0,23 episodes IDH per treatment), and in S-phase: 63 IDH episodes (0,70±0,25 episodes IDH per treatment).

Conclusions: According to the obtained results, we concluded that all three therapeutic options significantly decrease the number of IDH episodes compared to the first or monitoring phase (p<0,01). "Biofeedback" (with BVM and BTM) control of HD was more efficient way to prevent IDH than both other (midodrine or sertraline) options (p<0,01), and there were no significant difference between last two therapeutic options (p>0,05).

SaP239 PUROMYCIN AMINONUCLEOSIDE-INDUCED NEPHROTIC SYNDROME PRESENTS CARDIAC ATROPHY, CONTRACTILE DYSFUNCTION AND CYTOKINE ACTIVATION

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Introduction and Aims: In the nephrotic syndrome (NS), the impact of protein wasting and inflammatory activation on cardiac remodeling is still unknown. In the present study, cardiac morphometry, contractile function and myocardial gene expression were evaluated in puromycin aminonucleoside (PAN)-induced nephrosis.

Methods: Male Sprague-Dawley rats were studied 7 and 14 days after PAN (150 mg.kg⁻¹; ip) injection. Cardiac and skeletal muscle morphometry and protein concentration to DNA concentration ratio were evaluated. Renal function, blood pressure, cardiac hemodynamics and muscle strip contractile function were assessed. Evaluation of myocardial expression of cytokines, growth factors, calcium-handling and myofilament proteins was also performed. Statistical analysis was performed by one-way ANOVA followed by Student's *t*-test for unpaired comparisons.

Results: PAN injection consistently resulted in massive proteinuria and impaired creatinine clearance. Sodium retention was observed at day 7, while a negative sodium balance was present at day 14 with no changes in blood pressure or end-diastolic pressures. Skeletal and cardiac muscle atrophy were present in PAN treated animals 14 days after injection. This was accompanied by disturbed left ventricular (LV) systolic and diastolic function, and impaired performance of LV isolated muscle strips. Increased LV mRNA levels of cytokines TNF- α and IL-1 β and decreased mRNA and protein expression of SERCA2a were also observed. This resulted in a reduction of SERCA2a to PLB ratio in the PAN group on day 14.

Conclusions: PAN nephrosis associates with cardiac atrophy in the absence of altered loading conditions. This resulted in myocardial dysfunction in the presence of local cytokine activation and disturbed calcium-handling mRNA

and protein expression. These results suggest that, in the NS, systemic inflammatory activation and protein wasting induce cardiac remodeling and dysfunction.

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SaP240 ASSOCIATIONS OF SIALIC ACID WITH INDICES OF MALNUTRITION-INFLAMMATION AND ATHEROSCLEROSIS IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Sialic acid (SA) is a derivative of neuraminic acid, which is expressed on lipoproteins, glycolipids and acute phase reactants. SA has been shown to be a risk factor for cardiovascular (CV) morbidity and mortality in general population and in diabetics. It has been also shown to be elevated in patients with end stage renal disease, especially in those with CV disease. However, SA has not been evaluated as marker of atherosclerosis in non-diabetic, asymptomatic patients on chronic maintenance hemodialysis (MHD).

Aim of our study was to evaluate sialic acid as a marker of atherosclerosis in asymptomatic, non-diabetic chronic MHD patients.

Methods: Seventy stable, non-diabetic asymptomatic patients on chronic MHD (40 females and 30 males) and 30 healthy controls (15 females and 15 males) were examined for the presence of atherosclerosis with B-mode carotid ultrasound, estimating intima-media-wall thickness (IMT) bilaterally. All participants underwent clinical evaluation including assessment of antropometric indices and biochemical blood tests including high-sensitivity CRP and plasma fibrinogen, total SA and lipids.

Results: SA was significantly increased in MHD patients compared to controls in age-sex adjusted model (OR: 1.03, p=0.018). In univariate linear regression analysis SA correlated positively with CRP (r=0.79, p<0.0001), fibrinogen (r=0.44, p<0.0001), triglycerides (r=0.26, p=0.02) and carotid IMT (r=0.26, p=0.04) and negatively with serum albumin (r=-0.27, p=0.02) and predialysis serum creatinine (r=-0.37, p=0.001) in MHD patients. In stepwise multivariate regression analysis for carotid IMT SA (beta:0.0012, p=0.02), age (beta:0.004, p=0.012) and waist-to-hip ratio (beta:0.57, p=0.026) were found to be independent predictors of carotid IMT in non-diabetic MHD patients.

Conclusions: Serum SA is elevated in non-diabetic MHD patients and it seems to be strongly associated with established markers of CV disease (CRP, IMT). There is evidence that SA could be a marker of MIA syndrome in such patients, since it is seems to be associated with malnutrition (lower serum albumin and creatinine), chronic systemic inflammation (CRP, fibrinogen) and atherosclerosis (IMT) in chronic MHD patients. However, further clinical research is necessary to confirm this finding.

SaP241 LIPID PROFILE AND CARDIOVASCULAR RISK IN DIALYSIS: TWO-YEARS FOLLOW UP FROM RISCAVID STUDY

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Introduction and Aims: Atherosclerotic cardiovascular (CV) disease is the first cause of mortality and morbidity in uremic patients and both altered lipidic profile and chronic inflammatory state play an important role in its pathogenesis. The RISCAVID (Cardiovascular risk in Dialysis) study is an observational and prospective study, started on June 2004, of the over 800 patients in hemodialysis (HD) and peritoneal dialysis of the north-western

area of Tuscany. Aim of this study is to verify the predictive power of various risk factors regarding CV events in HD patients.

Methods: At the time of enrolment basal demographic, clinical and laboratory data of population were registered (n=757, m 60%, mean age 65.6±14 y, dialytic age 69±77 m, diabetes 19%). CV disease was established by anamnestic and instrumental data. Serum cholesterol (sC), serum tryglicerid (sTg) and HDL cholesterol (HDL-C) were directly measured (Beckman); LDL cholesterol (LDL-C) was indirectly calculated by Friedewald's formula. Chronic inflammatory state was evaluated by centralized dosage of CRP (highly sensitive nephelometric assay, Bering), IL-6 and IL-8 (EIA, Bender). The population was followed up for 24 months reporting CV major events (acute myocardial infarction, stroke and ictus), CV mortality and overall mortality.

Results: Patients with LDL-C >70 mg/dl (65% of the entire population) were associated with a significantly increased risk of CV mortality (RR 1.35, p<0.04). HDL-C >40 mg/dl was showed protective on fatal and non fatal CV events. Patients with HDL-C<40 mg/dl and LDL-C > 70 mg/dl were associated with an higher cumulative RR for non fatal CV events (1.42; p<0.05) and CV mortality (1.61; p<0.01). No predictive power was founded for total cholesterol and trygliceride values. Patients with pro-atherogenic lipidic profile (LDL-C>70 mg/dl) and inflammatory state (CRP>5 mg/L) showed an increased RR of mortality and morbidity in respect to patients with only one risk factor. Nevertheless, patients with low LDL-C (< 70 mg/dl) shower an increased RR for overall mortality (RR 1.22; p<0.05).

Conclusions: RISCAVID Study after a two-year follow-up confirms the importance of proatherogenic lipidic profile in the HD population. The combination of high levels of LDL-C, low levels of HDL-C and increased pro-inflammatory cytokines improves prognostic value of analysis for CV. Low levels of LDL-C are associated with an increased risk for overall mortality supporting the concept of "reverse epidemiology".

SaP242 PULMONARY HYPERTENSION IN END STAGE RENAL DISEASE PATIENTS: PREVALANCE AND RISK FACTORS

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Introduction and Aims: Cardiovascular complications are encountered frequently in end stage renal disease patients. Pulmonary hypertension has been reported in dialysis patients. The aims of this study were to find out the incidence of pulmonary hypertension, to determine the possible risk factors of pulmonary hypertension in dialysis patients and to find out the differences between two dialysis modalities.

Methods: Sixty seven haemodialysis patients (F/M) and nineteen peritoneal dialysis (F/M) patients were clinically evaluated for 24 months. Twenty-two of haemodialysis (HD)patients (32.8%) and 5 of peritoneal dialysis (PD) patients (26.3%) had diabetes mellitus. All patients had undergone Doppler echocardiography (pulmonary arterial pressure and left ventricular dimensions were evaluated) at least twice and haemodialysis patients were also undergone a Doppler USG of the arterio venous fistula (location and flow rate were evaluated) during the follow-up period. Pulmonary hypertension (PHT) was diagnosed when the mean of two levels of pulmonary arterial pressure (PAP) exceeded 35mmHg. Laboratory tests done included serum cholesterol, calcium, phosphorous, intact PTH, hemoglobin and ferritin levels.

Results: The incidence of PHT was 26.8% in HD and 31.6% in PD patients (p>0.05). The mean PAP was 23.6 mmHg in HD while it was 24.8% in PD patients. LVH was seen in 32.2% of HD and 36.4% of PD patients (p>0.05). Diabetes mellitus was a risk factor for patients under both types of dialysis (p=0.03). Serum levels of ferritin (p=0.04) was found to be significantly related to PHT while iPTH, hemoglobin and serum cholesterol levels were found to be unrelated in both HD and PD patients. Locations and flow rate of AVF of HD patients were also related with PHT. Patients with brachial fistulas were more prone to PHT but the difference was insignificant while the flow rate of the fistulas was significantly related with PAP (p=0.04).

Conclusions: In conclusion in this study PHT was found to be frequent in both dialysis types. Although the incidence was higher in PD patients the difference was insignificant. This higher incidence in PD patients in spite

of AVF in HD patients which is supposed to be a risk factor in some studies may be attributed to higher fluid overload in PD patients as can be seen with their higher incidence of LVH. Diabetes mellitus was found to be a risk factor for PHT which may be attributed to higher incidence of vascular atherosclerosis in dialysis patients. Serum ferritin levels which is a marker for inflammation was also found to be significantly related with PHT in dialysis patients. The significant effect of higher flow rates of AVF may be a result of increased cardiac output.

SaP243 PROGNOSTIC VALUE OF CAROTID INTIMA MEDIA THICKNESS AND WALL PLAQUES IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Cardiovascular disease and other complications of atherosclerosis are the most common cause of death in patients with chronic renal failure in maintenance hemodialysis (MHD). Carotid ultrasonography is a simple no invasive tool to investigate the vascular system, by means of intima media thickness (IMT) measurement and carotid wall plaques. Aim of the study was to determine IMT and its possible clinical relationships and to investigate whether IMT would predict cardiovascular morbidity and mortality in patients in MHD.

Methods: We studied 60 MHD patients (age 68 ± 13 years, 48% male, 50% diabetics, time on MHD 32 ± 11 months) and a control group of 274 people matched for age and sex. Follow-up period was 56 ± 10 months. Measurements: Demographic and clinical data, serum levels of homocysteine (tHcy), folic acid (FA) and B₆ and B₁₂ vitamins. IMT was measured by high-resolution B-mode ultrasonography.

Results: IMT was higher in MHD patients than in those in the control group (0.947 ± 0.308 vs 0.619 ± 0.176 mm; $P < 0.001$). IMT was related with age ($r = 0.268$, $P = 0.038$), diabetic ($r = 0.650$; $P < 0.001$) and hypertensive condition ($r = 0.333$, $P = 0.012$), but not with lipids, tHcy or FA. Similar findings were found with the presence or not of carotid plaques but serum LDL-cholesterol levels were also related ($r = 0.280$, $P = 0.031$). Patients who suffered from coronary artery disease, peripheral artery disease or stroke had higher IMT than those without those events (1.156 ± 0.371 vs 0.875 ± 0.285 mm, $P < 0.001$; 1.205 ± 0.374 vs 0.911 ± 0.231 mm, $P = 0.007$; 1.195 ± 0.264 vs 0.844 ± 0.251 , $P < 0.001$ respectively). Something similar occurred with the presence of plaques.

During the follow-up period 36 patients (60%) died, 67% of them due to cardiovascular causes. IMT was higher in patients who expired than those who survived (1.020 ± 0.264 vs 0.858 ± 0.334 mm; $P = 0.044$). The survival rate during the observation was significantly lower in the final IMT fourth (20%) than in the first (72%) ($P = 0.014$).

Conclusions: These findings suggests that measurement of carotid IMT and the presence of wall plaques are useful tools to predict cardiovascular events and mortality in patients in MHD.

SaP244 INCREASED RATIO OF EXTRACELLULAR TO TOTAL BODY WATER (ECW/TBW) IS RELATED TO COMORBIDITY AND FLUID OVERLOAD RATHER LOSS OF LEAN BODY MASS IN HAEMODIALYSIS (HD) PATIENTS

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Introduction and Aims: The application of Bioelectrical Impedance Analysis (BIA) has shown that increased ECW/TBW is associated with poor outcome in HD patients. It is less clear whether this is attributable to fluid overload leading to expanded ECW or loss of lean body mass leading to low TBW. The aim of this study was to combine relative measures of

TBW_{BIA} and the ECW/TBW ratio as measured by a multi-segmental and multi-frequency BIA device (InBody S20, Biospace, Korea) with absolute determination of TBW obtained in the dialysis unit from Deuterium Dilution using breath analysis using an on-line Flowing Afterglow Mass Spectrometer (Transpectra, UK).

Methods: 59 HD patients were studied (17 female, mean age 58.4 ± 16.1 years, mean BMI 27 ± 5.4). Body composition was determined post-dialysis. Co-morbidity was documented using the validated Stoke Co-Morbidity Index. SGA showed 84.7% of the patients were well-nourished and 15.3% were mildly malnourished.

Results: The mean post-dialysis ECW/TBW was 0.39 ± 0.01 and was significantly associated with increasing age ($R = 0.678$, $p < 0.001$) and co-morbidity grade (ANOVA $p = 0.000$) (Fig. 1). The Pearson's correlation between TBW_D and TBW_{BIA} was 0.94, $p < 0.001$. The mean difference between the absolute TBW_D and TBW_{BIA} was 1.61 ± 3.09 L (95% CI 0.80 to 2.41, $p < 0.001$). This difference between methods was greater in patients with higher ECW/TBW ($R = 0.404$, $p = 0.002$), in older patients ($R = 0.282$, $p = 0.031$), in patients with higher co-morbidity scores ($R = 0.474$, $p < 0.001$) and increased BMI ($R = 0.26$, $p = 0.049$). There was an incremental effect of co-morbidity on the difference between TBW_D and TBW_{BIA} (ANOVA $p = 0.004$) (Fig. 2).

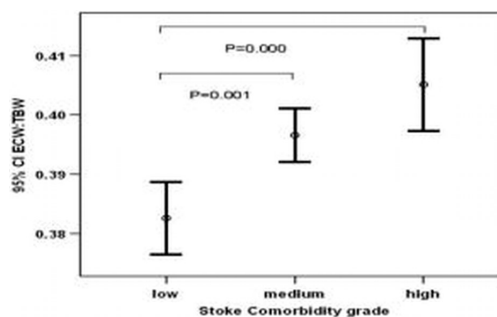


Fig. 1

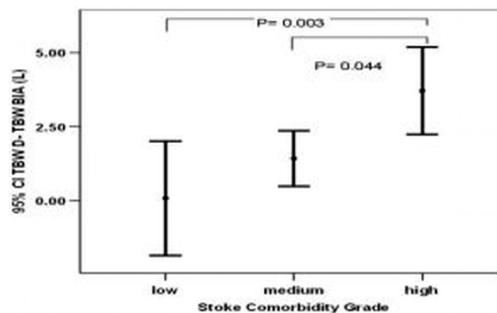


Fig. 2

Conclusions: In conclusion, by combining relative and absolute measures of body composition this study has shown that the increased ECW:TBW ratio observed in more co-morbid but not severely malnourished HD patients is associated with a higher TBW than that predicted from BIA. This suggests that there is added value in the absolute measurement of TBW when assessing fluid status.

SaP245 A COMPARATIVE STUDY OF THE EFFECTS ON PULSE WAVE VELOCITY (PWV) IN HEMODIALYSIS (HD) PATIENTS TREATED BY SEVELAMER WITH LOW DOSE CALCIUM CARBONATE OR CALCIUM CARBONATE ALONE

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Introduction and Aims: Cardiovascular disease is a major cause of mor-

bidity in patients with end-stage renal failure. Increasing evidence suggests that prolonged use of calcium carbonate increases the total body calcium load, and potentially increases the risk of cardiovascular and soft tissue calcification. Sevelamer is the first phosphate-binding agent that is non-absorbed, calcium-free, and metal-free. It may also attenuate coronary and aortic calcification and has a number of other beneficial effects on lipid metabolism. On the other hand, arterial stiffness measured by pulse wave velocity (PWV) is an independent risk factor for morbidity in end stage renal failure patients, and treatment with sevelamer was reported to attenuate the progressive increase in PWV in HD patients. The present study was performed to assess the effect of sevelamer administration on PWV in HD patients treated with calcium carbonate.

Methods: We performed a randomized clinical trial to compare the effect of calcium carbonate alone and sevelamer with low dose calcium carbonate on PWV. 44 HD patients (24 men and 20 women; mean age 63 ± 6 years; mean HD duration 6.3 ± 2.7 years), who had been treated with calcium carbonate as a phosphate binder, were enrolled into the study. The patients were randomly divided into the sevelamer with low dose calcium carbonate group (group A) and calcium carbonate alone group (group B). PWV was compared before and at the end of 2-year therapy of both. Serum biochemistry parameters were also assessed.

Results: All the variations found were evaluated through mean values \pm SD, t-tests. In group A, the dose of calcium carbonate could be reduced significantly from 2.8 ± 1.0 g/day to 1.2 ± 1.1 g/day with serum phosphate values maintained below 6 mg/dl by the addition of 2.5 ± 0.7 g/day sevelamer. Only in this group, intact parathyroid hormone rise from 94.9 ± 111.2 pg/mL to 188.2 ± 168.4 pg/mL ($P < 0.05$). However, there was not significant difference in PWV from 1874 ± 659 to 1939 ± 378 cm/sec ($P = 0.7$). In group B, the dose of calcium carbonate needed to be administered 1.9 ± 0.8 g/day to maintain serum phosphate values below 6 mg/dl. There was not significant difference in PWV from 2094 ± 697 cm/sec, to 1923 ± 501 cm/sec ($P = 0.27$). In both group serum calcium, phosphate and calcium x phosphate product remained unchanged.

Conclusions: The dosage of calcium carbonate was successfully reduced by adding sevelamer to maintain serum phosphate levels below 6 mg/dl. However, there was not the improvement in PWV, suggesting that more intensive long-term study is essential to evaluate the effects of sevelamer on PWV.

SaP246 LOW GLOMERULAR FILTRATION RATE IN PATIENTS PRESENTING WITH ACUTE CORONARY SYNDROME: IS EARLY CKD A RISK FACTOR FOR CAD?

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Introduction and Aims: Coronary artery disease (CAD) is the commonest cause of mortality in patients with CKD. Whether the patients with early fall in Glomerular filtration rate (GFR) are at risk to develop CAD is not known. We analysed the effect of Coronary artery disease on GFR in patients presenting with acute coronary syndrome (ACS).

Methods: We analyzed 305 consecutive patients admitted to acute coronary care unit over 6 months with the diagnosis of acute coronary syndrome and undergoing coronary angiogram (CAG). Diagnosis of acute coronary syndrome was made with classical history recent onset or rest angina with or without ECG changes. GFR was estimated by Creatinine clearance (Ccr) according to Cockcroft-Gault formula.

Results: Among 305 patients males were 269 (88.2%) and females were 36 (11.8%) with mean age of 52 ± 10 (25-81) years. Hypertensives were 168 (55%), 99 (32.5%) were diabetics, 137 (45%) were smokers and family history of CAD was present in 30 (9.8%) patients. Echocardiogram showed normal left ventricular (LV) function in 154 (50.5%), mild LV dysfunction (LVD) in 54 (17.7%), moderate LVD in 85 (27.9%), and severe LVD in 12 (3.9%) patients. CAG showed border line CAD ($> 30\%$ but $< 50\%$ stenosis in one or more coronary arteries) in 12 (3.9%), insignificant CAD ($> 50\%$ but $< 70\%$ stenosis) in 34 (11.1%), significant CAD ($> 70\%$ stenosis) in 221 (72.5%) patients and normal coronaries in 38 (12.5%) patients. Mean GFR in all was 70 ± 21 (18.6-128.8) ml/min. GFR in normal CAG was 78 ± 21 ml/min, with borderline CAD was 68 ± 21 ml/min, with insignificant CAD was 75 ± 21 ml/min and with significant CAD patients was 59 ± 19 ml/min. Analysis of variance between CAD and creatinine clearance was

significant ($p < 0.02$) more so when creatinine clearance of patients with significant CAD (221) was compared with creatinine clearance of those with insignificant CAD (84) using unpaired student t test. ($p < 0.004$). GFR correlated with the degree of LV dysfunction ($p < 0.01$).

Conclusions: Low GFR is common in patients with significant obstructive CAD presenting with ACS. This suggests that the patients with even early CKD are more at risk to develop significant CAD.

SaP247 ProBNP, BNP, AND NT-proBNP CIRCULATING LEVELS ARE ALTERED BY HEMODIAFILTRATION BUT STILL CORRELATE WITH VENTRICULAR FUNCTION IN CHRONIC HEMODIALYSIS PATIENTS

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Introduction and Aims: Brain natriuretic peptide (BNP) is released primarily as a prohormone proBNP that is enzymatically cleaved into the active hormone BNP and the inactive N terminal propeptide (NT proBNP). Increased circulating BNP and NT-proBNP, and in a lesser extent proBNP, have been associated with left ventricular dysfunction and with a poor outcome of patients with end stage renal failure. More recently, the prohormone proBNP determination was also available. However, the levels of circulating peptide values may be not only dependent on cardiac function and dimensions but also on renal function, fluid volume, and their removal by dialysis procedure including hemodiafiltration (HDF). The purpose of this study was (i) to assess in chronic dialysis patients the basal levels of BNP, NT-proBNP and the prohormone proBNP and their correlation with clinical and echocardiographic data (ii) to investigate their changes after a session of HDF.

Methods: 31 dialysis patients in maintenance HDF for at least 6 months without clinical or echocardiographic evidence of cardiac failure were included. Baseline clinical and echocardiographic parameters were collected. Pre and post-HDF BNP (Bayer), NT-proBNP (Dade Behring) and proBNP (Bio-Rad) plasma concentrations were measured. Correlations between echocardiographic measurements and basal circulating peptides, and between changes in peptide values and changes in fluid volume after HDF were investigated.

Results: Baseline plasmatic levels of natriuretic peptides were elevated (BNP = 517 ± 840 pg/ml, NT-proBNP = 5340 ± 6132 pg/ml and proBNP = 3569 ± 4683 pg/ml) and correlated with left auricular diameter ($r^2 = 0.25$ for BNP, $r^2 = 0.25$ for NT-proBNP and $r^2 = 0.14$ for proBNP) and left ventricular mass index ($r^2 = 0.19$ for BNP, $r^2 = 0.17$ for NT-proBNP and $r^2 = 0.12$ for proBNP). The HDF session led to a significant decrease of 39% for BNP, 59% for NT-proBNP and 36% for proBNP. This decrease was not correlated to post-HDF fluid removal or weight decrease.

Conclusions: Despite their elimination by hemodiafiltration, BNP, NT-proBNP and proBNP could be potential markers of left ventricular function in chronic renal failure patients on maintenance dialysis. According to our results, their cut-off values need to be reevaluated by further larger clinical trials.

SaP248 INFLAMMATION-RELATED IMBALANCE IN BONE MORPHOGENETIC PROTEINS (BMPs) PRODUCTION MAY FAVOUR THE PROGRESSION OF CARDIOVASCULAR DISEASE IN DIALYSIS PATIENTS (PTS)

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Introduction and Aims: Inflammation may directly modulate vascular calcification (VC) in end stage renal disease pts leading to high cardiovascular

mortality. There are evidences of BMP2 and 7 involvement in VC process, but it is still unclear whether uremic condition and chronic inflammatory status can regulate the expression of these proteins.

Methods: The relationship between BMP-2 and BMP-7 (ELISA, R&D and RayBiotech, respectively), high sensitive C-reactive protein (hsCRP), Fetuin-A (ELISA, Biovendor) serum levels and carotid intima-media thickness (cIMT, B-mode ultrasonography) were studied in 50 uremic pts, stably on hemodialysis (HD) (25 pts, mean age 60.5 years; dialytic age 49.5 months), or peritoneal dialysis (PD) (25 pts, mean age 59.1 years; dialytic age 45.4 months). The effect of inflammation on BMPs expression was evaluated in vitro in Eahy926 cells (an immortalized endothelial cell line) by RT-PCR and confocal microscopy.

Results: Significantly higher BMP-2 serum levels were found in HD compared to PD pts and normal controls (C) (C 8.1 ± 2.4 ; HD 65.1 ± 13 ; PD 28.5 ± 2.4 pg/ml; $p < .002$). On the contrary, lower BMP-7 (C 451.6 ± 59.9 ; HD 36.6 ± 6.1 ; PD 295.6 ± 60.1 pg/ml; $p < .0001$) and Fetuin-A (C 375.0 ± 78.2 ; HD 243.5 ± 42.0 ; PD 290.7 ± 58.4 mg/ml; $p < .0001$) serum concentrations were observed in HD pts as compared to PD pts and C. At univariate analyses BMP-2 serum levels were inversely correlated with Fetuin-A ($r = -.38, p < .02$) and positively correlated with CRP ($r = .3; p < .01$) and cIMT values ($r = .4; p = .003$). On the contrary, BMP-7 was directly correlated with Fetuin-A ($r = .35, p = .04$) and inversely associated with CRP ($r = -.7; p < .0001$) and cIMT ($r = -.6; p < .0001$). In a multiple regression model, cIMT was independently correlated with BMP-2, BMP-7 and CRP. Finally, an increased BMP-2 and a lower BMP-7 gene and protein expression were observed in Eahy cells upon incubation with TNF- α (100U/ml), a powerful pro-inflammatory cytokine.

Conclusions: In conclusion, inflammation-related high BMP2 serum levels along with low BMP7 and Fetuin-A concentrations are strictly correlated with progression of atherosclerotic lesions in dialysis pts.

SaP249 PREDICTIVE VALUE OF BOTH BNP AND NT-proBNP IS ENHANCED BY CRP LEVELS IN AN HEMODIALYSIS POPULATION

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Introduction and Aims: BNP and NT-proBNP levels are considered as an important diagnostic tool in congestive heart failure. They could be of predictive value in hemodialysis (HD) patients. However the relationship between cardiac natriuretic peptides levels and the HD-induced inflammatory state remains poorly investigated. The aim of this study was to explore the prognostic relevance to all-cause and cardiovascular mortalities in HD patients of BNP, NT-proBNP in combination with C-reactive protein (CRP).

Methods: We measured BNP, NT-proBNP, CRP at baseline (October to November 2001) in 130 HD patients [median age 69.0 years (range 23.4-87.7), 71 females, 59 males]. Patients were followed prospectively for mortality until January 2005. The adjusted relative risks (RRs) of death and 95% confidence intervals (CIs) were estimated using Cox proportional hazard models.

Results: During follow up, 36 patients died, 58.3% due to cardiac causes. Elevated BNP and NT-proBNP were associated with increased total and cardiovascular mortality [RR adjusted for age, gender and dialysis vintage 8.9 (2.0-39.7) for the third tertile of BNP versus the first tertile and 6.8 (1.9-24.7) for the third tertile of NT-proBNP versus the first tertile]. Moreover the combination of elevated CRP (>10.5 mg/l) impaired the HD survival rate especially the cardiovascular mortality. The combination of CRP >10.5 mg/l and BNP >75 pg/ml was associated with an increase in total (RR 5.70, 95% CI 2.38 to 13.67; $p < 0.0001$, after adjustment for age, gender and dialysis vintage) and cardiovascular mortality (RR 12.42, 95% CI 3.28 to 47.12; $p = 0.0002$, after adjustment for age, gender and dialysis vintage). Similarly, the combination of CRP >10.5 mg/ml and NT-proBNP >10204 pg/ml resulted in a raise in total (RR 5.84, 95% CI 2.32 to 14.68; $p = 0.0002$, after adjustment for age, gender and dialysis vintage) and

cardiovascular mortality (RR 20.12, 95% CI 4.24 to 95.52; $p = 0.0002$, after adjustment for age, gender and dialysis vintage).

Conclusions: Circulating BNP and NT-proBNP were associated with poor outcome, especially when combined with elevated CRP, strongly supporting their annual routine determination.

SaP250 PLASMA ADRENOMEDULLIN LEVEL PREDICTS CEREBRO AND CARDIOVASCULAR EVENTS IN MAINTENANCE HEMODIALYSIS PATIENTS

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Introduction and Aims: Adrenomedullin (AM), a vasodilative and natriuretic peptide, is correlated with cardiovascular condition and elevated in hemodialysis (HD) patients. Although the high prevalence of cerebro- and cardiovascular events (CCVE) in HD patients has been explained by several risk factors, it is still unknown whether the measurement of AM predicts subsequent CCVE in maintenance HD patients.

Methods: A total of 89 HD outpatients (age, 58.0 ± 12.9 years, mean \pm SD; male/female, 54/35; HD vintage, 97 ± 84 months) were followed up prospectively for 53 ± 13 months in a single dialysis center. At the start of this study, AM (IRMA kit, Shionogi Pharmaceutical Co.), high sensitivity C-reactive protein (hs-CRP) (N High Sensitivity CRP kit, Dade Behring Inc.), hemoglobin, albumin and lipids profiles were measured in blood samples taken just before HD treatment, in addition to blood pressure (BP) and pulse wave velocity (PWV) using form PWV/ABI (Colin Co.). The presence of death and hospitalization due to CCVE had been checked during the follow-up periods, and the prognostic values were tested by Cox's regression analysis.

Results: Plasma AM, serum hs-CRP and albumin were 27.5 ± 7.8 fmol/mL, 1.87 ± 3.53 mg/L, 3.7 ± 0.3 g/dL at baseline, respectively. Systolic BP and PWV were 155 ± 19 mmHg and 1779 ± 390 cm/sec, respectively. During the follow-up periods, 7 patients dropped out (2 with a renal transplantation and 5 with a transfer to another dialysis center) and 7 had died. Twenty-two patients had been hospitalized for and/or died of CCVE: new episodes of ischemic ($n = 8$) and non-ischemic ($n = 8$) heart disease, cerebral hemorrhage ($n = 5$) and infarction ($n = 1$). In stepwise Cox's regression analysis, CCVE was associated with age (per 10 years; relative risk [RR], 1.828; 95% confidence interval [95% CI], 1.241 to 2.6923; $p = 0.0022$) and plasma AM level (per 10 fmol/mL; RR, 1.731; 95% CI, 1.016 to 2.951; $p = 0.0436$). Divided into 3 groups by plasma AM levels (group I, <20 fmol/mL; group II, 20–30 fmol/mL; group III >30 fmol/mL), higher rate of CCVE in group III was observed compared with that in group II (RR, 4.354; 95% CI, 1.513 to 12.525; $p = 0.0064$; adjusted for age). There was no significant association between CCVE and hs-CRP or PWV in this study.

Conclusions: In maintenance HD patients, subsequent cerebro- and cardiovascular events may be predicted by the measurement of plasma AM.

SaP251 THE NITRIC OXIDE IN PATIENTS TREATED BY MAINTENANCE HEMODIALYSIS

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Introduction and Aims: Atherosclerosis is a very serious problem, especially in hemodialysed patients, because the frequency of this phenomenon in these patients is much higher than it is in general population. The endothelial nitric oxide (NO) is considered as an important atheroprotective mediator, and acquired defects in generation of NO associated with cardiovascular risk factors cause endothelial dysfunction and may lead to the development of atherosclerosis. The aim of this study was the assessment of NO serum concentration and finding factors that may influence it serum concentration in group of patients treated by maintenance haemodialysis (mHD).

Methods: To this study we enrolled 66 patients (20 of them had coronary artery disease, 12 suffered from diabetes mellitus) treated by mHD (mean

duration of HD 47.35±37.12 months). HD procedures were performed 3 times a week for 4 hours with polysulphone capillary dialyzers. The results from mHD patients were compared with reference values which were obtained from 20 healthy volunteers (HV). Serum samples were drawn at the start of the second HD from fasting patients and from fasting HV. The nitrite/nitrate (NO), vascular endothelial growth factor - 2 (VEGFR2), amino-terminal pro-brain natriuretic peptide (NT-proBNP) and soluble IL-6 receptor (sIL-6R), concentration were evaluated by the ELISA method. The concentrations of creatinine, total cholesterol, LDL-cholesterol and triglycerides were estimated by the routine laboratory tests.

Results: In mHD patients both NO (233.66±16.07 µmol/l) and VEGFR-2 (10012.3±4316.44 pg/ml) were slightly decreased but with no statistical significance if compared to HV: NO (260.11±21.24 µmol/l), VEGFR-2 (13745.35±5273.27 pg/ml). Whereas the serum concentration of NT-proBNP (152.2±68.6 fmol/ml) and sIL-6R (8051.48±2344pg/ml) were significantly higher (p=0.01, p=0.03, respectively) in comparison to HV: NT-proBNP (35.6±21.3 fmol/ml) and sIL-6R (2615.53±733.97 pg/ml). Total cholesterol, LDL-cholesterol and TG were slightly (with no statistical significance (p=0.07)) decreased in mHD patients. Serum concentration of NO inversely correlated with the presence coronary artery disease (r=-0.2, p=0.02), with the time of HD treatment (r=-0.235, p=0.004), and with serum concentration of total cholesterol (r=-0.232, p=0.004). The slightly inverse correlations but with weak statistical significance between NO and VEGFR2 (r=-0.15, p=0.058) was observed. There were no statistically significant correlations between NO and NT-proBNP, sIL-6R, triglycerides and serum creatinine.

Conclusions: mHD patients showed the propensity to the slightly lower serum concentration of nitric oxide. High serum NT-proBNP concentration confirms the increased risk of cardiovascular event in examined patients. This study suggest an important relationship between the release of NO and the duration of HD treatment and serum concentration of total cholesterol. Moreover, we found that this parameter may be slightly influenced by the regulation of VEGF-mediated blood vessel growth and development.

SaP252 SERUM VCAM-1 AND ICAM-1 INDICATED A DIFFERENT PATTERN BETWEEN SHUNT STENOSIS AND ARTERIOSCLEROSIS OBLITERANS COMPLICATED HEMODIALYSIS PATIENTS

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Introduction and Aims: Shunt stenosis is known as a life threatening factor for hemodialysis patients. In addition, some patients repeat shunt stenosis frequently. However, the mechanism of shunt stenosis has not elucidated. For coronary artery bypass grafting (CABG), graft occlusion of saphenous vein happened much more frequently than that of internal thoracic artery. Previous study showed vein grafting was weak against the blood pressure and the damage of their endothelial layer caused more severely than that of arterial grafting. For shunt vessels, stenosis occurred mainly on the connecting vein like a coronary vein grafting. The present study was undertaken to determine serum adhesion molecules levels in HD patients with shunt stenosis and arteriosclerosis obliterans (ASO).

Methods: Hundred nine shunt stenosis, 28 ASO and 50 age, gender and duration of HD matched control hemodialysis subjects were examined. Shunt stenosis determined the history of shunt occlusion or failure beyond 3 month of the operation day. The diagnosis of ASO was derived from Ankle Brachial Index (ABI) less than 0.90, and stenotic or obstructive change in angiogram. As parameters of adhesion molecules, we chose ICAM-1 and VCAM-1 and as an anti-sclerotic parameter, we chose adiponectin (ADN) respectively. The serum levels of ICAM-1, VCAM-1 and ADN were determined with ELISA. For static analysis, we use multiple regression analysis first and then use Fisher analysis for group comparison. P value less than 0.05 determined significant.

Results: In shunt stenosis group, increment of VCAM-1, decrement of ICAM-1 and ADN showed the significance by the multiple regression analysis. (p<0.001, p<0.001, p<0.005 respectively) on the other hand, ASO group also indicate increment of VCAM-1, decrement of ICAM-1 and ADN significantly (p<0.05, p<0.05, p<0.001 respectively), however, the value of regression was less than that of shunt stenosis group. For group

comparison, serum ICAM-1 levels was 191±24 ng/ml in the patients with shunt stenosis, 343±54 ng/ml in the patients with ASO and 470±31 ng/ml in control subjects. (p<0.01 among each groups) Serum VCAM-1 levels was 3255±200 ng/ml in shunt stenosis group and 3032±316 ng/ml in ASO group and 2550±149 ng/ml in control respectively. (p<0.01 only between shunt stenosis and control subjects).

Conclusions: The present results indicate that hypoalbuminemia and decrement of ICAM-1 are independent risk factors for both shunt stenosis and ASO in hemodialysis patients. For shunt stenosis, elevation of VCAM-1 is also another risk factor and suggests a different mechanism of ASO in hemodialysis patients.

SaP253 CORRELATIONS OF ARTERIAL STIFFNESS, ACE GENE I/D AND COLLAGEN1A1 GENE -1245G/T POLYMORPHISM IN PATIENTS WITH END-STAGE RENAL DISEASE

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Introduction and Aims: Arterial stiffness (AS) is an independent predictor of cardiovascular morbidity and mortality in patients with end-stage renal disease (ESRD). Structural changes in the vessel wall, like transformation of the collagen network and plaque formation can lead increased AS, a process, which can be modified by ACE-system. Human atherosclerotic lesions contain collagen type 1, which plays a pivotal role in atherosclerotic plaque stability. In contrast, the normal coronary arteries do not express this type of collagen. In our study, we evaluate the correlation between the parameters of AS, like augmentation index (AI) and pulse wave velocity (PWV), the ACE gene I/D and collagen type 1 A1 gene (COL1A1)-1245G/T polymorphism in ESRD patients.

Methods: In 81 patients on hemodialysis (HD) therapy, AS parameters (AI and PWV) were calculated twice using PulsePen device, both before and after HD procedure. COL1A1 and ACE gene polymorphisms were evaluated by RFLP techniques.

Results: Mean predialysis PWV (prePWV) and postdialysis PWV (post-PWV) were 11.0±2.9 and 11.6±2.9 m/s (P=0.0001), mean predialysis AI and postdialysis were 23.5±12.2 and 22.1±12.4% (NS), respectively. We found no correlation between the polymorphisms and prePWV or postPWV. The same was found in case of AI. In contrast, significantly different genotype pattern was found in case of collagen 1A1 gene in HD patients compared to healthy controls. The "ss" genotype of the COL1A1 gene was found to be significantly more frequent in HD patients, as compared to the control (9/94 vs. 7/212, p=0.01).

Conclusions: Our results suggest, that the studied polymorphisms of the ACE and COL1A1 genes has no significant predictive value for AS. Although, the different genotype pattern of the collagen type 1 A1 gene in HD patients - compared to controls - might be related to their higher propensity for vascular complications.

SaP254 EFFECTS OF SIMVASTATIN ON SOLUBLE MARKERS OF INFLAMMATION AND APOPTOSIS IN PATIENTS ON CHRONIC HAEMODIALYSIS (HD)

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Introduction and Aims: End-stage renal disease is considered to be a state of chronic inflammation. Emerging data reveal that HMG-CoA reductase inhibitors, beyond their lipid-lowering effects, exert pleiotropic and immune-regulatory actions as well. The purpose of the present prospective trial was to study the effects of a 6 month use of the HMG-CoA reductase inhibitor simvastatin on chronic inflammation in patients on HD. Serum levels of CRP, intracellular and vascular cell adhesion molecules (ICAM-1 & VCAM-1, respectively), E-selectin and monocyte chemoattractant protein (MCP-1)

were determined as markers of inflammation, and Fas and Fas-ligand (FasL) as markers of apoptosis.

Methods: We studied prospectively 21 patients (10 males, mean age 60 years, range 30-77) stabilized on HD (mean duration 63 months, range 7-242). In all patients 10mg of simvastatin tablets per day were prescribed for a period of 6 months. CRP was measured with the use of nephelometry. sICAM-1, sVCAM-1 and E-selectin were determined with the use of ELISA. All measurements were repeated at baseline, 3 and 6 months. Student's t-test and one-way ANOVA analysis with post-hoc multiple comparisons were used for the comparison of the levels of the parameters at different intervals.

Results: A significant reduction was found at 3 and 6 months compared to baseline levels in total cholesterol (184.7 ± 41 and 170.1 ± 44 vs 236.1 ± 40.7 mg/dL, $p=0.003$ and $p<0.0001$, respectively) and LDL (105.5 ± 37 and 102.9 ± 41 vs 152.5 ± 32 mg/dL, $p<0.001$ and $p<0.001$, respectively). Serum CRP levels in 6 months were also decreased compared to baseline (3.44 ± 0.7 vs 9.25 ± 8.3 mg/L, $p=0.012$). At 3 and 6 months, a decrease in sICAM-1 was found compared to baseline (450.9 ± 162.0 and 348.5 ± 104.1 vs 498.55 ± 133.75 ng/mL, $p=NS$ and $p=0.005$, respectively). Similarly, a significant reduction at 3 and 6 months compared to baseline was noticed in sVCAM-1 levels (2270.9 ± 680.7 and 1773.82 ± 506.7 vs 2553.9 ± 732.0 ng/mL, $p=NS$ and $p=0.002$, respectively). No significant differences were found between baseline, 3 and 6 months in the levels of MCP-1 and E-selectin. Fas was found decreased at 3 and 6 months compared to baseline (20968.7 ± 5824.4 and 17609.8 ± 2987.2 vs 21128.8 ± 6161.3 pg/mL, $p=NS$ and $p=0.03$, respectively). FasL showed a decrease as well at 3 and 6 months compared to baseline, which however did not reach statistical significance (92.6 ± 40.3 and 91.6 ± 36.1 vs 100.9 ± 31.4 pg/mL, $p=NS$ and $p=NS$, respectively).

Conclusions: A 6 month use of simvastatin, even at low dose, resulted in a significant lowering of CRP, ICAM-1, VCAM-1, and Fas but not E-selectin, MCP-1 or FasL levels, in parallel to the lowering in total and LDL cholesterol levels. These effects might be of potential therapeutic significance for the prevention of atherosclerosis in this patient group.

SaP255 PROGNOSTIC VALUE OF RIGHT VENTRICULAR SYSTOLIC AND DIASTOLIC FUNCTION ASSESSED BY DOPPLER TISSUE IMAGING IN DIALYSIS PATIENTS WITH HEART FAILURE

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Introduction and Aims: The presence of right ventricular systolic dysfunction is known to significantly worsen the prognosis of patients with heart failure. However, the prognostic impact of right ventricular diastolic dysfunction and of its combination with right ventricular systolic dysfunction and with other prognostic markers has not yet been systematically studied in dialysis patients. The aim of this study was to assess the prognostic impact of combined right ventricular systolic and diastolic dysfunction in patients with heart failure due to ischemic or idiopathic dilated cardiomyopathy.

Methods: The study included 152 patients on periodic hemodialysis (mean left ventricular ejection fraction of 29,2%) from 31 Italian clinics belonging to a clinic network using a prospective database (EuCliD). All patients underwent clinical and laboratory examination and standard echocardiography completed by Doppler tissue imaging of the tricuspid annular motion. They were followed up for a mean period of 18 months.

Results: During the follow-up, there were 25 cardiac-related deaths and 38 non-fatal cardiac events (33 hospitalizations for heart failure decompensation and 5 hospitalizations for malignant arrhythmias). The multivariate stepwise Cox regression, the right ventricular systolic (represented by the peak systolic tricuspid annular velocity-Sa) and diastolic (represented by the peak early diastolic tricuspid annular velocity-Ea) function to be the independent predictors of event-free survival or survival ($p<0.01$). The Sa was better predictor for the risk of cardiac events ($p<0.05$), while the Ea appeared to further distinguish patients with increased risk of early non-fatal event and early death rather than risk of late event from those at risk. The combination of Sa and Ea, creating the Sa/Ea categories, was the strongest predictor of

events: the Sa/Ea I category of patients ($Sa \geq 10.8$ cm s⁻¹ and $Ea \geq 8.9$ cm s⁻¹) had excellent prognosis; while the Sa/Ea IV category ($Sa < 10.8$ cm s⁻¹ and $Ea < 8.9$ cm s⁻¹) was found to be at a very high risk of cardiac events ($p<0.001$ vs. Sa/Ea I). Imbalanced categories of patients (Sa/Ea II and III) with only one component (Sa or Ea) pathologically decreased were at medium risk when assessing event-free survival. However, a significantly better survival ($p<0.05$) was found in patients with $Ea \geq 8.9$ cm s⁻¹ (Sa/Ea I and III categories) as compared with those having $Ea < 8.9$ cm s⁻¹ (Sa/Ea II and IV categories). In contrast to event-free survival, the survival pattern was determined mainly by the Ea value with only little additional contribution of Sa.

Conclusions: The assessment of right ventricular systolic and diastolic function provides complementary information with a very high power to stratify prognosis of patients with heart failure and on hemodialysis. The combination of right ventricular systolic and diastolic dysfunction identifies those with a very poor prognosis.

SaP256 CLINICAL EVIDENCE OF THE ROLE OF SECONDARY HYPERPARATHYROIDISM IN UREMIC LEFT VENTRICULAR HYPERTROPHY PROGRESSION

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Introduction and Aims: Left ventricular hypertrophy (LVH) is a very common finding in end-stage renal disease patients and represents an independent risk factor for mortality, whereas the occurrence of LVH may share a multifactorial origin. The impact of various PTH levels on left ventricular hypertrophy (LVH) progression in hemodialysis patients (pts) is still ill defined.

Methods: We retrospectively evaluated 60 of 118 HD pts who underwent echocardiography examination at baseline (B) and follow-up (F-U; 11.5 ± 1.0 months). From the study were excluded pts with: systemic disease; valvular disease; coronary heart disease; interdialytic body weight gain (IDBWG) greater than 6% b.w.; abnormal systolic function (ejection fraction less than 55%); previous parathyroidectomy. We identified three subgroups (G) according to PTH variations throughout the observation period. Group 1 ($n = 19$), with PTH values steadily < 200 pg/ml throughout the F-U; Group 2 ($n = 20$), with a progressive increase of PTH levels to values > 200 pg/ml, 16/20 pts received calcitriol intravenously after HD at a dose ranging from 1 µg to 3 µg twice/week; Group 3 ($n = 21$), with PTH levels > 200 pg/ml and $> 50\%$ reduction after intermittent calcitriol therapy intravenously at a dose ranging from 1 µg to 4 µg twice/week.

Results: PTH levels were correlated with LVMI ($r = 0.714$; $P < 0.001$), LV end diastolic diameter ($r = 0.464$; $P < 0.001$), interventricular septal thickness ($r = 0.395$; $P < 0.01$), and LV posterior wall thickness ($r = 0.279$; $P < 0.05$). Furthermore, significant correlations were found between mean systolic ($r = 0.338$, $P < 0.01$) and diastolic blood pressure ($r = 0.353$; $P < 0.01$) and LVMI. Patients with baseline PTH levels > 200 pg/ml ($n = 27$) had a higher LVMI with respect to those with PTH < 200 pg/ml ($n = 33$) (195 ± 50 vs 135 ± 31 g/m²; $P < 0.01$). In G1 LVMI did not change during F-U. In G2 LVMI increased from 146 ± 26 to 175 ± 46 g/m² ($P < 0.05$). In G3 LVMI decreased from 210 ± 44 to 154 ± 42 g/m² ($P < 0.001$). Multivariate analysis showed that PTH was the most important predictor for the progression of LVH followed by systolic blood pressure, while we failed to find any relationship between LVMI and IDBWG, calcitriol, serum calcium, and hemoglobin.

Conclusions: PTH per se may play an important role in the genesis and perpetuation of LVH, whereas partial correction of sHPT with injectable calcitriol may determine LVH regression.

SaP257 EFFECTS OF CHRONIC HAEMODIALYSIS THERAPY ON HEART RATE VARIABILITY IN CHRONIC KIDNEY DISEASE IN PATIENTS WITH AND WITHOUT DIABETES

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Introduction and Aims: Cardiac autonomic dysfunction is a common complication in patients with chronic kidney disease (CKD) and may contribute to increased cardiovascular morbidity and mortality in this population. Heart Rate Variability (HRV) is an established non-invasive method for the evaluation of autonomic nervous system activity at the heart level (CAN). Both type 2 diabetes mellitus (T2DM) and CKD have been repeatedly shown to affect HRV and their concurrence on the same patient results in poorer mid-term cardiovascular prognosis.

AIM: To evaluate CAN in diabetic and non-diabetic patients with stage 4 CKD, by means of HRV measurements, and to evaluate the effect of chronic haemodialysis on the same patients 3 months after initiation of dialysis.

Methods: This was a prospective study of 100 patients divided into four groups: Group 1: 25 patients with T2DM and CKD stage 4 (age 67±9 years, 11 men); Group 2: 25 non-diabetic patients with CKD stage 4 (age 65±7 years, 14 men); Group 3: 25 patients with T2DM but without CKD (age 67±7 years, 10 men); and Group 4: 25 healthy controls (age 65±3 years, 10 men). CAN was measured in all patients, using 24-hours ECG-Holter monitoring with HRV analysis in both time domain [min HR interval, maxHR, SDNN, ASDNN, SDANN, SD) and frequency domain (total power, LF, VLF, LF/HF ratio). For the Groups 1 and 2, HRV measurements took place before and 3 months after initiation of haemodialysis.

Results: Both time and frequency domain parameters were worse in the Groups 1-3 in comparison with the Group 4 (p<0.05). Among Groups 1, 2 and 3 no significant differences were observed, except for the LF/HF ratio, which was higher in Group 1 in comparison with the Group 2 (p = 0.001) and Group 3 (p = 0.02). Three months after initiation of haemodialysis, patients in Group 2 showed improvement in several time domain parameters (maxHR (p = 0,021), meanRR (p = 0,025), HR (p = 0,024), SDNN (p = 0,036), SDANN (p = 0,013) and SD (p = 0,032), while patients in Group 1 had improvement only in (SDANN, p = 0.04). No significant difference was observed in the frequency domain parameters after the initiation of haemodialysis in either study group.

Conclusions: The lack of significant difference in most of the HRV parameters among the patients with CKD or diabetes probably reflects the dual cause of autonomic dysfunction in these patients, namely uremia and hyperglycaemia. Haemodialysis improved only the time domain parameters of HRV in the non-diabetic patients with CKD but not in the patients with diabetes and CKD. This finding suggests that diabetic patients with CKD may have poorer prognosis in terms of cardiovascular events and overall survival.

SaP258 IMPACT OF MYELOPEROXIDASE (MPO) ON LIPIDS OXIDATION AND CAROTID PLAQUE FORMATION IN HEMODIALYSIS PATIENTS (HD pts)

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Introduction and Aims: MPO is an important source of oxidative stress in HD pts, however, associations between MPO, lipid oxidation, and atherosclerosis in those pts are not fully evaluated.

Methods: In one hundred and eighty-six HD pts (aged 65±13 years, 58% males, diabetes mellitus: DM 31%, HD vintage 77 months: range 1.0-346), WBC count including differential WBC, high sensitive C-reactive protein (hsCRP), s-albumin (s-Alb), lipids (Cholesterol: chol, HDL-chol, LDL-chol,

oxidized(ox) HDL-chol, oxLDL-chol), MPO and oxα1 antitrypsin(AT) as an activated PMN-linked oxidative stress marker were measured before HD session. Carotid artery intima-medial thickness (IMT) was analyzed by B mode ultrasonography and the maximum value of IMT (max IMT) measured in the bilateral carotid artery in each patient.

Results: MPO levels were correlated with WBC (rho=0.18, p=0.01), ox LDL-chol (rho=0.44, p<0.0001), ox HDL-chol (rho=0.32, p<0.0001), ox AT (rho=0.60, p<0.0001) and max IMT (rho=0.25, p=0.001). Ox HDL-chol (179.8±49.1 ng/mL versus 155.9±64.1 ng/mL, p<0.0001) and ox AT levels (83.6±40.4 ng/mL versus 44.1±22.9 ng/mL, p<0.0001) and ox LDL-chol (56.8±27.5 U/L versus 35.6±11.9 U/L, p<0.0001) as well as max IMT (1.57±0.79 versus 1.18±0.4, p=0.001) were significantly increased in a high MPO group divided by median MPO level, while HDL-chol and LDL-cho levels did not differ between a high and a low MPO group. In univariate model MPO, oxLDL and oxAT associated to max IMT but not for oxHDL-chol. MPO (β=0.11, p=0.04) and ox LDL-chol (β=0.13, p=0.008) were independently associated with max IMT by a backward stepwise multivariate regression analysis included age, gender, DM, hsCRP, WBC, MPO, HDL-chol, oxLDL-chol, and oxAT as independent factors (adjusted r²=0.28). In this model ox AT tended to be linked to max IMT (β=0.09, p=0.08).

Conclusions: In conclusion, MPO seems to influence lipid oxidation and plaque formation as a consequence of excess oxidative stress in HD pts.

SaP259 HEMODIALYSIS EFFECTS ON PULSE WAVE ANALYSIS: MEMBRANE BIOINCOMPATIBILITY AND ULTRAFILTRATION EFFECTS

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Introduction and Aims: Cardiovascular disease is a major cause of morbidity in dialysis patients. Among other, repetitive endothelial damage from dialysis membrane bioincompatibility has been proposed as a contributing factor of accelerated atherosclerosis. Increased aortic stiffness has emerged as a powerful predictor of survival in dialysis and can be measured non invasively using pulse wave analysis technology (PWA). It is not clear whether hemodialysis (HD) per se acutely affects endothelial function or mechanical vessel wall properties as a result of the membrane bioincompatibility or ultrafiltration. **Aims:** To analyse separately the effects on arterial stiffness of membrane bioincompatibility and ultrafiltration during an HD session.

Methods: PWA was obtained by applanation tonometry (SphygmoCor®). Studied variables included: the augmentation index (AI), subendocardial viability ratio (SEVR), ejection duration (ED), and aortic systolic and diastolic blood pressure. Membrane bioincompatibility was detected by successive white blood cell counts in the ADVIA autoanalyzer and C3a generation (enzyme immunoassay Quidel).

a) Bioincompatibility effects analysis: leucocyte count, C3a levels and PWA were monitored before, at 15, and at 30 minutes of HD session in 10 patients using a cellulose diacetate membrane (Baxter). In order to avoid the effects of intravascular volume changes on PWA, fluid removal was completely avoided (ultrafiltration=0) during the 30 minutes of monitoring.

b) Ultrafiltration effects analysis: PWA was performed before and after a conventional HD session with the same membrane in 19 patients (mean ultrafiltration: 2,41±1,04 kg).

Results: a) A significant decrease in leucocyte count occurred at the beginning of HD: 6801±1186 vs 4412±1333 at 15 minutes (p<0,001), while C3a levels sharply increased from 427±269 to 3501±1638 ng/ml at 15 minutes (p<0,000), being both parameters inversely correlated (r² = 0,74, p=0,01). No changes were demonstrated in any of the variables analysed in PWA: AI (28±11 vs 29±15), ED (38±6 vs 36±5), SEVR (124±30 vs 139±29). Only aortic systolic BP was lower at 15 minutes: 118,5±16 vs 107,2±22 (p=0,009), in agreement with a reduction of brachial systolic BP: 154,7±24 vs 134,0±32 (p=0,01), without changes in aortic or brachial diastolic BP.

b) In contrast, important changes in PWA were observed during the HD session due to ultrafiltration: AI 31 ± 11 vs 19 ± 16 , ED 37 ± 4 vs 32 ± 4 , SEVR 124 ± 20 vs 171 ± 36 , central aortic systolic BP 139 ± 25 vs 119 ± 27 (all $p<0.00$), central aortic diastolic BP 75 ± 13 vs 75 ± 17 (p:ns).

Conclusions: HD with cellulose diacetate acutely induced a transient state of immunoactivation due to bioincompatibility, non detectable by PWA. Ultrafiltration during HD session leads to important changes in PWA.

SaP260 AVERAGE SYSTOLIC BLOOD PRESSURE AND PULSE PRESSURE IN 48-HOUR AMBULATORY BLOOD PRESSURE MONITORING AND POSTDIALYSIS N-TERMINAL proBNP LEVEL REFLECT LEFT VENTRICULAR HYPERTROPHY IN STABLE HEMODIALYSIS PATIENTS

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Introduction and Aims: Hypertension and left ventricular hypertrophy (LVH) are risk factors for mortality in hemodialysis patients. We investigated whether N-terminal pro-brain natriuretic peptide (NT-proBNP) and the parameters of ambulatory blood pressure monitoring (ABPM) are associated with cardiac abnormalities in hemodialysis (HD) patients.

Methods: We measured pre- and postdialysis NT-proBNP and 48h-ABPM and performed echocardiography. The HD day was defined as the 24hr period beginning at 1h after the start of HD, and the interdialytic day was defined as the subsequent 24h. The study involved 68 stable HD patients: 35 males, 33 females; mean age 49.5 ± 14.3 years; mean HD duration 53.1 ± 44.9 months; 27 (39.7%) with diabetes mellitus (DM).

Results: Mean pre- and postdialysis NT-proBNP were 8832.4 ($209.9 - 25786.0$) and 10500.1 ($226.8 - 34215.5$) pg/ml, respectively. Patients with LVH ($n=42$) had a higher average systolic blood pressure (SBP) and pulse pressure (PP) on the HD day (151.9 ± 19.8 vs. 130.3 ± 23.1 ; 73.1 ± 19.5 vs. 53.4 ± 18.4 mmHg), the interdialytic day (153.2 ± 14.7 vs. 141.6 ± 23.5 , 72.2 ± 23.2 vs. 63.4 ± 17.6 mmHg) and 48h (152.5 ± 27.4 vs. 140.1 ± 23.0 mmHg, 70.8 ± 24.4 vs. 62.7 ± 18.4 mmHg, respectively) than those without LVH ($p<0.05$), and pre- (14231 ± 10377.4 vs. 5490.0 ± 4754.0 pg/ml) and postdialysis (16218.5 ± 11407.0 vs. 6960.2 ± 5963.0 pg/ml, respectively) NT-proBNP levels were also greater in patients with LVH ($p<0.05$). Simple regression analysis, average SBP, PP on the HD day ($r = 0.58$, $r = 0.31$), the interdialytic day ($r = 0.56$, $r = 0.27$), and 48 h ($r = 0.59$, $r = 0.22$), and pre- and postdialysis NT-proBNP ($r = 0.86$, $r = 0.84$, respectively) was significantly correlated with LVM index ($p<0.05$), and average SBP, PP on the HD day ($r = -0.304$, $r = -0.317$), 48 h ($r = -0.276$, $r = -0.379$), and pre- and postdialysis NT-proBNP ($r = -0.255$, $r = -0.272$, respectively) inversely correlated with ejection fraction (EF). On multiple regression analysis, average SBP on the HD day and postdialysis NT-proBNP were the only variable linked to LVM index ($R^2=0.566$, $p=0.006$), and postdialysis NT-proBNP to EF ($R^2=0.204$, $p=0.012$).

Conclusions: These results suggest that the absolute value of the average SBP on the HD day and postdialysis NT-proBNP may predict LVH and cardiac dysfunction in stable HD patients.

SaP261 ESTIMATED GLOMERULAR FILTRATION RATE FORMULA AND RELATIONSHIP TO EARLY PATIENT OUTCOME POST CARDIAC SURGERY

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Introduction and Aims: Pre-operative Kidney function is a powerful predictor of operative mortality in patients undergoing coronary artery bypass surgery. Modification of Diet in Renal Disease (MDRD) study equation gives an estimated glomerular filtration rate (eGFR) adjusted for body-surface area. The aim of this study was to explore relationship between assessment of kidney function by the MDRD equation and patient outcome.

Methods: The eGFR was calculated for a patients undergoing cardiothoracic surgery over a 6 month period. The presence of additional risk factors, hypertension and diabetes was recorded.

Results: Retrospective analysis of patient records regarding renal complications and outcome to discharge was available for all patients & at 6 weeks for 78% ($n=264$). The mean age was 65 ± 11.8 years: (range 26-90). The Male female ratio was almost 4:1. 43% had treated hypertension pre-surgery, 19% had hypertension and diabetes and 6% had diabetes alone. Total Diabetes ($n=65$) The mean serum creatinine was $104\pm 44\mu\text{mol/l}$. 25% ($n=63$) had a raised serum creatinine. 1% ($n=3$) had a serum creatinine $>200\mu\text{mol/l}$. 4% ($n=12$) had creatinine $>150\mu\text{mol}$. The MDRD formula identified significantly higher incidence of renal dysfunction. Mean eGFR was 60 ± 15.8 mls/min/1.72m^2 . 178 (59%) patients had an eGFR >60 mls/min/1.72m^2 . 111 (37%) had an eGFR >30 mls/min/1.72m^2 . 9 (3%) patients had more severe renal failure, 1 of which was on dialysis pre surgery. For patients with Diabetes, the corresponding incidence was 59%, 34% and 6.5%. For hypertension, 51%, 43% and 5.5%.

There were 10 deaths at 6 weeks post surgery – overall mortality 3.3%. 3 patients with eGFR >60 mls/min/1.72m^2 required dialysis post operatively and 2 died (1.2%). 8 patients with eGFR >30 mls/min/1.72m^2 required dialysis, 4 died. & 4 other deaths in this group. Total (7.6%). Nopatients with more severe renal failure died though 2 required dialysis post operatively. 13 patients required dialysis post operatively (6 died – 46% mortality). 16 had a significant rise in creatinine $>25\%$, 1 died.

Conclusions: There is a high prevalence of chronic kidney disease in patients undergoing cardiothoracic surgery. Risk factors such as hypertension or diabetes were not a strong predictor to the likelihood of renal disease. Patients with pre-existing renal disease were at a higher risk of death and a need for dialysis post surgery.

SaP262 THE DIFFERENCE OF CHANGE OF B TYPE NATRIURETIC PEPTIDE (BNP) AND N-TERMINAL-proBNP DURING HEMODIALYSIS

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Introduction and Aims: The most important cause of mortality in end-stage renal disease (ESRD) patients receiving maintenance hemodialysis (HD) is cardiovascular diseases, such as ischemic heart disease and congestive heart failure (HF). The cardiovascular risk factors are lipoprotein(a), inflammation, abnormal calcium/phosphate metabolism, uremic toxin and volume overload. Blood measurements of B type natriuretic peptide (BNP) and N-terminal-proBNP (NT-proBNP) have been used to identify patients with HF and they are biochemical marker of cardiac mortality. BNP is cleaved with NT-proBNP from pre-proBNP by ventricular myocyte stretch. But, the elimination by dialysis of this two peptides are different. BNP is easy eliminated by HD due to small sizes and short half-life. We evaluated the difference of this two natriuretic peptides before and after HD and the relationship with echocardiography. And we compared this relationship according to left ventricular (LV) geometry.

Methods: We measured BNP, NT-proBNP and echocardiography before and after HD in patients without HF who had been undergoing regular HD for a period of at least 3 month at Eulji university hospital from March 1, 2004 to February 30, 2006 ($n=34$). Patients are divided to normal and abnormal (concentric remodeling, eccentric LV hypertrophy and concentric LV hypertrophy) group by LV geometry.

Results: The effect of HD on plasma concentrations of BNP and NT-proBNP was different. BNP was significantly decreased after HD (preHD vs postHD, 187.0 ± 237.0 vs 138.5 ± 187.5 pg/mL, $p<0.001$), and NT-proBNP was significantly increased after HD (6258.7 ± 7331.2 vs 8368.0 ± 9352.0 pg/mL, $p<0.001$). BNP was related to left atrial volume index (LAVI) at preHD ($r=0.435$, $p=0.018$) and postHD ($r=0.503$, $p=0.005$). NT-pro BNP was related to interventricular septum in diastole (IVSd) at preHD ($r=0.498$, $p=0.003$) and postHD ($r=0.453$, $p=0.007$) and LV mass index (LVMI) at preHD ($r=0.413$, $p=0.019$) and postHD ($r=0.455$, $p=0.009$). But amount of ultrafiltration and Kt/V were not related to BNP and NT-proBNP. Abnormal LV geometry group compared with normal group was higher BNP (243.3 ± 300.3 vs 120.0 ± 97.8 pg/mL, $p=0.126$) and NT-proBNP (9362.8 ± 8479.2 vs 2787.8 ± 3514.0 pg/mL, $p=0.006$). The changes of BNP(postHD, abnormal vs normal group, 119.9 ± 97.8 vs 99.1 ± 88.1

pg/mL), and NT-proBNP(12396.7±10517.5 vs 3835.8±5065.4 pg/mL) during HD in both groups were same with previous results.

Conclusions: BNP and NT-proBNP were correlated with LV geometry and NT-proBNP was superior than BNP in our HD patients. This is similar to the results of cardiac patients with normal renal function. BNP was decreased and NT-proBNP was increased during HD. The cause of increase in NT-proBNP could be suggested to increased production during HD and late elimination due to large molecular weight and long half-life of NT-proBNP and characteristics of hemodialyzer. So, further study for the clearance of natriuretic peptides according to different hemodialyzer and evaluation for cause of increase of natriuretic peptide production and secretion during HD session is necessary.

SaP263 SPATIAL QRS-T ANGLE IN PERITONEAL DIALYSIS PATIENTS: ASSOCIATION WITH COMMON CAROTID ARTERY INTIMA-MEDIA THICKNESS AND CORONARY ARTERY CALCIFICATION

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Introduction and Aims: The spatial angle between the directions of ventricular depolarization and repolarization (QRS-T angle), is a combined measurement of the electrical activity of the heart and predicts cardiovascular morbidity and mortality in various groups of patients.

We designed this study with 2 objectives: (1) to estimate the spatial QRS-T angle in a group of selected peritoneal dialysis (PD) patients, and (2) to assess the possible association between QRS-T angle and coronary artery calcium burden, atherosclerosis, and some biochemical measurements.

Methods: The angular differences between the maximum spatial QRS and T vectors were reconstructed from the digitally stored 12-lead ECG in 52 PD patients and in 65 controls. In PD patients coronary artery calcification (CAC) score was performed by using multi-row computed tomography. Atherosclerotic disease was assessed by measuring common carotid artery (CCA) intima-media thickness (IMT) and plaque score (sum of maximum thickness in millimeters of all plaques on both sides) by using an ultrasound scanner.

Results: QRS-T angle values were more than twofold higher, in PD patients compared with controls (31.42±12.88 and 13.05±7.87 respectively; p<0.001).

Median CAC score equaled 16.1 Agatston units (range, 0 to 2478). No calcification (CAC score < 10 Agatston units) was found in 26,3%. Agatston score was > 400 units in 36,8% of patients. IMT was increased (>1.0 mm) in 78,8%, and atherosclerotic plaques were detected in 84,6% of patients. The plaque score was 7.57±5.49. In 32,7% of patients, troponin T values were > 0.1 mmol/l.

QRS-T angle values were higher in patients with CAC score > 400 Agatston units compared with patients with CAC score < 400 Agatston units (p=0.015). QRS-T angle values were also higher in patients with IMT > 2 mm compared with those with IMT < 2mm.

The Pearson test showed significant correlation between QRS-T angle and HDL (r= - 0.322, p=0.015), troponin T (r= 0.359, p=0.006), CAC score (r= 0.418, p=0.001), and plaque score (r= 0.339, p=0.010). The relation between QRS-T angle and hemoglobin was borderline (r= - 0.253, p=0.058).

Using multivariate analysis, either CAC score or troponin T level were found to be independent predictors of QRS-T angle values.

Conclusions: The spatial QRS-T angle is high in PD patients and is mainly associated with coronary artery calcium burden and troponin T elevation. The possible clinical importance of the higher QRS-T angle in PD patients remains to be confirmed in further studies.

SaP264 ULTRASOUND GUIDED COMPRESSION (USGC) ON IATROGENIC FEMORAL PSEUDOANEURYSMUS (FPA) IN HEMODIALYSED (HD) PATIENTS

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Introduction and Aims: As the femoral artery cannulation (FAC) appeared to be the most reliable access for diagnosis and therapy of cardiovascular diseases in HD pts, the risk of FPA especially in aged pts with more advanced atherosclerosis should be considered.

Methods: We assessed the occurrence of FPA as well as usefulness of USGC as the first line conservative therapy of FPA in the group of 37 consecutive HD pts (23M, 14F, aged 55,5±8,2 years, on HD 24,2±22,6 mths) who after FAC underwent regular femoral duplex USG (FdUSG). Indications for FAC were as follows: cardiac angiography (31/37); coronary angioplasty (4/37); renal artery angioplasty (2/37). Only 4 pts were on systemic anticoagulation. FdUSG was performed immediately after release the compression of artery after FAC.

Results: FPA was found in 9/37 (24%) pts, had size from 2,3 to 5,8cm (mean 3,6cm) with size of neck of PA 1,3 to 3,0mm (mean 1,8mm), aged 12±8 hours after release of the FA compression. Our protocol of USGC included vascular surgery standby, identification of PA channel to native artery (it means neck of PA), then two consecutive 20min compression intervals to obliterate blood flow with 9MHz probe and restudy after 24hrs. USGC resulted in successful thrombosis in 5/9pts but failed in 4 other patients, who required standard surgical operation. The failed group was older (64±8 years) with more advanced atherosclerosis. The size of PA, especially the neck of PA, as well as the age of PA was similar in both groups of patients.

Conclusions: In conclusion, we recommend USGC as the first line conservative therapy of FPA being in our material rather frequent complication of FAC in HD pts.

SaP265 LOW CHOLESTEROL ALONG WITH HIGH INFLAMMATION LEVEL PREDICT MORTALITY IN HEMODIALYSIS PATIENTS

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Introduction and Aims: An inverse association between total serum cholesterol (TChol) and mortality has been observed in hemodialysis (HD) patients. The verification of this "reverse epidemiology" as well as the potential role that inflammation concomitantly plays in this phenomenon is being explored in the present study.

Methods: A group of 136 stable HD patients was prospectively followed and cardiovascular disease (CVD) as well as all-cause mortality was recorded for a time period of 24 months. Baseline characteristics, lipid profile and inflammatory indexes were investigated as potential survival predictors.

Results: During follow-up 21 deaths (11 due to CVD), 9 renal transplantations and 5 losses to follow-up occurred. In univariate Cox regression survival analysis, decreasing TChol, increasing C-reactive protein (CRP), Interleukin-6 (IL-6) and IL-6 x soluble IL-6 receptor/soluble gp130 ratio were common predictors for both CVD and all cause mortality. Decreasing body mass index and decreasing interleukin-10 (IL-10) level were additional predictors for CVD mortality. In multivariate Cox regression analysis, decreasing TChol was the common significant predictor for CVD (RR 0.98, 95% CI 0.96-1.00, p = 0.03, mean±SD TChol 167.4±47.9 in survivors vs. 122.0±26.5 mg/dl in non-survivors) and all cause mortality (RR 0.98, 95% CI 0.97-0.99, p = 0.04), while increasing IL-6 and decreasing IL-10 were additional predictors for CVD (RR 7.14, p = 0.05 and RR 0.97, p = 0.05 respectively, mean±SD IL-6 9.5±8.9 in survivors vs. 18.2±15.9 pg/ml in non-survivors and IL-10 11.3±21.5 in survivors vs. 5.5±4.6 pg/ml in non-survivors) and increasing CRP for all-cause mortality (RR 6.28, p

= 0.001, mean±SD CRP 9.4±11.6 in survivors vs. 23.1±18.8 mg/ml in non-survivors).

Conclusions: Increased pro-inflammatory and decreased anti-inflammatory activity in concert with low cholesterol seems to influence survival in HD patients. Thus, it seems that reverse epidemiology applies in the case of low cholesterol levels, though it could be largely explained by the increased inflammatory activity observed in this population.

SaP266 THE INFLUENCE OF SPIRONOLACTONE ON PLASMA LEVEL OF PLASMINOGEN-ACTIVATOR INHIBITOR TYPE 1 (PAI-1) IN ANURIC HEMODIALYSIS PATIENTS

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Introduction and Aims: It was established that aldosterone mediates fibrosis, collagen formation and target organ dysfunction particularly by induction of vascular smooth muscle cell hypertrophy, and endothelial dysfunction. Such effect of aldosterone is realized mainly by the modulation of PAI-1 expression.

The aim of our study was to assess the effect of aldosterone receptor blockade by spironolactone on plasma PAI-1 level in anuric hemodialysis patients.

Methods: 83 anuric hemodialysis patients (mean age – 50,74±9,44 years) have been studied, dividing in 2 groups. Group 1 patients (n= 42) received usual therapy, group 2 (n=41), in addition to standard therapy, received spironolactone (25 mg per day) during the 6 months. PAI-1 activity levels were measured using an assay with standardized commercial kits (Biopool Inc.), with results expressed as units per milliliter.

Results: The basal levels of PAI-1 in group 1 and group 2 were 6,1±0,11 U/ml and 5,2±0,05 U/ml, respectively (the upper limit of normal is 3,5 U/ml). After 6 months of follow up the level of PAI-1 in group 1 decreased significantly (3,1±0,11 U/ml, p < 0,0001). In group 2 mean PAI-1 level remained unchanged (p>0.05).

No patients developed hyperkalemia during the spironolactone treatment period.

Conclusions: (1) Blocade of aldosterone receptors by spironolactone in hemodialysis anuric patients reduces PAI-1 level, thus, preventing endothelial dysfunction and vascular smooth muscle cell hypertrophy.

(2) In such patients long-term (6 months) treatment with spironolactone in low doses does not induce hyperkalemia.

SaP267 VITAMIN E-COATED CELLULOSE ACETATE DIALYSIS MEMBRANE: LONG TERM EFFECT ON INFLAMMATION AND OXIDATIVE STRESS

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Introduction and Aims: Chronic inflammation and oxidative stress association is prevalent in patients undergoing hemodialysis (HD). Vitamin E is a fat-soluble antioxidant that reduces lipid peroxidation and the generation of reactive oxygen species. Our aim was to investigate the influence of a vitamin E-coated cellulose acetate (CAE) membrane on oxidative and inflammation biomarkers.

Methods: Nine stable HD patients (median age: 66 years, range: 50-71; median HD duration: 52 months, range: 8-142) dialyzed 3 times a week with polysulfone (PS) low flux membrane, for 12 hours/week (9-15), were switched to CAE membrane for 3 months and then changed back to PS membrane again for 6 months. Diabetics, patients on ACE inhibitors, statins, corticosteroids or with evidence of inflammatory disease were excluded. Oxidative stress biomarkers measured were: Reactive oxygen metabolites and derivatives (d-ROMs) (d-ROMs Test™-FRAS 4, Grosseto, Italy) and total anti-oxidant capacity (TAC) by spectrophotometry, and superoxide dismutase (SOD) by ELISA. Inflammation biomarkers measured were:

High sensitivity CRP (Hs-CRP), IL-6 and TNF-α by ELISA. Blood samples were taken, before dialysis session, at baseline, 3 (end of use of CAE) and 9 months after, then centrifuged and frozen at -70°C. All patients underwent HD with low molecular weight heparins and received rHuEpo, iron, carnitine and folic acid. During the study all dialysis parameters, except membranes, were kept unchanged. Non-parametric tests were applied for statistical analysis.

Results: The results are reported in the Table 1: Oxidative stress biomarker d-ROMs lowered significantly 6 months after CAE treatment. TAC rose, also significantly, by the same time while SOD increased rapidly and immediately after the end of CAE treatment. Inflammation markers Hs-CRP, TNF-α and IL-6 were significantly lowered, late, at 6 months after CAE treatment.

Table 1: Changes of inflammation and oxidative stress biomarkers

	Baseline	3 months	9 months	P
Hs-CRP (µg/ml)	15.9±8.7*	13.6±9.3	2.9±1.9*	*<0.03
IL-6 (pg/ml)	12.6±7.6*	11.0±10.1	5.8±4.3*	*<0.02
TNF-α (pg/ml)	15.5±6.6	23.9±23.4*	9.3±8.4*	*<0.04
d-ROMs (Units)	321.7±48*	338.4±99.4	288.2±63.7*	*<0.03
TAC (mmol/l)	1.3±0.3*	1.4±0.3	1.5±0.3*	*<0.02
SOD (U/ml)	9.2±6.6*	14.3±8.3*	13.4±6.8	*<0.009

Conclusions: Vitamin E-coated cellulose acetate dialysis membrane leads to an increase in anti-oxidant serum activity, as evidenced by SOD, immediately, and on the long-term by TAC rise and d-ROMs decrease. This was associated with a delayed effect on inflammation indices as evidenced by Hs-CRP, TNF-α and IL-6 lowering by the end of the study.

SaP268 CARDIOVASCULAR OUTCOME IN ASYMPTOMATIC HAEMODIALYSIS PATIENTS SUBMITTED TO AGGRESSIVE MEDICAL THERAPY: A 30-MONTH FOLLOW UP

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Introduction and Aims: During May and June 2004 a baseline 99mTc sestamibi stress myocardial perfusion scintigraphy (SPECT) was performed in thirty-one asymptomatic HD patients with no history of cardiovascular disease (CVD) nor clinical, electrocardiographic or ultrasonographic signs of myocardial ischemia. Silent myocardial ischemia (SMI) consisting in significant reduction of myocardial perfusion under stress in otherwise asymptomatic subjects was reported in 18 of 31 patients (58.1%) (Tedesco M, NDT 2005, 20s6). All patients underwent aggressive medical therapy for primary prevention of major adverse cardiac events (MACEs). Here we investigated the cardiovascular outcome of these patients during a thirty-month follow up.

Methods: Both patients with and without SMI at SPECT (SPECT+ and SPECT-, respectively) received an aggressive medical regimen consisting in Pravastatin 40mg daily regardless serum LDL cholesterol, antiplatelet drugs, hypotensive medications associated to ACE-I and/or ARBs to maintain blood pressure below 130/80mmHg, insulin and/or glucose lowering drugs to keep baseline blood glucose between 80 and 120mg/dL and glycosylated hemoglobin below 7% in diabetic patients, Sevelamer and calcium carbonate to keep serum phosphate below 5.5mg/dL, calcitriol to keep serum i-PTH between 150 and 300ng/mL.

Results: A total of six patients died during the follow up, four among SPECT+ (22.2%) and two among SPECT- patients (15.4%); causes of death were acute myocardial infarction, rupture of abdominal aneurysm and neoplastic disease (2) in SPECT+ patients; stroke and intestinal infarction in SPECT- patients. Coronary arteriography was performed in five SPECT+ patients; subsequent successful PTCA was necessary in two. Among SPECT- patients two developed unstable angina and underwent coronary arteriography and subsequent successful PTCA, three received kidney transplantation. In both groups no drop out was observed due to intolerance to the prescribed medications.

Conclusions: After a 30-month follow up under aggressive medical therapy cardiovascular outcome of the patients of the two groups, who as previously reported showed no significant differences in conventional and emerging cardiovascular risk factors (Manca di Villahermosa S, NDT 2006, 21s7), is comparable regardless the presence or absence of SMI. Hence, as CVD is by far the first cause of death in ESRD, an aggressive medical management may be highly advisable for the primary prevention of MACEs in all HD patients.

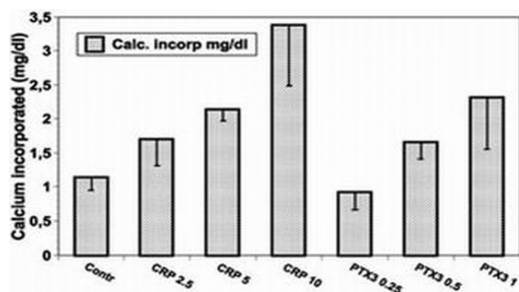
SaP269 THE PENTRAXINS C-REACTIVE PROTEIN (CRP) AND PENTRAXIN 3 (PTX3) AUGMENT CALCIFICATION OF HUMAN VASCULAR SMOOTH MUSCLE CELLS (SMC)

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Introduction and Aims: Cardiovascular mortality is greatly increased in patients suffering from end stage renal disease (ESRD). Both proteins are elevated in plasma of patients with chronic inflammatory conditions such as ESRD and plasma levels of CRP and PTX3 are associated with future cardiovascular events. In addition, CRP as well as PTX3 are markedly expressed in atherosclerotic plaques. Whether pentraxins play a causal role in the pathogenesis of atherosclerosis is controversially discussed. We investigated whether recombinant, endotoxin-free CRP and PTX3 have direct effects on calcification of SMC in vitro. In addition, cytokine induction in PBMC by pentraxins was also investigated.

Methods: Human SMC were isolated from umbilical veins, cultured and used for experiments in their 4th passage. Confluent cells were incubated for 48h with a calcification-inducing medium (2 mM Calcium and 2 mM phosphate) containing either PTX3, CRP (both R&D systems) or endotoxin (L55:B5, Sigma). After incubation, intracellular calcium content was determined via the o-cresolphthalein-complex method (Wako) and the von Kossa method. Expression of the calcification inhibitor Matrix G protein (MGP Ia) was investigated via RT-PCR. Furthermore, PBMC of healthy individuals were isolated and incubated with CRP, PTX3 or endotoxin for 24 hours. Induction of interleukins IL-1, IL-6 and TNF alpha was determined by ELISA. Endotoxin was measured by chromogenic Limulus-test (BioWhittaker, sensitivity 0.03 U/ml).

Results: After incubation with CRP or PTX3 SMC incorporated significantly greater amounts of calcium compared to controls (table). Similar findings were observed microscopically using the von Kossa stain. mRNA expression of MGP Ia in SMC decreased after incubation with CRP. In PBMC PTX3 and CRP dose-dependently induced production of all studied cytokines. The concentration of endotoxin in CRP and PTX3 preparations were always below the threshold for cytokine induction.



Conclusions: The pentraxins PTX and CRP augment calcification of SMC in vitro. This effect appears not to be related to endotoxin contamination. The clinical association between cardiovascular risk and pentraxin plasma concentration might reflect activation of PBMC and augmentation of calcification in SMC by pentraxins that appear as possible mediators in the pathogenesis of atherosclerosis. Our results support the link between inflammation and atherosclerosis.

SaP270 RISK FACTORS FOR CALCIFICATION AND MORTALITY IN UREMIA: RESULTS FROM THE BASCH STUDY

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Introduction and Aims: Patients with chronic kidney disease have a drastically increased cardiovascular mortality. Risk factors contributing to uremic vascular calcification include chronic inflammation, hyperphosphatemia, and an increased calcium x phosphate product. Recently, we established a simple calcification score to assess the degree of cardiovascular calcification in hemodialysis patients in the BASCH (Belgrade Aachen Study on Calcification in Hemodialysis patients) study.

Methods: In the BASCH study we included 97 patients (55±9 years). Patients were enrolled between December 2003 and January 2005 and observed for 18-26 months. Calcification was assessed using the Adragao score (X-rays of pelvis and hands; NDT 19:1480, 2004) and a composite calcification score (Adragao score plus X-ray of AV-fistula plus ultrasound of carotid arteries, mitral and aortic heart valves). Tertiles of both calcification scores were used to perform a survival analysis (Kaplan-Meier).

Results: In the multivariate analysis diabetes (p=0.04), male gender (p=0.001) and phosphate (p=0.04) were independent predictors of calcification. Diabetes was the only clinical risk factor for mortality (p=0.0003) while other risk factors like serum calcium, phosphate, ultrasensitive CRP, fetuin-A or osteoprotegerin were not associated with mortality. The tertile with lowest calcifications in the composite calcification score but not the Adragao score was associated with a better survival (p=0.037).

Conclusions: In our study, diabetes and cardiovascular calcifications were the most important risk factors for mortality. The novel composite calcification score is a cost-effective method to assess cardiovascular risk.

SaP271 CAROTID-INTIMA MEDIA THICKNESS AND ENDOTHELIAL FUNCTION RELATIONSHIP IN PERITONEAL DIALYSIS PATIENTS

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Introduction and Aims: Detection of atherosclerosis in the early stage is one of the important tool for the planning of future treatment. It has been well known that there is an increased carotid intima media thickness (CIMT) and existence of endothelial dysfunction (ED) in the early stage of atherosclerosis, both of which are also risk factors for future coronary events. It has been shown that peritoneal dialysis (pd) patients are characterized by increased CIMT and ED. In this study, we investigated whether there is a relation between CIMT and endothelial function in PD patients.

Methods: We included 54 PD (female/male: 28/26, mean age: 42±11) patients who were not characterized by diabetes mellitus, atherosclerotic disease, presence of active infection and history of peritonitis in the last three months and age and gender matched 30 controls (female/male: 16/14, age: 43±10). After demographic data was recorded, 24 hr ambulatory blood pressure and biochemical parameters were measured in each subject. Moreover, CIMT and endothelial function of each subject were measured by non-invasive technique described by elsewhere.

Results: CIMT were higher in PD patients than in controls (0.84±0.08 mm vs 0.75±0.06 mm, P<0.01). It was also found that flow mediated dilatation % (FMD %) were lower in PD patients than those of controls (8.2±5.0% vs. 11.7±5.5% P<0.01). In addition; nitrate mediated dilatation % (NMD %) were also lower in PD patients than in controls (18.1±8.5% vs. 26.4±4.6%, P<0.01). Correlation analysis showed that there was no relation between CIMT and FMD % (r=-0.004, p=0.94).

Conclusions: PD patients were characterized by increased CIMT and endothelial dysfunction expressed as low FMD %. No existence of relation between CIMT and endothelial function in our PD patients may show that these modalities indicate different stage of atherosclerosis.

SaP272 DETERMINANTS OF CORONARY ARTERY CALCIFICATION PROGRESSION IN PATIENTS WITH CHRONIC KIDNEY DISEASE NOT ON DIALYSIS

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Introduction and Aims: Vascular calcifications (VC) are predictors of morbidity and mortality in patients on dialysis (ESRD-patients). VC and particularly coronary artery calcification (CAC) proceed over time. Abnormal mineral metabolism as well as reduction of "protective" proteins (e.g. fetuin-A) are involved in progression of CAC. Rapid progression is regarded as additional factor responsible for morbidity and mortality. Determinants of CAC progression have not been evaluated in patients with kidney disease not undergoing dialysis (CKD-patients). This study assesses CAC progression and determinants in CKD-patients. Awareness of rate and potential determinants of CAC can allow early therapeutic interventions and expectantly hinder cardiovascular morbidity and mortality.

Methods: Consecutive out-patients (age 18-70 years) with normal or reduced renal function (stage 3-5 CKD not on dialysis) were enrolled. Exclusion criteria were: symptomatic coronary disease; arrhythmia; myocardial infarction; diabetes. In patients with diabetes CAC progression is greater and independent of mineral metabolism and renal function. Serum calcium, phosphorus, parathyroid hormone, homocysteine, C-reactive protein, triglycerides, total cholesterol, high- and low-density lipoprotein cholesterol were serially measured. Fetuin-A was assessed at the entry and at the end of the study. CAC progression was detected by measuring total calcium score (TCS) with computed tomography. Follow-up lasted 24±4.2 months (mean±SE).

Results: n.53 patients had CKD and 60 had normal renal function (NRF-patients). Patients with CAC were older with lower fetuin-A. TCS increased from 73±17 to 80±20 (mean±SE; p=NS) in NRF-patients and from 384±116 to 602±140 (mean±SE; p<0.01) in CKD-patients. Despite the majority of patients had normal concentration, phosphorus [O.R.=1.97 (1.14-3.41, 95% C.I.); p=0.015] correlated with CAC progression. N.11 CKD-patients, 45-70 years old, experienced fatal or not fatal cardiovascular event. All but one patient presented progression of CAC. In contrast, no event occurred in NRF-patients.

Conclusions: CAC progression was prominent in CKD-patients and correlated with serum phosphorus. Cardiovascular events were more frequent in CKD-patients. Studies are required to ascertain whether the attainment of serum phosphorus lower than that suggested by guidelines may reduce CAC progression, and ultimately mortality.

SaP273 LOW DENSITY LIPOPROTEIN (LDL) APHERESIS FOR HEMODIALYSIS PATIENTS WITH PERIPHERAL ARTERIAL DISEASE (PAD) REDUCES REACTIVE OXYGEN SPICES (ROS) PRODUCTION VIA SUPPRESSION OF NADPH OXIDASE GENE IN LEUKOCYTE

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Introduction and Aims: Peripheral arterial disease (PAD) is the major complication in hemodialysis (HD), especially with diabetes mellitus. Previous reports indicated that the Low density lipoprotein (LDL) apheresis improves arteriosclerosis in PAD patients; however, mechanism of LDL apheresis for PAD is still not clear. In this study, we hypothesized that LDL apheresis attenuates reactive oxygen species (ROS) production in HD patients with PAD.

Methods: Twenty HD patients who have ischemic symptoms due to PAD were investigated in present study. All subjects agreed with a protocol named EDDEN (Effective drugs and/or dialysis evaluated NADPH oxi-

dase) study that was approved by medical ethics committee of faculty medicine, Kagawa University (# H15-12). Informed consent was obtained from all subjects before LDL apheresis was performed. The symptoms of PAD were assessed by Fountain classification. The clinical effects were evaluated by thermography and angiography. Blood samples were obtained before and after LDL apheresis. We measured the serum levels of LDL cholesterol, high density lipoprotein (HDL) cholesterol, malondialdehyde-modified LDL (MDA-LDL), high sensitive C reactive protein (HSCRP), bradykinin, fibrinogen, international normalized ratio of pro-thrombin time (PT-INR), vascular endothelial growth factor (VEGF) and transforming growth factor-beta (TGF-β). Oxidative stress in serum was evaluated by TBARS (thiobarbituric acid reactive substances) and mRNA of leukocyte was separated by PAXgene Blood RNA kit (PreAnalytiX Company, Switzerland). Gene expression of mRNA in leukocyte was measured by real time PCR method.

Results: The ischemic symptoms due to PAD were gradually improved in 13 patients (65%) after starting LDL apheresis. One session of LDL apheresis removed approximately 75% of LDL from the serum. Some patients showed dramatically improvement of severe PAD symptoms such as ulcer of skin after a serial of LDL apheresis. LDL cholesterol, MDA-LDL, HSCRP, VEGF PT-INR and bradykinin were decreased between before and after single session of LDL apheresis. However, there were no changes between before and after 10 times LDL apheresis. The levels of fibrinogen and p22phox mRNA were decreased in single session of LDL apheresis and the effects on them were prolonged during whole observation periods. More than 50% of down-regulation of p22phox mRNA expression in leukocytes was observed after 10 times apheresis.

Conclusions: LDL apheresis improved the ischemic symptoms in HD patients with PAD via the reduction of ROS production with the suppression of NADPH oxidase gene expression in leukocyte. We conclude that LDL apheresis is good therapy for HD patients complicated with PAD.

SaP274 IMPEDANCE CARDIOGRAPHY A NON-INVASIVE METHOD FOR HEMODYNAMIC MONITORING OF HAEMODIALYSED PATIENTS

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Introduction and Aims: Impedance cardiography (ICG) represents a non invasive method for hemodynamic assessment and fluid status measurement in haemodialysed patients.

Hemodynamic monitoring of haemodialysed patients using impedance cardiography.

Methods: We included in the study 20 chronic haemodialysed patients (12 male and 8 female) with the age range 28 to 68 (mean 53,2±11,48) years. Using ICG, we studied the following parameters: blood pressure (BP), cardiac index(CI), heart rate(HR), ejection fraction (EF), systemic vascular resistance index (SVRI), thoracic fluid content (TFC). This parameters were recorded pre and after haemodialysis (HD) session and the changes of each parameters during HD were correlated with amount of fluid removed. All patients underwent a adequate haemodialysis kt/v ≥ 1.2. For patients had uncontrolled hypertension, 10 patients had normal values of BP and 6 patients had hypotension. Mean arterial pressure of the patients was 130±27,22 mmHg.

Results: TFC decreased in all patients during HD session (average reduction 0,012±0,008 ohms (-1)), and it was significant correlated with amount of fluid removed. The amount of ultrafiltration was 2.45±0,46 L. Others hemodynamic parameters were insignificantly correlated with fluid removed. EF increased in all patients after HD but significantly only in hypotensive patients. SVRI decreased after HD only in hypotensive patients. The patients with hypertension and normal BP had an increased values of SVRI during HD.

Conclusions: ICG represents an accessible and useful method for hemodynamic monitoring in haemodialysed patients. Optimising hemodynamic control we can improve heart failure management and subsequent decreased of cardiovascular risk.

SaP275 LEFT ATRIAL VOLUME IS A RELEVANT PREDICTOR OF CARDIOVASCULAR OUTCOMES IN DIALYSIS PATIENTS

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Introduction and Aims: Left atrial volume (LAV) is an important component of heart geometry but the potential prognostic relevance of this echocardiographic parameter in end stage renal disease (ESRD) patients is still unexplored. In this prospective cohort study we have therefore tested the prognostic value for CV events of single and repeated measurements of LAV.

Methods: Two hundred and forty nine dialysis patients were enrolled into the study and 191 of these (age: 59±15 yrs; 110 M and 81 F) repeated echocardiography after an average interval of 17±2 months. LAV was measured by the disk method (Lester SJ et al, Am J Cardiol 1999), i.e. a method showing a satisfactory day to day reproducibility.

Results: LAV (height^{2.7} indexed) was significantly higher in dialysis patients than in healthy subjects (P<0.001). During the follow-up, 113 patients died. LAV had an independent prognostic power for all cause mortality in a multivariate Cox model [hazard ratio (1 ml/height^{2.7} increase in LAV): 1.07, 95% CI: 1.03-1.12, P<0.001] adjusting for Framingham risk factors (age, sex, smoking, diabetes, blood pressure and previous CV events) and non traditional risk factors as well (albumin, CRP and treatment modality). Furthermore, LAV maintained a significant predictive value for death (P=0.03) also when LV mass and LV systolic function were jointly introduced into the Cox's model. Between the first and the second echocardiographic study LAV rose from 10.5±5.0 ml/height^{2.7} to 11.6±5.6 ml/height^{2.7} (P<0.001). After the second study, 85 patients had fatal and non fatal CV events. The rate of increase in LAV was significantly higher (P<0.001) in patients with incident fatal and non fatal CV events (median 0.59 ml/height^{2.7}/yr, inter-quartile range: 0.00-2.62 ml/height^{2.7}/yr) than in events free patients (0.11 ml/height^{2.7}/yr, -0.27-0.58 ml/height^{2.7}/yr). In a multiple Cox regression model taking into account a series of potential confounders including baseline LAV and LV geometry a 1 ml/m^{2.7}/yr increase in LAV was associated with a 12% increase in the relative risk of fatal and non fatal CV events. The association between changes in LAV and CV outcomes remained substantially unmodified [hazard ratio (1 ml/m^{2.7}/yr increase in LAV): 1.13, 95% CI: 1.06-1.21, P<0.001] also after the inclusion of LV mass.

Conclusions: In patients with ESRD, a single measurement of LAV added a significant prediction power to a Cox model including LV mass and function. Furthermore, changes in LAV showed an independent prognostic value for CV events beyond and above that provided by a single measurement. Left atrial volume measurements provide prognostic information beyond that given by LVH and LV ejection fraction and repeated echocardiographic studies of left atrium are useful for CV risk monitoring in dialysis patients.

SaP276 MONOCYTE EXPRESSION OF ADHESION MOLECULES DURING LOW AND HIGH FLUX POLYSULPHONE HAEMODIALYSIS AND THE EFFECTS OF ATORVASTATIN ADMINISTRATION

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Introduction and Aims: It has been suggested that inflammation is implicated in the pathogenesis of cardiovascular disease and involved in haemodialysis-related morbidity. We report part of the results of an ongoing crossover study aiming to identify alterations in several inflammatory markers in patients on low (LFD) or high flux (HFD) polysulphone haemodialysis and the influence of statin use.

Methods: We studied CD11b, CD18 and CD62L expression on monocytes in 32 patients, 16 on LFD and 16 on HFD polysulphone haemodialysis, before and after dialysis and also after administration of atorvastatin 20 mg/day for 6 months. The two groups were matched for age, sex,

duration of dialysis, with same prevalence of diabetes, and dialyzed with an spKT/V₀ ≥ 1.3. 16 healthy blood donors were used as controls (C). Monocytes were identified and analysed by flow cytometry after incubation of blood with monoclonal antibodies against CD11b, CD18 and CD62L. Antigen expression was defined as mean fluorescence intensity (MFI).

Results: Baseline pre-dialysis expression of CD11b and CD62L on monocytes was significantly lower in dialysis patients compared to that in healthy controls (P= 0.05 and P= 0.03 respectively), whilst no difference was found for CD18. There was no statistically significant difference of baseline expression of all three molecules between LFD and HFD dialysis groups. After dialysis there was an increase in the expression of CD11b and CD18 compared to pre-dialysis baseline values (P< 0.001 and P= 0.03 respectively), but expression of CD62L remained unchanged. No statistically significant differences were found in post-dialysis expression and in the change (Δ) pre and post-dialysis, of all three examined molecules, between the two dialysis groups. After 6 months of treatment with atorvastatin there was a decrease in pre-dialysis monocyte expression of CD11b and CD18 and an increase in the expression of CD62L compared to pre-dialysis baseline values (P= 0.004, P= 0.05 and P= 0.001 respectively). Again there were no statistically significant differences in after atorvastatin treatment pre-dialysis expression and in the Δ before and after treatment, in all three molecules, between patients on LFD and HFD haemodialysis (table).

	MFI C	Pre-dialysis (MFI)		Post-dialysis (MFI)		After statin (MFI)	
		LFD	HFD	LFD	HFD	LFD	HFD
CD11b	17.1±4.3	14.5±5.6	14.4±4.9	22.2±10	24.4±9.5	11.3±6	11.5±4.8
CD18	17±2.5	17.3±3.9	17.7±2.4	19.6±4.2	18.9±2.7	14.6±4.1	16.4±5.1
CD62L	4.5±1.2	4.02±2	3.1±1.5	3.8±2.5	2.9±1.7	4.8±1.9	4.8±1.9

Conclusions: Patients on haemodialysis seem to have phenotypic alterations in the expression of adhesion molecules on monocytes, which are further influenced by the process of dialysis itself, irrespectively of the membrane flux. Atorvastatin use induces changes in the expression of these inflammatory mediators. Further studies are needed to evaluate the role of inflammation and the clinical impact of statin use in dialysis patients.

SaP277 VASCULAR CALCIFICATION AND BONE DISEASE IN HEMODIALYSIS PATIENTS ASSESSMENT, ASSOCIATION AND RISK FACTORS

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Introduction and Aims: Vascular calcification and bone disease are commonly associated, highly prevalent in HD patients, associated with adverse prognosis, increased morbidity and all-cause mortality.

The aim of our study is to evaluate the extent of vascular calcifications using aortic calcium score and the association between calcium score, cardiovascular risk factors and the severity of bone disease using heel quantitative ultrasound.

Methods: We conducted a retrospective study which enrolled 90 consecutive non-diabetic patients receiving maintenance HD, 50.6% men, age 53.8±21.8 years, 31.5% of patients over 65y. The etiology ESRD: glomerular nephropathy 33.7%, ADPKD 20.5% and vascular nephropathy 19.1%. None of the patients had diabetic nephropathy. The mean HD duration was 4.32±3years and 34% of patients had >5years HD vintage. 73.5% pts were hypertensive and 72% of them were controlled. 44% were treated with statins, 89% with calcium based phosphate binders and 58% with alfacalcidol.

Results: Mean calcium score was 4±4.8 (median value 2 [0-19]). No vascular calcifications were found in 22% of patients. Mean T score was -1.7±0.9, but 43% of patients had T scores below -2.5 and only 19% had positive values. Mean estimated BMD was 0.4±0.14g/cm³ (0.17-0.99). Patients with calcium scores >2 compared with those without aortic calcifications are older (61.5±12.8yrs vs 44.9±12.9yrs), have a longer history of hypertension (11±9.7yrs vs 3.8±6.1yrs), are obese (20% vs 5%), had a marked inflammatory syndrome (CRP >3mg/dl 73% vs 25%; serum albumin <3.5mg/dl 80% vs 30%; ferritin >500ng/ml 56% vs 30% despite lower doses of iron supplements). They also had more frequently aortic

valve (52.2% vs 10.5%) and/or mitral valve calcifications (33.3% vs 5.3%), carotid atherosclerotic plaques (89% vs 25%) particularly of heterogeneous echographic structure (37% vs 5%), with higher calcium content (84.8% vs 15%) and higher intima-media thickness index (1.13 ± 0.15 vs 0.9 ± 0.15 mm). There were no differences between the 2 groups regarding HD vintage, calcium-phosphorus metabolism markers (serum calcium, serum phosphate, CaP product and PTH) or lipid metabolism (cholesterol, triglycerides, HDL and LDL cholesterol). The patients with vascular calcification have significantly lower T scores (-2 ± 0.9 vs -1.4 ± 0.7) with a higher percentage of patients in the lower than 2.5 range (57 vs 20%).

Conclusions: We can conclude that there is a strong relationship between aortic calcium score and valvular calcifications or carotid atherosclerotic plaques. Aortic calcium score is significantly associated with bone disease in our group. Age, obesity, personal history of hypertension and inflammatory syndrome are risk factors for vascular calcification. This simple aortic calcification score seems to be a good marker of cardiovascular and bone pathology in HD patients.

SaP278 VASCULAR CALCIFICATION IN INCIDENT DIALYSIS PATIENTS

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Introduction and Aims: Vascular calcification plays an important role in the pathophysiology of cardiovascular disease in dialysis patients. The impact of dialysis initiation on the progression of calcification has not previously been described. The objective of this study was to prospectively investigate the progression of vascular calcification in incident haemodialysis and peritoneal dialysis patients.

Methods: 46 CKD stage 4 subjects entered this study. Patients were studied at 12-month intervals. Vascular calcification was assessed using multi-slice spiral CT scanning of a 5 cm standardised segment of superficial femoral artery (SFA). Calcification scoring (CaSc) was undertaken using the Agatston score. All medications were recorded and biochemical parameters were time averaged over 12 months.

Results: After 24 months, 14 patients initiated PD, 12 initiated HD and 17 patients had not started dialysis (CKD 4) (2 died and 1 withdrew). Mean age was comparable between the three groups (61 ± 13 , 57 ± 15 and 62 ± 13 years respectively). Incident HD patients had significantly higher CaSc at baseline than the other two groups (median CaSc 221 (IQR 2-524) in HD compared to zero (IQR 0-108) in PD and CKD 4, $P < 0.01$). Significant progressive calcification was observed in all patients with a positive calcification score at baseline, calcification increased from a median of 103 (IQR 5-367) to 253 (IQR 13-582). 4 patients initiated calcification from a baseline CaSc of zero (3 CKD 4 patients and one PD patient). 19 patients who started with a CaSc of zero had no change over 12 months (8 CKD 4, 8 PD and 2 HD). Delta CaSc correlated with baseline CaSc ($P < 0.001$) delta residual renal function ($P < 0.01$) and number of months on dialysis ($P < 0.01$). Biochemical variables associated with delta CaSc were osteoprotegerin ($P < 0.01$) and negatively with total cholesterol ($P < 0.01$) and LDL cholesterol ($P < 0.05$). There were no significant differences in plasma phosphate, calcium or PTH between patients. 18/46 patients used calcium-based phosphate binders at baseline, 9 with and 9 without calcification.

Conclusions: Arterial calcification begins prior to the initiation of dialysis. Pre-existing vascular calcification is the most important factor determining its progression, however HD was associated with higher CaScs. Given its associations with cardiovascular mortality, therapies targeting the progression of vascular calcification should begin prior to starting renal replacement therapy.

Cardiovascular complications of CKD 3

SaP279 COMPARISON BETWEEN HEMODIALYSIS PATIENTS WITH DIFFERENT ARTERIAL CALCIFICATION STATUS

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Introduction and Aims: The aims of this study were to evaluate presence of different arterial calcifications, as well as to compare atherosclerotic findings and risks between hemodialysis (HD) patients with different arterial calcifications status.

Methods: In a cross-sectional study we examined 135 HD patients (84 men; mean age 54.75 ± 14.82 years; HD duration 101.87 ± 64.89 months). Primarily we evaluated the presence of arterial intima (AIC) and arterial media calcifications (AMC) using plain radiography of the pelvis, and the presence of atherosclerotic lesions using high resolution B-mode ultrasonography of the common carotid arteries (CCA). Then we compared the potential clinical, biochemical risk factors and different atherosclerotic findings among the groups of the patients with different arterial calcifications.

Results: Our results showed frequent presence of AIC ($n=61$; 45.2%) and AMC ($n=46$; 34.1%) in our HD patients. The patients ($n=28$; 20.7%) without arterial calcifications and with AMC had high percentage of carotid atherosclerotic plaques (28.6%/47.8%) and documented cardiovascular diseases (46.4%/76.1%) respectively. Patients with AIC had significantly ($p < 0.05$) older age (59.4 ± 11.8 vs 50.2 ± 11.7 , 47.1 ± 10.9 years), smoking habits (22.9 vs 8.7, 7.1%), diabetes (41.8 vs 19.6, 3.6%), male gender (70.5 vs 35.7%), poorer dialysis adequacy (kt/v 1.23 ± 0.17 vs 1.3 ± 0.19 , 1.32 ± 0.2), lower body mass index (22.67 ± 2.61 vs 25.44 ± 6.47 , 24.0 ± 3.9 kg/m²), higher serum triglycerides (2.49 ± 1.01 vs 1.88 ± 0.86 mmol/L), lower serum albumin (38.25 ± 2.97 vs 39.51 ± 2.92 g/L), increased CCA intima media thickness (1.54 ± 0.27 vs 1.42 ± 0.29 mm), hypertensive nephropathy (31.1%) as a cause of renal failure, CCA atherosclerotic plaques (80.3%), calcified intimal plaques (59.1%), documented cardiovascular (85.2%), cerebrovascular (36.1%) and peripheral arterial diseases (49.2%) in comparison with other patients. Significantly ($p < 0.05$) frequent presence of male gender (67.4 vs 35.7%), diabetes (19.6 vs 3.6%) and internal diameter on CCA (7.64 ± 1.1 vs 7.07 ± 0.95 mm) were found in patients with AMC in comparison with patients without arterial calcifications. We did not find statistically differences in other atherosclerotic (blood pressure, other serum lipids, C-reactive protein) and in HD specific risks (doses of prescribed calcium carbonate and vitamin D₃, serum levels of phosphate, calcium phosphate product, intact parathyroid hormone and duration of HD).

Conclusions: Arterial calcifications in HD patients are frequent. The patients with AMC and without arterial calcifications have high percentage of atherosclerotic lesions and complications. In our patients AIC were associated with older age, smoking habits, diabetes, male gender, poorer dialysis adequacy, lower body mass index, higher serum triglycerides, lower serum albumin. AMC were associated with male gender and diabetes. In our patients the role of HD specific risks in formation of different arterial calcifications needs to be further elucidated in additional large scale study.

SaP280 AN UNUSUAL CAUSE OF PLEURAL EFFUSION IN A HAEMODIALYSIS PATIENT

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Introduction and Aims: Pleural effusion is not usually the first sign of constrictive pericarditis. The aim of this report was to highlight that constrictive pericarditis should, however, always be considered as a possible cause of pleural effusion in haemodialysis patients, as the prognosis depends on an early diagnosis.

Methods: We present a case of constrictive pericarditis occurring in a 66-year-old man on haemodialysis. Previously the patient had received a cadaveric renal transplantation, but after 14 years, haemodialysis was resumed on account of chronic allograft nephropathy. A few months later, bilateral pleural effusion was diagnosed. To establish the cause of the pleural effusion, several assessments were carried out. They included