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DIABETES CLINICAL

MP273 NOVEL MANAGEMENT OF DIABETIC NEPHROPATHY WITH CHRONIC RENAL FAILURE IN TYPE-2 DIABETES MELLITUS BY LIVING DONOR RENAL TRANSPLANTATION USING PRETRANSPLANT INSULIN-SECRETING CELLS WITH STEM CELL THERAPY AND REGULATORY T-CELL THERAPY POSTTRANSPLANT

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Introduction and Aims: Diabetes mellitus type-2 (T2DM) is a metabolic disorder leading to diabetic nephropathy (DN) responsible for approximately 35% chronic renal failure (CRF) on waiting list of renal transplantation (RT). RT is a well accepted therapy for these patients however life-long immunosuppression mandatory to prevent the allograft rejection exposes them to high risk of recurrence, toxicity, infections and malignancy. Stem cell therapy (SCT) holds promise of minimizing immunosuppression, diabetogenicity and immune injuries.We present early experience of Institutional Review Board approved study of pre-transplant SCT with insulin-secreting cells and posttransplant T-regulatory cell (Treg) therapy in T2DM patients with DN-CRF subjected to living-donor renal transplantation (LDRT).
Methods: Seven T2DM male patients with DN-CRF were subjected to thymic and portal co-infusion of in-vitro generated donor adipose-derived mesenchymal (AD-MSC), hematopoietic stem cells (HSC) and insulin-secreting cells (ISC) pre-transplant under conditioning of subtotal lymphoid irradiation, rabbit antithymocyte globulin and Bortezomib. Mycofenolate, Tacrolimus and Prednisone were given for initial immunosuppression to be stepped down after 3 months of stable graft function. In vitro generated Tregs (CD127low/-/CD25high/CD4+) were infused 1 month posttransplant.Mean age of patients was 44.4 ± 6.5 years, suffering from DM for mean 12.4 ± 2.15 years. Donors were wives in 5 patients, brother in 1 and mother in 1 patient. Mean donor age was 44 ± 8.2 years. Mean HLA-match was 2.3 ± 1.25.
Results: Mean CD34+ infused were 0.8 ± 0.75 x106, AD-MSC were 1.47 ± 1.24 x104 with ISC, 1.73 ± 0.99 x104 and Tregs, 55.13 ± 82.96 x104/kgBW. There were no adverse effects of cell therapy/ conditioning.Over a mean follow-up of 10.6 ± 6.2 months, glycosylated haemoglobin reduced from 9.46 ± 0.72% to 7.1 ± 0.86%. Daily insulin requirement of 49.4 ± 23.45 IU before transplant decreased to 25.67 ± 3.39 IU. Mean C-peptide decreased from 9.96 ng/mL to 2.8 ng/mL (reference range: 1.1- 4.4 ng/mL). All grafts are functioning well without rejection and mean serum creatinine of 1.09 ± 0.36 mg/dL. Six patients are on 2 immunosuppressants (Prednisone, 10 mg/day or Mycofenolate 360 mg, 3 tabs/day and Tacrolimus, 0.05 mg/kgBW/day or Sirolimus, 1 mg/day) and 1 patient is on Prednisone, Sirolimus and Mycofenolate (same dose as above).
Conclusions: Thymic and portal co-infusion of donor AD-MSC, HSC, ISC pre-transplant and thymic infusion of Tregs posttransplant in T2DM with DN-CRF subjected to LDRT is safe. It offers graft protection from immune injury with acceptable glycemic control.

MP274 BLOOD PRESSURE LEVELS AND CARDIOVASCULAR EVENTS IN PATIENTS WITH TYPE 2 DIABETES AND RENAL IMPAIRMENT-A NATIONAL-WIDE OBSERVATIONAL REGISTER STUDY

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Introduction and Aims: We assessed the relationship between blood pressure and risk of cardiovascular events (CV) and all-cause mortality in patients with type 2 diabetes (T2D) and renal impairment (RI) treated and followed up in clinical practice.
Methods: 33,304 patients (47% men, age 75±9 years, BMI 29.1±4.8 kg/m^2, diabetes duration 10±8 years) with at least one serum creatinine and blood pressure (BP) value available in the Swedish National Diabetes Register (NDR) between 7 January 2005 and 31 December 2007 were followed until 31 December 2011 or death. RI was defined as estimated glomerular filtration (eGFR) <60ml/min/1.73m^2 according to MDRD. BP values were the mean of all reported values during the follow-up period. First CV event and all-cause mortality were the primary outcomes in the study. Linkages were performed with the hospital discharge, cause of death, and prescribed drug registers. Patients were categorized into deciles according to systolic (SBP) or diastolic BP (DBP) (approx. 3300 patients in each group). The relationships between mean BPs, CV events and all-cause mortality were examined by time-dependent Cox models, to estimate hazard ratios (HR), adjusting for CV risk factors and ongoing medications.
Results: During the follow-up period (median 5.3 years), 11,899 CV events and 10,691 deaths occurred. The most common causes of death were cardiovascular disease (34%) and malignancies (15%).The lowest risks of CV events and all-cause mortality were observed with SBP 135-139 and DBP 72-74 mmHg, respectively (reference levels). The highest risks were found with mean SBP 80-120 and 160-230 mmHg (CV HR 2.5, 95% CI 2.2-2.8 and mortality HR 2.6, 2.3-2.9) and (CV HR 2.0, 1.8-2.3 and mortality HR 3.1, 2.8-3.5), respectively, and for mean DBPs 40-63 mmHg and 83-125 mmHg (CV HR 2.0, 1.8-2.2 and 1.6, 1.4-1.8) and (mortality HR 2.2, 2.0-2.5 and 2.0, 1.7-2.2), respectively. Adjustments for presence of albuminuria did not markedly alter the results.
Conclusions: The risk of CV events and all-cause mortality increased significantly with both high and low SBP and DBP. In patients with T2D and RI, SBP 135-139 and DBP 72-74 mmHg were associated with the lowest risks of CV events and death.

MP275 ASSOCIATION OF CUTANEOUS ADVANCED GLYCATION END PRODUCTS (AGES) WITH CHRONIC KIDNEY DISEASE (CKD) IN DIABETES MELLITUS TYPE 2 (DM2): A SUBGROUP ANALYSIS OF THE DIACORE STUDY BASELINE VISIT

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Introduction and Aims: AGEs are generated by oxidative stress in hyperglycemia, accumulate in the skin and vascular wall and are implicated in diabetic complications. Cutaneous AGEs in skin biopsies correlate with skin autofluorescence (SkinAF). SkinAF may thus represent a simple noninvasive test to determine risk for diabetic complications. Here, we investigate the association of skinAF with traditional risk factors and CKD in a large cohort study of DM2.
Methods: Each individual's mean SkinAF was obtained from three measurements with the AGE-reader (DiagnOptics, Groningen, NL) at the baseline visit of a random subgroup of patients of the DIACORE study. DIACORE is a prospective cohort study of Caucasian diabetes mellitus type 2 (DM2) patients not on renal replacement therapy. We investigated the association of variables potentially affecting SkinAF, and the association of SkinAF with urine albumin/creatinine ratio (UACR,mg/g), elevated albuminuria (defined as UACR≥30), eGFR (CKD-EPI equation), chronic kidney disease (CKD2012, defined according to KDIGO 2012 as eGFR<60ml/min/1.73m2 or [≥60ml/min/1.73m2 and UACR≥30mg/g]). Means are provided ±1 standard deviation.
Results: SkinAF was measured in 759 patients. In these, mean skinAF was 2.4±0.5, 463 (61%) were male, mean age was 65.8±9.2yrs, mean DM2 duration 10.1±8.4yrs, 207 (27.3%) patients were treated with insulin, 290 (39.4%) had CKD2012 and 192 (25.3%) had elevated albuminuria. 154 (20.3%) patients had UACR 30-300, 38 (5.0%) had UACR >300. Higher age ($p<0.0001$), DM2 duration ($p<0.0001$), systolic blood pressure ($p=0.004$), HbA1c ($p=0.02$), ever smoking ($p=0.0004$), waist hip ratio ($p=0.002$) were significantly associated with higher SkinAF, as was lower diastolic blood pressure ($p=0.02$). Squared correlation coefficients (r2) ranged from 0.1 (age) to 0.006 (diastolic blood pressure). Insulin resistance (HOMA-IR), determined in fasting individuals at least 10 hours after the last insulin injection (if any), and BMI were not associated with skinAF.Higher mean skinAF was associated with lower eGFR and higher lnUACR ($p<0.0001$, r2=0.07 and 0.03 respectively). Mean skinAF in those with CKD2012 or eGFR<60ml/min/1.73m2 was higher than in those without (skinAF: 2.6 vs 2.3, $p<0.0001$; 2.5 vs. 2.3, $p=.0001$ respectively), and increased across increasing UACR categories (UACR300: 2.6, $p=0.0004$).
Conclusions: In this cross-sectional analysis of the baseline visit of DIACORE patients, cutaneous AGEs, quantified by SkinAF, is affected by multiple factors, with age showing the strongest association. SkinAF in turn is higher in patients with different definitions of CKD. Further work is needed to determine the degree of independent association of SkinAF with CKD in DM2 in cross-sectional and prospective analyses, which is ongoing work in DIACORE.

MP276 ASSOCIATION OF INFLAMMATION, ALBUMINURIA AND KIDNEY FUNCTIONS IN ELDERLY DIABETIC PATIENTS

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Introduction and Aims: Diabetic nephropathy (DN) is a major manifestation of microangiopathy in patients with Diabetes Mellitus (DM).The current data have proven the role of inflammation in the development of micro and macro vascular complications in diabetes. Recently, neutrophil-to-lymphocyte ratio (NLR) was found to positively correlated with inflammatory markers including tumor necrosis factor-α (TNF- α) and interleukin (IL)-6 in cardiac and noncardiac patients and NLR was introduced as potential marker to determine inflammation. This study aimed to determine the relationship between inflammation,hyperglycemia, kidney functions and albuminuria in elderly diabetic patients.
Methods: Two-hundred and twenty five diabetic patients who were between the ages of 65 and 100 years were included in this cross-sectional study. Hemoglobin A1c (HbA1c), serum uric acid and creatinine, urinary albumin levels were measured. NLR was calculated as the ratio of the neutrophils to lymphocytes obtained from the same automated blood sample. Patients were divided into three groups according to albuminuria levels as normoalbuminuric, microalbuminuric and macroalbuminuric. After calculating median of NLR, patients were divided in two groups. Albuminuria, creatinine, uric acid, HbA1c and NLR levels, age of patients and sex distribution of patients were compared according to albuminuria group and NLR medians with nonparametric tests. Statistical significant differences between the groups were determined by chi-square test for categorical variables. Associations between the variables were explored using the Spearman's rho. Data are expressed as median (minimum-maximum). Two-sided P values less than 0.05 were considered significant.
Results: The baseline characteristics of the 225 subjects are shown in Table 1. There were statistically significant differences in the creatinine, HbA1c and NLR according to albuminuria groups while there were no significant differences in age, sex and uric acid. As shown in Table 2, a significant increase was observed in HbA1c and albuminuria levels in parallel to increase in NLR. Albuminuria was significantly correlated with creatinine, HbA1c and NLR (r:0.163 p: 0.014, r: 0.315, p: <0.001, r: 0.312, p: <0.001, respectively). Binary logistic regression analysis was also performed to define the variables of albuminuria. Serum creatinine, HbA1c and NLR levels were found to be independently associated with albuminuria.
Conclusions: This study demonstrated that inflammation, uncontrolled hyperglycemia and diminished kidney functions were closely associated with albuminuria in elderly diabetic patients. Further prospective and randomised studies are needed to highlight pathogenesis of diabetic microvascular diseases.

MP276 Table 1.

Parameters	Normal group [median (min-max)] N=149	Microalbuminuric group [median (min-max)] N=57	Macroalbuminuric group [median (min-max)] N=19	P value
Age (year)	71 (65-94)	70 (65-87)	70 (65-77)	0.392
Sex (f/m)	88/61	31/26	11/8	0.831
Creatinine (mg/dL)	0.78 (0.30-3.10)	0.79 (0.50-2.70)	1.31 (0.50-4.70)	0.009
Uric acid (mg/dl)	5(1-10)	5 (2-10)	5 (2-7)	0.919
HbA1c(%)	7.5 (5-12.6)	8.4 (5.3-13.2)	9.6 (5.5-15.6)	<0.001
NLR	1.69 (0.64-5.34)	1.83 (0.89-9.95)	2.41 (0.85-9.64)	0.001

MP276 Table 2.

Parameters	Group 1(NLR≤1.819) [median(min-max)] N=113	Group2(NLR>1.819) [median(min-max)] N=112	P value
Age (year)	71 (65-94)	70 (65-87)	0.351
Sex (f/m)	65/48	65/47	0.938
Creatinine (mg/dL)	0.79 (0.30-3.10)	0.83 (0.50-4.70)	0.076
Uric acid (mg/dl)	5 (1-10)	5 (2-11)	0.837
HbA1c (%)	7.5 (5-12.6)	8.4 (5.3-15.6)	<0.001
Albuminuria (mg/g)	0.004 (0.000-0.012)	0.047 (0.013-1.878)	<0.001

MP277 METABOLIC ACIDOSIS IS ASSOCIATED WITH MONOCYTE ACTIVATION IN DIABETIC KIDNEY DISEASE (DKD)

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Introduction and Aims: Systemic inflammation has been linked to adverse cardiovascular outcomes and it is thought to contribute to CKD progression in DKD. CD74 is a receptor for the cytokine MIF. MIF promotes kidney injury and CD74 expression is increased in renal biopsies from DKD patients and in atherosclerotic lesions. CxCl16 is a scavenger receptor and chemokine that has been associated to kidney and cardiovascular injury. However, the expression of CD74 and CxCl16 in circulating leukocytes from DKD patients has not been previously explored.
Methods: We have assessed the cell surface expression of CD74 and CxCl16 in peripheral blood leucocytes from 88 DKD patients (Mean age 67 ± 13, 75 % males, eGFR 55 ± 22,1 ml/min/1.73 m2, median albuminuria/ creatinine ratio 140 [30 - 480] mg/g) and 6 controls (mean age 41 years).
Results: CD74 and CxCl16 were mainly expressed by monocytes. Median CxCl16 expression in controls was 12, 28 and 33 fluorescence units in CD14++/CD16-, CD14+ +/CD16+, CD14+/CD16++ monocytes, respectively. Controls presented a median CD 74 expression of 28, 32 and 8 fluorescence units in CD14 ++/CD16-, CD14++/CD16+, CD14+/CD16++ monocytes, whilst DKD patients presented a higher median CD74 expression (44, 54, 21 fluorescence units for the same populations, respectively). Thus, DKD monocytes presented a pattern of activation even in classic (CD14 ++/CD16-) monocytes. In DKD, there was correlation between CD74 and CxCl16 expression in CD14++/CD16- (r 0.55, p<0.001), CD14++/CD16+ cells (r 0.26, p 0.012), CD14 +/ CD16 ++ (r 0.78, p<0.001).In DKD, median CD74 fluorescence in CD14++/CD16- monocytes correlated directly with serum phosphorus (r 0.2, p 0.005), HbA1c% (r=0.41, p0.02) and correlated inversely with eGFR (r -0.27, p 0.05) and CO2 (r -0.38, p 0.0003).Median CD74 fluorescence also correlated indirectly with CO2 in the following subpopulations: CD14++/CD16+ monocytes (r 0.79, p 0.002), CD14++/CD16++ monocytes (r 0.23, p 0.02), in neutrophils (r 0.28, p 0.0007), NK CD56+ (r 0.25, p 0.01) and NK CD56++ (r 0.24, p 0.024)Median CxCl16 fluorescence correlated indirectly with CO2 in CD14++/CD16- monocytes (r -0.24 p 0.02), as well as in neutrophils (r 0.27, p 0.01).In a multivariate analysis, the main factors associated with CD74 fluorescence in CD14++/CD16- were CO2 (p 0.04) and HbA1c% (p 0.0006). The r2 adjusted for the model was 0.24. In another multivariate analysis, CO2 was associated with median CD74 expression in CD14++/CD16+ monocytes (r2 adjusted 0.12, p 0.003), CD14+/CD16++ (r2 adjusted 0.04, p 0.001), and neutrophils (r2 adjusted 0.14, p 0.03).
Conclusions: CD74 expression in monocytes and in neutrophils was inversely correlated with CO2 in a cross sectional analysis. This suggests that acidosis may be a driver of monocyte and neutrophil activation in DKD. The cohort is being followed in order to assess the relationship between these inflammatory markers and outcomes.

MP278 PROXIMAL TUBULE DYSFUNCTION IS ASSOCIATED WITH URINARY NEPHRIN AND VASCULAR ENDOTHELIAL GROWTH FACTOR EXCRETION IN NORMOALBUMINURIC TYPE 2 DIABETES MELLITUS PATIENTS: A CROSS-SECTIONAL STUDY

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Introduction and Aims: The proximal tubule (PT) may be involved in the uptake of urinary nephrin and VEGF in the course of diabetic nephropathy (DN), even in its early stages. The aim of the study was to document a potential association between PT dysfunction and urinary nephrin and VEGF excretion, as biomarkers of podocyte involvement, in patients with type 2 diabetes mellitus (DM). Also, we queried if this association could be related to advanced glycation end-products (AGE) intervention, which may impact on both the PT and podocytes.
Methods: A total of 70 patients with type 2 DM and 11 healthy subjects were enrolled in a cross-sectional study. All patients were assessed concerning urinary albumin: creatinine ratio (UACR), urinary alpha1-microglobulin, urinary kidney injury molecule-1 (uKIM-1), urinary nephrin, urinary vascular endothelial growth factor (uVEGF), urinary AGE, and serum cystatin C.
Results: Urinary alpha1-microglobulin, uKIM-1, urinary nephrin, and VEGF displayed increased levels in normoalbuminuric as well as in microlabuminuric patients. Urinary alpha1-microglobulin and uKIM-1 correlated directly with UACR (p<0.0001; p<0.001), nephrinuria (p<0.0001), uVEGF (p<0.0001), urinary AGE (p<0.0001), serum cystatin C (p<0.001), and inversely with GFR (p<0.0001). Nephrinuria and urinary VEGF correlated directly with UACR (p<0.0001), urinary AGE (p<0.0001), serum cystatin C (p<0.0002; p<0.0001), and inversely with GFR (p<0.007; p<0.0001). In multivariate regression analysis, urinary alpha1-microglobulin and uKIM-1 correlated directly with UACR (p<0.0001; p<0.001), urinary AGE (p<0.0001; p<0.011), nephrinuria (p<0.001), VEGF (p<0.0001), serum cystatin C (p<0.0001), and inversely with GFR (p<0.008; p<0.001), while nephrinuria and VEGF correlated directly with UACR (p<0.0001), serum cystatin C (p<0.0001), and inversely with GFR (p<0.006; p<0.001).
Conclusions: In patients with type 2 DM there is an association between PT dysfunction, and nephrinuria and VEGF excretion, even in the normoalbuminuria stage. This observation documents a potential role of the PT in urinary nephrin and VEGF processing in early DN. Moreover, this hypothesis raises the question of whether urinary nephrin and VEGF excretion, and PT dysfunction precede the onset of

microalbuminuria. AGE could be involved in nephrinuria and VEGF excretion, as well as in PT dysfunction in patients with type 2 DM. It may be assumed that the PT delays the expression of glomerular involvement in early DN and explains development of normoalbuminuric renal insufficiency.

MP279 GENETIC VARIATION IN THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM AND RENAL SURVIVAL IN JAPANESE PATIENTS WITH DIABETIC NEPHROPATHY

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Introduction and Aims: Genetic polymorphism renin-angiotensin-aldosterone system (RAAS) may play a pivotal role in the development and progression of diabetic nephropathy. Therefore, we aimed to investigate whether genetic variation in the RAAS is related to renal survival in patients with diabetic nephropathy.
Methods: We enrolled 290 Japanease patients with diabetic nephropathy who consulted nephrologists in our hospital between January 1995 and December 2010. One hundred and sixty-three (56.2%) patients progressed to end stage renal disease (ESRD) at an average age of 58.6 years. We estimated the association between 5 polymorphisms of RAAS and cumulative renal survival. We investigated the following genetic polymorphisms: renin enhancer region (REN) C-5312T, angiotensinogen (AGT) M235T, angiotensin converting enzyme (ACE) insertion/deletion, angiotensin II type I receptor A1166C, and aldosterone synthase CYP 11B2 C-344T. We cumulative survival analysis using the Kaplan - Meier method with the log-rank test statistical analysis of the time course of progression to ESRD.
Results: Cumulative renal survival in diabetic nephropathy was significantly lower with those the TT genotype of the (M235T polymorphism) (log-rank, P=0.036; $\chi 2$ =4.383). There was no association between cumulative survival and the REN C-5312T , ACEI/D, A1166C, and C-344T polymorphisms.
Conclusions: The AGT M235T polymorphism may play a role in diabetic nephropathy progression in that it may directly affect prognosis in these patients.

MP280 QUALITY OF LIFE AFTER SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION AND KIDNEY TRANSPLANTATION ALONE IN TYPE 1 DIABETIC PATIENTS WITH END-STAGE RENAL DISEASE

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Introduction and Aims: Simultaneous pancreas-kidney transplantation (SPK) and kidney transplantation alone (KTA) have been demonstrated to prolong survival in patients with type 1 diabetes mellitus (T1DM) and ESRD. However, it is controversial whether SPK and KTA equally yield benefit in terms of quality of life compared with dialysis. We therefore conducted this study to compare quality of life (HRQOL) and psychological status of diabetes in patients with T1DM undergoing chronic dialysis, KTA, and SPK.
Methods: 93 T1DM patients with ESRD (65 women and 28 men) were studied, comprising of 52, 25 and 16 patients undergoing dialysis, KTA and SPK, respectively. Patients were excluded if they had second or more transplantations, or if they had kidney or pancreas graft loss. We compared comprehensive HRQOL, psychological status of diabetes and severity of hypoglycaemic awareness among the three renal replacement therapy (RRT) groups. Comprehensive HRQOL was assessed using the Medical Outcome Health Survey Short Form-36 (SF-36 v2), consisting of 36 questionnaire items, and 8 subscale scores and physical and mental composite scores were calculated using the standard deviation of ordinary Japanese nationals. Psychological status of diabetes was evaluated by calculating amount of problem area in diabetes survey (PAID) scores, consisting of 20 questionnaire items. Severe psychological status of diabetes was defined as a PAID score $\geq$ 50. Severity of hypoglycaemic awareness was assessed using the Clarke hypoglycaemic score, consisting of 8 questionnaire items. Hypoglycaemic unawareness was defined as a Clarke Score $\geq$ 4.
Results: There were no significant differences among the three RRT groups in terms of age, sex and duration of diabetes. Duration of dialysis was significantly longer in SPK and dialysis than KTA patients. Recipient's age and posttransplant observational period were not different between the two transplant groups. The SF-36 scores of vitality (VT), general health perception (GH), and physical and mental component summary in patients with SPK were significantly higher than those with KTA. There was no significant difference in any of SF-36 scores between patients treated with dialysis and KTA. The scores in SPK patients ranged from 44 to 53 points, which were almost identical to those in the Japanese national standard range. The PAID Score in patients with SPK (30±10) were significantly lower than those with dialysis (59±18) and those with KTA (50±18). There were also no significant differences in PAID Score between patients treated with dialysis and KTA. The Clarke Score in patients treated with SPK (1.3±1.2) and KTA (2.2±1.7) were significantly lower than those with dialysis (3.4±1.9).
Conclusions: QOL for T1DM patients receiving SPK may be superior to that of patients undergoing dialysis. KTA is unlikely to improve QOL except for improvement of hypoglycaemic unawareness.

MP281 CONVERSION OF IMMUNOSUPPRESSION FROM TACROLIMUS TO CYCLOSPORINE A IMPROVES INSULIN SENSITIVITY AND OVERALL GLUCOSE TOLERANCE IN HCV-POSITIVE RENAL TRANSPLANT RECIPIENTS

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Introduction and Aims: New onset diabetes after transplantation (NODAT) relates to lower renal graft and patient survival and increased cardiovascular morbidity. HCV-infection and immunosuppression (IS) predict the development of NODAT, however, a more accurate metabolic characterization, i.e. effects of IS on both insulin sensitivity and insulin secretion, remains pending.
Methods: 2h-75g-oral glucose tolerance tests (OGTT) were performed in 10 HCV-positive renal transplant recipients (RTR) before and 3 months after the conversion from tacrolimus (Tac) to cyclosporine A (CyA). Mathematical modelling was used to analyse kinetics of glucose, insulin and C peptide providing total B cell insulin secretion rate (TIS) and hepatic insulin extraction (HIE). Basal and dyamic insulin sensitivity were estimated using QUICKI and the oral glucose insulin sensitivity index (OGIS), respectively. Beta cell-function was quantified by the adaptation index (ADAPT; OGIS×dynamicTIS), which yields an estimation of the pre hepatic insulin secretory capacity of beta cells, i.e. unaffected by HIE, in response to the prevailing insulin sensitivity, and the disposition index (DISP; OGIS×dynamicAUCinsulin), which represents a marker of overall glucose metabolism considering both insulin secretion and HIE.
Results: Following the conversion of IS, plasma glucose levels decreased at all time points of the OGTT ($p<0.05$). Dynamic insulin sensitivity as evaluated by OGIS and beta cell-function as evaluated by DISP and ADAPT improved significantly ($p<0.05$).
Conclusions: The conversion of IS from Tac to CyA significantly improves insulin sensitivity and overall glucose tolerance. With regard to the high prevalence of pre-and post-transplant diabetes, a CyA-based immunosuppressive regimen might be favourable in HCV-positive renal transplant recipients at high risk for cardiovascular events.

MP282 GLYCAEMIC CONTROL AMONG PEOPLE WITH TYPE 2 DIABETES RECEIVING RENAL REPLACEMENT THERAPY

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Introduction and Aims: The increasing prevalence of type 2 diabetes (T2DM) will lead to a higher absolute number of people who require renal replacement therapy (RRT). Data investigating the control of T2DM in this population are contradictory and some studies suggest that very tight control might be associated with increased mortality. We therefore aimed to describe the control of T2DM by RRT status, separate for people with diabetic nephropathy (DN) or another primary renal disease (PRD).
Methods: Data from the Scottish Renal Registry and the Scottish Care Initiative-Diabetes Collaboration were linked to identify patients with known T2DM who were receiving RRT on 31/05/2008 in Scotland. Mean HbA1c was estimated between 01/01/2007 and 31/12/2008 and categories defined as shown in the table. Logistic regression analyses were used to investigate whether the association between HbA1c>7% in people with DN or another PRD on RRT differed from people not on RRT. Adjustments were made for age, sex and diabetes duration.
Results: 495 people with T2DM and HbA1c measurements available were receiving RRT on 31/05/2008. Of these 495 people 199 had DN as PRD and 296 had an other underlying PRD. Characteristics per patient group are shown in the table below. Adjusted Odds ratios for HbA1c>7% for people with DN or another PRD on RRT compared with people not on RRT were 0.54 (0.40-0.72) and 0.49 (0.39-0.62), respectively.
Conclusions: Glycaemic control in people with T2DM on RRT with DN or another underlying PRD appears to be better than in people with T2DM not on RRT. Furthermore, a large proportion of people on RRT with another PRD have HbA1c <6% in this cross-sectional analysis. Prospective studies will be useful to investigate causality, the role of selection bias and effects of glycaemic control on outcomes among people receiving RRT.

MP282

	Percentage people per HbA1c category					Characteristics per group		
	<6%	6-6.9%	7-7.9%	8-8.9%	≥9%	Age (yrs)*	Sex (%Male)	Duration T2DM (yrs)*
RRT, PRD DN, n=199	17.6	26.1	26.6	14.1	15.6	69.0(60.0-75.0)	59.8	17.3(11.0-22.5)
RRT, other PRD, n=296	24.0	32.8	23.3	12.8	7.1	66.0(56.5-73.0)	57.1	7.0(3.6-12.6)
No RRT, n=170,784	11.4	32.6	27.6	14.1	14.3	68.0(59.0-76.0)	54.3	5.8(2.9-10.0)

*Expressed as median and interquartile range.

MP283 RED BLOOD CELL COUNT IS ASSOCIATED WITH GLOMERULAR FILTRATION RATE AND ALBUMINURIA IN NORMOALBUMINURIC TYPE 1 DIABETIC PATIENTS WITH NORMAL OR MILDLY IMPAIRED RENAL FUNCTION

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Introduction and Aims: Anemia is a common feature in diabetic patients with chronic kidney disease (CKD). Anemia in diabetic patients develops earlier than in subjects with renal disease from other causes and those with reduced hemoglobin have higher risk of progressive renal disease and have a more rapid decline in glomerular filtration rate (GFR). The aim of this study was to investigate relationship between red blood cell count (RBC) and renal function parameters in type 1 diabetic patients (T1DM) with normal or mildly impaired renal function.
Methods: Study included 313 normoalbuminuric T1DM with normal or mildly decreased (eGFR > 60 $mlmin^{-1}$ 1.73 m^2) renal function and before any interventions with statins, ACE inhibitors or angiotensin II receptor blockers. eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula. Microalbumin was measured spectrophotometrically by turbidimetric immuno-inhibition. Urinary albumin excretion rate (UAE) was measured from at least two 24-h urine samples and determined as the mean of 24-h urine collections. Complete blood count was determined on an automatic blood counter.
Results: Estimated GFR was significantly associated with hemoglobin (Hb) (r=0.11), hematocrit (Hct) (r=0.18) and erythrocytes (E) (r=0.17). Hb (133 vs 141 vs 141 g/L, p=0.01), Hct (0.38 vs 0.41 vs 0.41 L/L, p=0.001), and E (4.4 vs 4.7 vs $4.7x10^{12}$/L, p=0.003) levels were significantly lower in subjects with mildly decreased (eGFR=60-90 ml/min) renal function compared to those with normal renal function (eGFR=90-125 ml/min) or renal hyperfiltration (eGFR≥ 125 ml/min). Stratifying RBC markers for the degree of eGFR, trends across different groups for Hb (133 vs 140 g/L, p=0.01), Hct (0.38 vs 0.41 L/L, p=0.001), and E (4.4 vs $4.7x10^{12}$/L, p=0.003) were statistically significant. Stratifying RBC for degree of UAE, trends across quartiles was statistically significant for Hb (140 vs 135 g/L, p=0.03) and Hct (0.41 vs 0.39 L/L, p=0.03)
Conclusions: Significant associations between RBC and renal function parameters even in normoalbuminuric T1DM with eGFR >60 ml/min suggest that the interplay between RBC and renal function exist in the absence of nephropathy.

MP284 ELIMINATION AND DEGRADATION OF THE INCRETIN HORMONES GLUCAGON-LIKE PEPTIDE-1 AND GLUCOSE-DEPENDENT INSULINOTROPIC POLYPEPTIDE IN PATIENTS WITH END-STAGE RENAL DISEASE

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Introduction and Aims: The impact of the kidneys in elimination and degradation of intact incretin hormones and their truncated metabolites is unclear. We evaluated elimination and dipeptidyl peptidase 4 (DPP-4)-mediated degradation of glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) in patients with end-stage renal disease (ESRD).
Methods: 12 non-diabetic ESRD patients treated with chronic haemodialysis and 12 matched control subjects were examined in a double-blinded, randomised, observational study. Over 4 separate study days, synthetic human GIP or GLP-1 was infused with or without concurrent inhibition of DPP-4 using sitagliptin (100 mg) or placebo. Plasma concentrations of glucose, insulin, glucagon, and intact and total forms of GLP-1 and GIP were measured. Plasma half-life ($T_{½}$), metabolic clearance rate (MCR), area under curve and volume of distribution for intact and metabolite levels of GLP-1 and GIP were calculated.
Results: Fasting concentrations of intact GLP-1 and GIP were increased in ESRD patients (P < 0.001), whereas fasting levels of GLP-1 and GIP metabolites did not differ between groups (P > 0.738). MCRs of intact GLP-1 and GIP, and the GLP-1 metabolite were reduced in ESRD patients on the placebo day (P < 0.009), while $T_{½}$ of intact and metabolite forms of GLP-1 and GIP were comparable between groups (P > 0.121).
Conclusions: Unexpectedly, degradation and elimination of the intact and metabolite forms of GLP-1 and GIP appeared preserved, although reduced, in patients with ESRD. This may be taken into consideration prior to potential introduction of incretin-based therapy in patients with impaired renal function.

MP285 LIFE-THREATENING DUODENAL GRAFT ULCERATIONS FOLLOWING SINGLE PANCREAS TRANSPLANTATION

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Introduction and Aims: Standard technique for pancreas transplantation (Ptx) in the last era has been whole-pancreaticoduodenal grafts. Complications related to the duodenal graft segment have been reported. We hereby report a patient who experienced severe duodenal graft complication after PTx
Methods: A 40-year old woman with brittle diabetes for 20 years received a PTx in spring 2013 (HLA-mismatch 3-1, CMV + to +). Immunosuppression consisted of ATG induction, prednisolone, tacrolimus (trough 8-12µg/L) and mycofenolate mofetil (MMF) 1 g x2. The postoperative course was excellent without sign of rejection. Surveillance of plasma CMV PCR revealed a positive test after six weeks and was treated preemptively with oral Valganciclovir for 4 weeks. Enteric drainage to the native duodenum allowed endoscopic surveillance of both graft duodenum and pancreas. Endoscopic ultrasound guided surveillance biopsies at weeks 3 and 6 post-transplant were normal.
Results: At week twelve post PTx the patient suffered diffuse abdominal pain and decreased hemoglogin. Gastroscopy showed multiple ulcers in donor duodenum. Biopsies verified duodenal graft rejection grade 4 but no signs of pancreas rejection. She was treated with high-dose i.v. methylprednisolon (total of 1.375 g over 5 days) followed by an increased oral prednisolone dose. Follow-up biopsy showed successful rejection-treatment with some regression of the duodenal ulcers.Fifteen weeks post PTx the patient had increasing abdominal pain. A gastroscopy showed large ulcers in each end of the donor duodenum. Biopsies did not show rejection or signs of viral, bacterial or fungal infection by standard techniques. A CMV PCR test of the biopsy material was positive although CMV immunostaining was negative. The patient received iv ganciclovir with some clinical effect.The duodenal ulcers were extensive and considered at risk for perforation, but surgical intervention was not considered feasible without risk for graft loss. Treatment consisted of high-dose of proton-pump inhibitor, prednisolone reduction and discontinuation of acetylsalicylic acid. Persistence of ulcers at week 17 post PTx led to reduction of MMF to 500mg x 2 since there were no signs of rejection. Pancreas function remained stable with C-peptides about 900pmol/l . Repeated gastroscopies showed no sign of heeling and the abdominal pain persisted. She maintained treatment for CMV. At month 7 after PTx she experienced acute severe abdominal pain and CT scan showed occluded arteries, and severe damage of the pancreatic head and graftectomy was performed without further complications. Histological examination of the resected graft showed chronic inflammation, ulceration in duodendum and no signs of rejection; staining for CMV, Herpes 1, adeno- and polyomavirus were also negative.
Conclusions: The etiology of the severe transplant duodenal ulcerations remains unknown. Initially rejection of the duodenal graft was suspected and later biopsies also indicated CMV infection as a causal factor. However, several other factors such as duodenal ischemia, enteral enzymes and treatment with steroids, MMF and ASA may be have contributed.

MP286 ASSOCIATION OF URINARY TRACT INFECTION WITH PROGRESSION OF DIABETIC KIDNEY DISEASE IN TYPE 2 DIABETIC WOMEN

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Introduction and Aims: Urinary tract infection is frequently observed in diabetic patients, especially in diabetic women; however, information is scares in terms of the risk of urinary tract infection for progression of diabetic kidney disease. We therefore conducted this study to determine the relationship between urinary tract infection and progression of diabetic kidney disease in type 2 diabetic women.
Methods: This was a single-center observational cohort study, involving 478 Japanese type 2 diabetic women with normoalbuminuria and an eGFR ≥ 60 mL/min/1.73 m2. The mean age was 51 ± 29 years. In this study, urinary tract infection was defined by qualitative test strips detecting various degree of urinary leukocytes. Qualitative results of leukocytes in the urine of negative, 1+, 2+, and 3+ were converted into numerical scores from 0 to 3, respectively. According to the mean value of the three consecutive urinary leucocyte score on separate visit days, patients were classified into the following three groups: 236 patients with the mean score of 0 (no infection), 124 patients with the score ranging 0.33 to 0.67 (less frequent infection), and 118 patients with the mean score ≥ 1.0 (more frequent infection). Two independent outcomes were defined, progression to microalbuminuria and decrease in eGFR less than 60 mL/min/1.73 m2. Cumulative incidence of these outcomes was calculated by means of Kaplan-Meier method and compared using log-rank test. Hazard ratios were assessed using the Cox proportional hazard model.
Results: 5-years cumulative incidence of developing microalbuminuria in the three groups was 9.7%, 10.4%, and 10.0% in women with no, less frequent, and more frequent infection, showing no significant difference (p=0.7856 by log-rank-test). In the multivariate Cox model with several clinical parameters as covariates, urinary tract infection was not associated with higher risk of developing microalbuminuria. There was also no statistically significant difference in the 5-year cumulative incidence of decrease in eGFR less than 60 ml/min/1.73 m2: 11.8% for women without infection, 13.2% for those with less frequent infection, and 15.8% for those with more frequent infection (p=0.1182, by log-rank test). In the multivariate Cox regression analysis, hazard ratio for patients with either less or more frequent urinary tract infection was not significant in reference to that for patients without infection.
Conclusions: It is unlikely that diabetic women who have urinary tract infection are at significantly increased risk of progression of diabetic kidney disease.

MP287 WHAT IS THE SIGNIFICANCE OF THE ASSOCIATION OF SOLITARY KIDNEY WITH DIABETES MELLITUS ?

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Introduction and Aims: Due to the shortage of living kidney donors and the current Diabetes Mellitus (DM) pandemics, studying the association of the solitary kidney (SK) with DM is of paramount importance. The aim of our study was to assess the significance of the association between SK and the presence or absence of DM.
Methods: Eighty-four patients with SK and DM (group A), mean age: 62.46+/-12.72 y, 36M and 48F, with a mean duration of a SK of 15.7+/-15.15 y were enrolled into the study. Six pts (7.14%)had a congenital SK.The control group (group B) comprised 84 SK pts without DM of similar age and duration of existence of a SK: mean age: 61.58 +/-8.22 y, 23M and 61F, and mean duration of existence of a SK: 15.26+/-13.76 y. Four pts (4.76%) had a congenital SK.The inclusion criteria were history of unilateral nephrectomy in pts with surgically acquired SK and presence of a SK confirmed by at least two imaging methods in pts with congenital SK.All patients were assessed for serum Creatinine, GFR(CKD-EPI), glycemia, cholesterol, triglycerides, serum uric acid, proteinuria/24h, systolic blood pressure (SBP), dyastolic blood pressure (DBP), BMI. Pts from group A were also assessed for HbA1c. Data is presented as mean value ± standard deviation. Mean values were compared using the t-student test (parametric variable) or the Mann-Whitney U-test (non-parametric variables). Percentages were compared using the chi-square test.
Results: The comparative assessment of SK pts with DM (group A) vs. SK pts without DM (group B)is presented in Table 1. The group of pts with SK and DM (group A) had a significantly higher BMI (p=0.0007), glycemia (p<0.001), triglycerides (p=0.0004), uric acid (p=0.019) and proteinuria/24h (p=0.006). The group of pts with SK without DM (group B) presented higher DBP than the study group A (p=0.001). The study group also had a higher prevalence of arterial hypertension (p=0.003) and coronary artery disease (p=0.031).
Conclusions: Our study showed a higher value of proteinuria due to the phenomena of hypertrophy and hyperfiltration in the study group as well as a higher prevalence of arterial hypertension. Patients with SK and DM should be carefully monitored from a nephrological viewpoint for proteinuria, GFR and arterial hypertension and for cardiovascular diseases.

MP288 SERUM LEVELS OF METHYLGLYOXAL AND CARBOXYMETHYL LYSINE ARE INCREASED IN PATIENTS WITH TYPE 1 DIABETES AND REDUCED KIDNEY FUNCTION

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Introduction and Aims: Advanced glycation end-producs (AGEs) are considered markers, and potentially also mediators of chronic vascular complications in diabetes. Inhibition of AGE accumulation reduces the progression of atherogenesis and diabetic nephropathy in experimental models. The role in clinical diabetes of either methylglyoxal (MG), one of the most potent precursors of AGEs, and carboxymethyl-lysine (CML), a well-studied AGE, has not been established. Aim of this study was to determine the circulating levels of MG and CML-modified proteins in patients with type 1 diabetes (T1D) and their association to progression of diabetic nephropathy.
Methods: Serum MG and CML were measured in 350 adults with T1D and in 114 healthy control subjects as part of the Finnish Diabetic Nephropathy (FinnDiane) study. MG was determined by HPLC after derivatization with 1,2-diamino-4,5-dimethoxybenezene. CML was determined by an ELISA-based method. Glomerular filtration rate (GFR) was estimated using the CKD-EPI formula.
Results: Serum MG was higher in patients with T1D as compared to control subjects (411±8 vs 340±12 nM, $P<0.05$). Patients with reduced kidney function (GFR <30 ml/min per 1.73m^2) had significantly higher MG levels than those with GFR >90 (476±32 vs 395±11 nM, $P<0.05$). MG was negatively correlated with GFR ($r=-0.113$, $P=0.035$). The CML levels were higher in the T1D patients with GFR 90 (510±26 vs 459±7 nM, $P90$. CML was negatively correlated with GFR in patients with T1D ($r=-0.121$, $P<0.05$). The urinary albumin excretion rate (AER), age, gender, or HbA_{1C} were not associated with serum MG or CML levels in T1D patients or in controls in our study. The correlation between MG or CML and GFR remained statistically significant also after adjustment for age and gender.
Conclusions: The deterioration of the kidney function is strongly associated with increased levels of MG and CML in patients with T1D. These results support the role of AGEs and their precursors in the development of vascular complications in diabetes.

MP289 NEW FORMULAE FOR MORE PRECISE ESTIMATION OF RENAL FUNCTION IN DIABETIC PATIENTS – EGFR CORRECTED BY HEMOGLOBIN AIC

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Introduction and Aims: Serum creatinine levels are lower in diabetic patients compared with their non-diabetic counterparts. Therefore, estimated glomerular filtration rate (eGFR) is higher in the former than in the latter group. Factors associated with overestimation of renal function in diabetic patients were examined, and new formulae reflecting precise eGFR were created.
Methods: Eighty subjects (age 56.5±15.4 years; 35 males (43.8%); 40 diabetics and 40 non-diabetics subjects) were enrolled. GFR was directly measured by inulin clearance (C_{in}). Estimated GFR (eGFR) values were calculated based on serum creatinine and/or serum cystatin C levels; $eGFR_{cr}$, $eGFR_{cys}$, and $eGFR_{cr\text{-}cys}$. The factors related to the dissociation between each of three eGFR and C_{in} in diabetic patients were examined. The agreement between each of three eGFR and C_{in} were compared.
Results: Although C_{in} was not significantly different between the diabetic and non-diabetic subjects (p=0.2866), each of three eGFR measures from the diabetic patients was significantly higher than that of the non-diabetic subjects (p<0.01). As shown in figure 1, correlation coefficients between each of three eGFR measures and C_{in} in diabetic patients were weeker than those of non-diabetic subjects, and the intercepts of the regression lines in the diabetic patients were significantly higher than those of the non-diabetic subjects. The intraclass correlation coefficients between each of eGFR and C_{in} in diabetic patients were weaker than those in the non-diabetic subjects. As shown in figuire 2, there were significant and positive correlations between the ratio of each of three $eGFR/C_{in}$, hemoglobin A1c and glycated albumin. According to the regression line between $eGFR/C_{in}$ and glycemic control indices, new formulae of eGFR corrected by glycemic control indices of hemoglobin A1c and glycated albumin

MP287 Table 1.

Parameter		Group A(n=84)	Group B(n=84)	P Value
Age (years)		62.46±12.72	61.58±8.22	0.594
Gender	Male (%)	42.85% (n=36)	27.38% (n=23)	0.036
	Female(%)	57.14% (n=48)	72.62% (n=61)	0.043
Duration of SK (years)		15.7±15.15	15.26±13.77	0.931
Age at nephrectomy for pts with surgically acquirred SK (years)		50.36±13.88 (n=78)	48.64±13.01(n=80)	0.425
Duration of DM (years)		8.78±8.55	-	-
BMI (kg/sqm)		30.85±6.88	27.62±5.04	0.0007
Systolic BP (mmHg)		134.52±21.37	140.47±22.22	0.078
Dyastolic BP (mmHg)		76.96±10.86	83.63±13.69	0.001
Serum creatinine (mg/dl)		1.77±1.38	1.5±0.82	0.34
Glycemia (mg/dl)		170.25±87.17	97.75±16.02	<0.001
Serum cholesterol (mg/dl)		201.54±59.69	215.94±62.28	0.137
Serum triglicerides(mg/dl)		225.21±179.81	152.28±73.39	0.0004
Uric acid (mg/dl)		6.59±2.09	5.89±1.75	0.019
HbA1c (%)		8.67±2.09 (n=41)	-	-
Proteinuria (g/24h)		0.64±1.07	0.29±0.52	0.006
GFR (ml/min/1.73sqm)		50.6±25.68	50.77±20.61	0.962
Arterial hypertension (%)		86.9% (n=73)	67.85% (n=57)	0.003
Coronary artery disease (%)		55.95% (n=47)	39.28% (n=33)	0.031

Figure 1

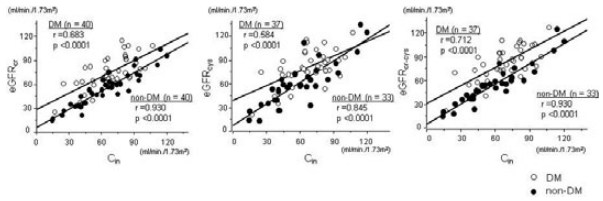

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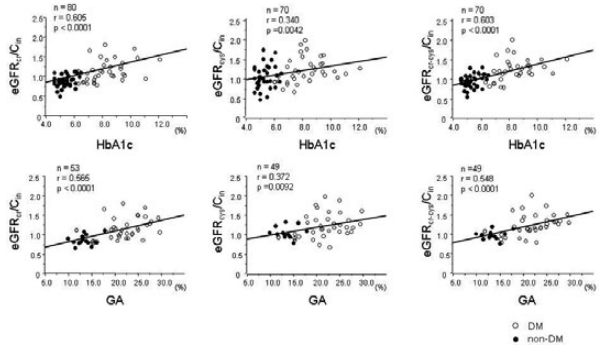
Figure 2



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were created. The intraclass correlation coeffficients of new formulae of eGFR corrected by the glycemic control indices of hemoglobin A1c and glycated albumin were higher than the original eGFR, particularly in diabetic patients. For clinical feasiblity, eGFR corrected by hemoglobin A1C, i.e., $eGFR_{cr}$ / (0.428 + 0.085 × HbA1c), would be useful.
Conclusions: eGFR overestimates C_{in} as glycemic controls worsen. eGFR corrected by hemoglobin A1c is considered to be clinically useful and feasible for precise assessment of renal funtion in diabetic patients.

MP290 CHRONIC KIDNEY DISEASE (CKD) AND OBESITY IN DIABETES MELLITUS TYPE 2 (DM2): BASELINE CHARACTERISTICS OF THE DIABETES COHORTE STUDY (DIACORE)

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Introduction and Aims: DM2, a major risk factor for CKD and adverse cardiovascular outcomes, is increasing in prevalence. We have established DIACORE to systematically explore the mechanisms in DM2 complications. Here, we report baseline characteristics of the center with completed recruitment, focusing on CKD, macrovascular disease and obesity.
Methods: DIACORE is a prospective, observational, two-center cohort study of Caucasian DM2 patients with 2-yearly follow-ups. Inclusion criteria: DM2, Caucasian, age >= 18yrs. Key exclusion criteria: renal replacement therapy, active cancer or viral hepatitis, HIV, autoimmune disease with potential renal disease. Standardized phenotyping by study personnel at each center comprises a questionnaire, physical examination and central laboratory investigations. Descriptive baseline characteristics are given as mean±1SD or median [25% interquartile range].
Results: Between 4/2010 and 8/2013, we recruited 2492 participants in one center, with the following baseline characteristics: 60.3% male, age 65.6±9.0yrs, duration of DM2 10.3±8.5yrs, HbA1c 6.9±1.1%, BMI 31.4±5.7kg/m2, waist hip ratio (WHR) 0.96±0.09, blood pressure 139±18 / 76±10 mmHg. At baseline, 11.1%, 7.5%, 14%, 4% and 5.3% of patients had had previous myocardial infarction, coronary bypass operation, percutaneous coronary intervention, peripheral arterial angioplasty or laser treatment for diabetic retinopathy respectively.Mean creatinine-based eGFR (CKD-EPI formula) was 78.1±20.0ml/min/1.73m2 and median albumin-creatinine-ratio (UACR) from spot urine 10.7 [4.9,31.7] mg/g. 447 (17.9%) patients had eGFR<60ml/min/1.72m2, n=635 (25.5%) had UACR≥ 30mg/g; 10.6% had eGFR<60 ml/min/1.72m2 without elevated UACR (Table 1).10.1%, 35.2%, 31.6% and 22.9% of patients had BMI <25, 25-29, 30-35 and >35 respectively. Higher BMI and higher WHR were both associated with higher HbA1c, higher prevalence of eGFR<60 and UACR≥30mg/g, higher insulin resistance (HOMA-IR) and lower HDL (p<0.001). In contrast, higher WHR but not higher BMI were associated with male sex and longer DM2 duration (p<0.001).
Conclusions: There is significant micro- and macrovascular comorbidity in this large cohort of DM2 patients, with a positive correlation between obesity and CKD. CKD prevalence compares well with data from UKPDS patients with similar DM2 duration. Recruiting of an additional 500 patients in the second center will be completed in April 2014. A comparison with other DM2 cohorts and DM2 subgroups of population based studies to assess the representativeness of DIACORE as an outpatient DM2 population is ongoing work.

MP290 Table 1: CKD prevalence (KDIGO 2012)

		UACR Categories		
		<30mg/g	30-300mg/g	>300mg/g
eGFR Categories (ml/min/1.73m2)	≥ 90	618 (25.5%)	149 (6.2%)	20 (0.8%)
	60-89	904 (37.3%)	242 (10.0%)	43 (1.8%)
	45-59	188 (8.8%	77 (3.2%)	22 (0.9%)
	30-44	63 (2.6%)	38 (1.6%)	9 (0.4%)
	15-29	15 (0.6%)	18 (0.7%)	15 (0.6%)
	<15	0 (0%)	0 (0%)	2 (0.008%)

MP291 EFFECT OF GLYCAEMIC AND ELECTROLYTE VARIATION ON CARDIAC ELECTRICAL ACTIVITY DURING HAEMODIALYSIS IN PEOPLE WITH INSULIN TREATED DIABETES

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Introduction and Aims: The annual mortality among diabetic dialysis patients is high, with 1-year survival rate of 84.7% in 2010 cohort or UK Renal Registry. Cardiovascular deaths account for 22% of mortality on (UK Renal Registry 2012 report). Rapid electrolyte shifts, QT dispersion, Left ventricular hypertrophy, myocardial structural and functional abnormalities and sympathetic hyperactivity are potential causative factors. Arrhythmia accounts of more than half of these CV deaths as in USRDS report. Hypoglycaemia has been linked to sudden death in insulin treated diabetes.We aimed to explore the relation between glycaemic variation and heart rate, rhythm and QTc interval 4hrs before, during (3 to 4hrs) and 4hrs after haemodialysis (HD) and on non-HD days.
Methods: In our ongoing study, we undertook week-long continuous glucose monitoring and Holter monitoring, for 1 to 3 weeks in insulin deficient patients. Baseline echocardiogram was done. Serum electrolytes and 12 lead ECG's were obtained at the beginning, middle and end of HD during the 1st study week.
Results: 7 patients (3 male and 4 female, mean age 46.7±5.7 yrs) were monitored covering 48 HD sessions. 6 patients had Type 1 diabetes and 1 had MODY3.Mean glucose levels during HD were significantly lower than pre-HD (9.4±4.0 vs11.9 ±4.9mmol/L, p<0.01, n=28) and post-HD period (9.3±3.8 vs 13.4±4.5mmol/L, p13.0mmol/L) during pre-HD compared to HD (83.5±99.6mins vs 27.9±57.3mins, p<0.005, n=29) and also during post-HD compared to HD period (105.5±81.2 vs 25.5 ±51mins, p<0.001, n=40) on paired samples. Hypoglycaemia (<3.5mmol/L) occurred infrequently during pre-HD (2 episodes, avg 50mins), and post-HD periods (3 episodes, avg 63.3mins) compared to HD period (6 episodes, avg 30mins) with no statistical significance.Mean QTc interval was not significantly different between pre-HD and HD (420±22 vs 421±19ms, n= 31), but was longer during post-HD compared to HD period (427±19 vs 423±20ms, p<0.005, n= 45) on paired samples. Multiple short episodes of asymptomatic tachy- and brady-arrhythmias were noted in 5 out of 7 patients, including atrial tachycardia, non-sustained ventricular tachycardia, sinus bradycardia, ventricular bigeminy/trigeminy & junctional rhythm.Mean post-HD serum electrolytes were significantly lower than pre-HD levels (n=21): potassium 3.3±0.3 vs 4.5±0.8 mmol/L (p<0.0001), magnesium 0.80±0.07 vs 0.98 ±0.11mmol/L (p<0.0001) and corrected calcium 2.18±0.06 vs 2.25±0.16 mmol/L (p=<0.05) respectively (all patients dialysed with standard dialysate with potassium of 2.0mmol/L). Mean QTc interval was significantly prolonged on post-HD ECG compared to pre-HD ECG (507±58 vs 469±45 ms, p<0.005).
Conclusions: Periodic Holter monitoring of diabetic patients on haemodialysis reveals frequent episodes of arrhythmias, some of which are potentially life threatening. Larger study is required to understand the pathophysiological basis of these arrhythmias and their relation to glycaemia.

MP292 TNF-A AND MICROALBUMINURIA IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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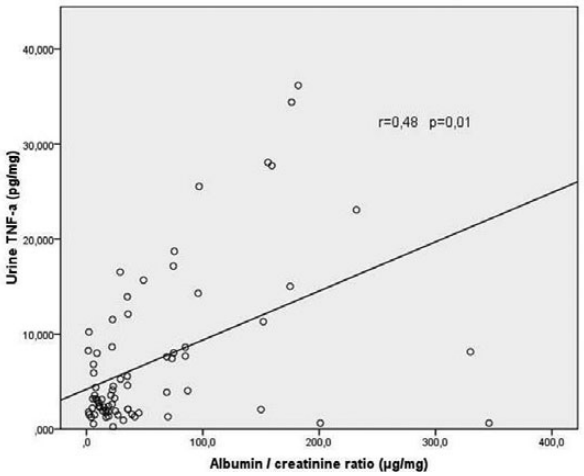
Introduction and Aims: Diabetic nephropathy is a major microvascular complication of diabetes mellitus (DM) and a main cause of mortality. Recent evidence suggests that chronic subclinical inflammation play a key role in the pathogenesis diabetic nephropathy. Aim of the present study was to investigate whether there are associations between inflammatory markers and albuminuria in patients with type 2 DM.
Methods: Eighty patients with type 2 DM (32 male, median age 68 years) were enrolled in the study. The presence of diabetic neuropathy, retinopathy and cardiovascular disease as well as the administered drugs were recorded. Blood pressure was measured and estimated glomerular filtration rate (eGFR) was calculated. Blood samples were collected for laboratory tests, C-reactive protein (CRP) and fibrinogen.
Albumin-creatinine ratio (ACR) was calculated in first morning urine samples. Serum and urinary levels of TNF-α were determined by immunoabsorbent assay (ELISA) using commercially available standard kits (Research & Diagnostic Systems, Europe Ltd, Abington CK).
Results: ACR was significantly correlated with the presence of cardiovascular disease, hypertension, administration of clopidogrel, ACEs-ARBs and glycosylated hemoglobin levels. ACR was not correlated with serum CRP, fibrinogen or TNF-α levels, but had a strong correlation with urinary levels of TNF-α. The latter were also associated with the presence of diabetic retinopathy. Forty-five patients had normoalbuminuria, 33 microalbuminuria and 2 macroalbuminuria. Compared to patients with normoalbuminuria, patients with microalbuminuria were older and had longer duration of DM and higher glycosylated hemoglobin levels. In addition, a greater percentage of patients in the latter group had diabetic retinopathy, neuropathy and cardiovascular disease and were on treatment with ACEs/ARBs. Additionally, urinary levels of TNF-α were significantly higher in patients with microalbuminuria compared to patients with normoalbuminuria. Serum levels of TNF-α did not differ significantly between two groups. Finally, serum TNF-α levels did not correlate with urinary TNF-α levels.
Conclusions: In patients with type 2 diabetes mellitus, urinary, but not serum TNF-α levels are associated with the presence and severity of microalbuminuria. Further studies are needed to determine the exact role of this cytokine in the development and progression of diabetic nephropathy.

MP292 Clinical features, laboratory findings and drugs in diabetic patients with normo- and microalbuminur

Parameters	Patientswith normoalbuminuria (n = 45)	Patients with microalbuminuria (n = 33)
Age (years)	64 (37-78)	70 (51-78) *
Sex (male/ female)	17/28 (37.8/ 62.2)	15/18 (45.5 / 54.5)
Duration of DM (years)	12 (1-38)	18 (2-35) **
Body mass index (kg/m2)	27 ± 5.1	28.5 ± 4.5
Mean blood pressure (mmHg)	98.33 ± 8.6	101 ± 8.57
Systolic blood pressure (mmHg)	133.4 ± 13.1	137.9 ± 13.1
Diastolic blood pressure (mmHg)	80.8 ± 9.9	82.6 ± 9.2
Hypertension	23 (51.1)	29 (87.9)
Cardiovascular disease	13 (28.8)	19 (57.6) **
Retinopathy	12 (30)	19 (59.3) **
Diabetic neuropathy	19 (50)	17 (80.1) ***
Statins	32 (71.1)	28 (84.8)
Acetylosalicylic acid	12 (26.7)	9 (27.3)
Clopidogrel	9 (20)	14 (42.4)
ACEi/ARBs	18 (40)	27 (81.8)
Fibrinogen (g/l)	3.3 ± 0.45	3.26 ± 0.67
Glycozylated hemoglobin (%)	6.7 ± 0.7	7.06 ± 0.5
Total cholesterol (mg/dl)	177.2 ± 38.1	171.7 ± 33.4
LDL cholesterol(mg/dl)	108.5 ± 26.6	104.5 ± 25.9
HDL cholesterol (mg/dl)	46.96 ± 9.1	43.18 ± 9.28
Triglycerides (mg/dl)	125.8 ± 56.9	129.9 ± 46.5
C- reactive protein (mg/dl)	0.53 (0.22-1.9)	0.53 (0.13-0.79)
Serum TNF-α (pg/ml)	3.79 ± 5.1	4.99 ± 5.06
Urinary TNF-α (pg/mg creatinine)	3.8 ± 3.3	11.4 ± 10.3



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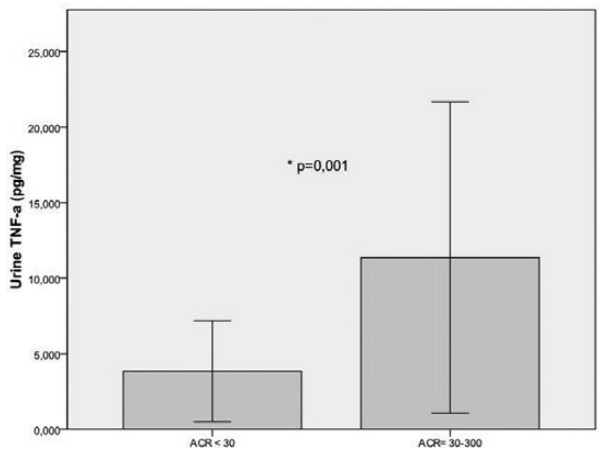

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MP293 HYPOXIA AS A REVERSIBLE CAUSE OF CARDIOVASCULAR AUTONOMIC NEUROPATHY IN PATIENTS WITH TYPE II DIABETES AND IMPAIRED RENAL FUNCTION

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Introduction and Aims: Cardiovascular autonomic neuropathy (CAN), characterized by an imbalance between sympathetic and parasympathetic activities, is common in patients with diabetes mellitus. Although CAN is conventionally considered to be an organic, irreversible disorder, it has already been demonstrated in patients with type 1 diabetes that BRS could be corrected by deep breathing, thus suggesting a functional component to the disorder. In this study we tested this hypothesis in the clinical setting of type 2 diabetic patients with or without renal impairment.
Methods: 27 patients affected by type 2 diabetes were enrolled. Mean ± SEM age was 61.1±0.8 years; diabetic duration was 11.2 ±2 years and BMI 29.9±0.7 kg/m2. GFR, estimated by CKD-EPI formula was 69.1± 5.4 ml/min (range 18-105 ml/min), 6 patients presented microalbuminuria and 6 macroalbuminuria. 24 healthy subjects (age 58.5±1) were enrolled as controls.CAN was assessed by measurement of blood pressure (BP), heart rate (HR) and arterial baroreflex sensitivity (BRS) obtained from recordings fluctuations in the RR interval and BP during spontaneous and normal (15 breaths per min) or slow, deep (6 breaths per min) controlled breathing. Then, the entire protocol was repeated in condition of hyperoxia, breathing 5 L/min oxygen.
Results: During normal controlled breathing diabetic patients presented higher HR and lower BRS compared with the control participants (5.5±0.6 vs 11.8 ±2.1 ms/mmHg, p<0.05).Neither duration of diabetes, nor BMI, BP values and presence of micro/macroalbuminuria were associated to autonomic function parameters. Interestingly, allocating diabetic patients according to the presence of chronic kidney disease (CKD, i.e. GFR ≤ 60 ml/min) we found that patients with renal impairment (n 11) presented significant lower BRS values respect to not-CKD patients (3.9±0.8 vs 6.5 ±0.8 ms/mmHg, respectively, p<0.05).Deep breathing and oxygen administration

significantly reduced HR and increased BRS in both the control group and diabetic patients (15.3±2.3 ms/mmHg and 9.6 ± 1.8, respectively, P<0.05 vs normoxia). Notably, a similar this trend was also observed in the subgroup of CKD diabetic patients (BRS during hyperoxia 7.6±1.6 ms/mmHg; P<0.05 vs normoxia).
Conclusions: Our results show that CAN present in type 2 diabetic patients is further aggravated in CKD.However, this condition can be partially reversed by increasing oxygen supply, suggesting a possible role of hypoxia in the origin of diabetic complications. This finding supports the hypothesis that interventions, like physical activity, may be useful in the prevention and management of complications in diabetic patients.At the same time, the severity of CAN and good response to oxygen in CKD call attention on hypoxia as a reversible pathogenic factor of the renal damage in diabetic patients.

MP294 FGF-23 IS ASSOCIATED WITH INSULIN RESISTANCE IN OBESE NON-CKD PATIENTS AND IN PRE-DIALYSIS CKD PATIENTS

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Introduction and Aims: Fibroblast growth factor 23 (FGF-23) acts to reduce renal phosphorus re-absorption (increasing renal phosphorus excretion) by decreasing the expression of renal proximal tubule NaPi-II co-transporters. In CKD, as nephron mass decreases, renal phosphorus elimination becomes impaired, and FGF-23 increases to maintain normo-phosphatemia. Consequently, it has been suggested that increased FGF-23 is an early biomarker indicating renal phosphorus homeostasis is disrupted, even in the absence of overt hyperphosphatemia. Insulin directly induces NaPi-II, and is therefore anti-phosphaturic, promoting renal phosphorus retention. Previously, we have reported a positive association between insulin resistance (HOMA-IR) and FGF-23 in pre-dialysis CKD patients (Garland J et al, *Journal of Diabetes and its Complications*, 2013). We wished to determine if the association between FGF-23 and insulin resistance could also be demonstrated in a non-CKD population.Aim: Our primary objective was to compare the associations between insulin resistance and FGF-23 in non-CKD and CKD populations.
Methods: Subjects: Cross sectional study of 72 predialysis stage 3-5 CKD patients and 66 obese, non-diabetic, non-CKD patients receiving care in Ontario, Canada. Insulin resistance was assessed using the homeostasis model assessment of insulin resistance (HOMA-IR), and plasma carboxyl terminal FGF23 (ctFGF-23) was measured in duplicate by enzyme-linked immunosorbent assay. Kidney function was estimated (eGFR) using the abbreviated MDRD formula.
Results: CKD patients were older, had greater systolic but lower diastolic blood pressure, lower eGFR, and had higher HOMA-IR and FGF-23 levels compared to non-CKD patients (see table). By partial correlation, in CKD patients (N=72), accounting for kidney function (eGFR) and phosphorus level, ctFGF-23 was positively associated with HOMA-IR (r=0.4;P=0.001). This assocation remained in non-CKD patients (N=66) (r=0.26;P=0.04), and when considering all patients together (N=138) (r=0.25; P=0.003).
Conclusions: The association we described previously between HOMA-IR and ctFGF-23 in a CKD population remained robust in an obese non-CKD cohort. These data suggest that insulin resistance may impact on renal phosphorus handling in CKD, and in patients with preserved kidney function. Studies evaluating urinary renal phosphorus excretion in insulin resistance are needed.

MP294 Study Participants

Variable	CKD N=72	non-CKD N=66	P
Age	64 +/- 14	59 +/- 13	0.003
BMI	30.2 +/- 8	32.1 +/- 4	0.08
Waist (cm)	101.6 +/- 22	109.3 +/- 10	0.01
BP (Sys)	130.7 +/- 16	124.9 +/- 18	0.04
BP (Dia)	74.8 +/- 11.7	79 +/- 9.2	0.02
Glucose	5.8 +/- 1.2	5.5 +/- 0.6	0.06
Phosphorus	1.27 +/- 0.24	0.95 +/- 0.21	<0.0001
eGFR	25.8 +/- 13	63 +/- 13	<0.0001
HOMA-IR	2.66 (1.4 - 5)	2.15 (1.3 - 3)	0.02
ctFGF-23	132 (58 -300)	67 (56-79)	<0.0001

MP295 ASSOCIATION OF NLR AND ALBUMINURIA IN DIABETIC PATIENTS.

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Introduction and Aims: Diabetic nephropathy (DN) is a major manifestation of microangiopathy in patients with Diabetes Mellitus (DM). The current data have proven the role of inflammation in the development of micro and macro vascular complications in diabetes. Recently, neutrophil-to-lymphocyte ratio (NLR) was found to positively correlated with inflammatory markers including tumor necrosis factor-α (TNF- α) and interleukin (IL)-6 in cardiac and noncardiac patients and NLR was introduced as potential marker to determine inflammation. This study aimed to determine the relationship between inflammation, kidney functions and albuminuria in diabetic patients.
Methods: Five hundered and seventy-two diabetic patients who were between the ages of 18 and 65 years were included and assessed in this cross sectional study. HbA1c, uric acid, creatinine, urinary albumin levels were measured. NLR was calculated as the ratio of the neutrophils to lymphocytes, obtained from the same automated blood sample. Patients were divided into three groups according to albuminuria levels as normoalbuminuric, microalbuminuric and macroalbuminuric. After calculating median of NLR, patients were divided in two groups. Statistical significant differences between the groups were determined by chi-square test for categorical variables. Associations between the variables were explored using the Spearman's rho (for data that was not normally distributed). Data are expressed as median (minimum-maximum). Two-sided P values less than 0.05 were considered significant.
Results: The baseline characteristics of the 572 subjects enrolled in the study are shown in Table 1. There were statistically significant differences in the age, creatinine, uric acid, HbA1c, NLR according to albuminuria groups. As shown in Table 2, a significant increase was observed in creatinine and albuminuria levels in parallel to increase in NLR. Albuminuria was significantly correlated with age, creatinine, HbA1c and NLR levels (r: 0.202 p: <0.001, r: 0.094, p: 0.024, r: 0.387, p: <0.001, r: 0.164 p: <0.001 respectively) . Age, serum creatinine, HbA1c and NLR levels were found to be independently associated with albuminuria.
Conclusions: This study demonstrated that inflammation, uncontrolled hyperglycemia and diminished kidney functions were closely associated with albuminuria in diabetic patients. Further prospective and randomised studies are needed to highlight pathogenesis of diabetic microvascular diseases.

MP295 Table 2.

Parameters	Group1 (NLR≤1.594) [median(min-max)] N=286	Group 2(NLR>1.594) [median(min-max)] N=286	P value
Age (year)	52(18-64)	53(21-64)	0.533
Sex (f/m)	183/103	149/137	0.004
Creatinine (mg/dL)	0.68(0.20-2.90	0.73(0.30-5.50)	0.002
Uric acid (mg/dl)	4(1-8)	4(1-10)	0.224
HbA1c (%)	7.4(4.8-17.5)	7.6(4.8-14.5)	0.070
Albuminuria (mg/g)	0.006(0.000-1.093)	0.010(0.000-3.333)	0.004

MP296 CLINICAL AND METABOLIC PREDICTORS OF NONPROLIFERATIVE AND PROLIFERATIVE/LASER TREATED RETINOPATHY IN NORMOALBUMINURIC TYPE 1 DIABETIC PATIENTS WITH NORMAL OR MILDLY IMPAIRED RENAL FUNCTION

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Introduction and Aims: It is assumed that retinopathy and nephropathy, as most important microvascular complications in diabetes, occurs at the same time and that retinovascular pathology reflects renal disease. However, several studies demonstrated

MP295 Table 1.

Parameters	Normoalbuminuric group [median(min-max)] N=434	Microalbuminuric group [median(min-max)] N=98	Macroalbuminuric group [median(min-max)] N=40	P value
Age (year)	51.50(18-64)	56.00(24-64)	57.50(18-64)	<0.001
Sex (f/m)	263/171	51/47	18/22	0.067
Creatinine (mg/dL)	0.68(0.20-2.90)	0.73(0.40-3.60)	1.11(0.40-5.50)	<0.001
Uric acid (mg/dl)	4(1-9)	4(1-10)	5(1-9)	<0.001
HbA1c (%)	7.1(4.8-14.5)	8.9(5-17.5)	8.9(5.3-13.0)	<0.001
NLR	1.56(0.46-4.61)	1.64(0.35-5.31)	2.24(0.94-10.89)	<0.001

that albuminuria is not a risk factor for diabetic retinopathy and that retinopathy might be present already in normoalbuminuric state in type 1 diabetic patients (T1DM). The aim of this study was to evaluate the prevalence and predictors of nonproliferative (NPR) and proliferative/laser-treated retinopathy (PR) in normoalbuminuric T1DM.
Methods: Study included 333 (198 without retinopathy, 114 with NPR and 21 with PR) normoalbuminuric T1DM with normal or mildly decreased renal function (estimated glomerular filtration rate (eGFR) > 60 $mlmin^{-1}1.73m^{-2}$) and before any interventions with statins, ACE inhibitors or angiotensin II receptor blockers. eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula. Microalbumin was measured spectrophotometrically by turbidimetric immuno-inhibition. Urinary albumin excretion rate was measured from at least two 24-h urine samples and determined as the mean of 24-h urine collections. Diagnosis of retinopathy was made by fundoscopy after pupillary dilatation.
Results: Patients without retinopathy compared to those with NPR and PR were younger (31 vs 39 vs 45 years, p<0.001), had longer duration of diabetes (7 vs 18 vs 23 years, p<0.001), lower hemoglobin A1c (7.2±1.5 vs 7.8±1.6 vs 7.8±1.4%, p=0.003), lower total cholesterol (4.8±0.9 vs 5.0±0.9 vs 5.6±1.0 mmol/L, p=0.02), lower LDL cholesterol (2.7 ±0.7 vs 2.8±0.7 vs 3.1±0.9 mmol/L, p=0.03), lower heart rate (HR) (70 vs 78 vs 85 beats/min, p<0.001) and higher eGFR (104 vs 94 vs 81 $mlmin^{-1}1.73m^{-2}$). Stratifying clinical and metabolic characteristics of patients for degree of eGFR, trends across quartiles for age (43 ±9 vs 23±4 years, p<0.001), duration of diabetes (17±10 vs 9±6 years, p<0.001), hemoglobin A1c (7.1±1.2 vs 8.4±1.9%, p=0.002), total cholesterol (5.1±0.7 vs 4.6±0.7 mmol/L, p=0.02), and LDL cholesterol (2.9±0.7 vs 2.4±0.7 mmol/L, p=0.006) were statistically significant.
Conclusions: Retinopathy might be present already in normoalbuminuric state in T1DM. Age, duration of diabetes, hemoglobin A1c, total and LDL cholesterol are major risk factors associated with progression of retinopathy and renal disease.

MP297 THE ADIPOSE TISSUE AND THE RISK FOR OBESITY HYPOVENTILATION SYNDROME DEVELOPMENT IN DIABETIC PATIENTS WITH CHRONIC KIDNEY DISEASE

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Introduction and Aims: Obesity hypoventilation syndrome (OHS) is a diagnosis of exclusion. In its simplest form, it is defined as daytime hypercapnea with elevated awake PCO2 >45mmHg, BMI >35 kg/m2 with the exclusion of pulmonary, neurologic and neuromuscular disorders. In up to 90% of the cases, obstructive sleep apnea-hypopnea syndrome (OSAHS) is also present. Obesity and Diabetes Mellitus (DM) are independent risk factors for the development of obstructive sleep apnea-hypopnea syndrome. Patients with DM have OSAHS up to 23% and likewise 40% of the patients with OSAHS tend to have diabetes. The purpose of this study was to investigate whether there is a relation between the adipose tissue mass and the carbon dioxide partial pressure (PCO2) in diabetic patients with CKD using bioimpedance spectroscopy technique (BCM-Body Composition Monitor).
Methods: This is a single center cohort study of 53 patients with DMT2 and CKD (29M,24F) with mean values of age 70±9 years, body weight 84.4±18.5 Kg, serum creatinine 1.5±0.6 mg/dl, eGFR 49.7±21.7 ml/min/1.73m2,serum albumin 4.2±0.5 g/dl, CRP 0.5±0.12 mg/d, Urine protein to creatinine ratio (P/Cr) 0.88±0.22,Systolic Blood Pressure (SBP) 153±19.26 mmHg, Diastolic Blood Pressure 79.3±12.6 mmHg and BMI 31.91±5.83 kg/m2. The patients' acid base status was estimated by measuring arterial blood gas values(means : pH 7.4±.04 PaCO2 39.84±4.93 mmHg, PaO2 95.7±2.9 mmHg, HCO3 24.99±3.92 mmol/lt) and their body composition (e.g. hydration, fat tissue) by using bioimpedance spectroscopy technique. The scope of the study was to investigate the possible correlation between BCM measurements with arterial blood gas values.
Results: In this study, PaCO2 was statistically significant correlated (Spearman's correlation) with BMI (r=0.28,p=0.03),with the Adipose Tissue Mass (ATM, r=0.28 and p=0.04) and with the Fat Tissue Index (FTI, r=0.33 and p=0.014). Additionally there was a negative statistically significant correlation between the PaCO2 and the Lean Tissue Mass (LTM, r=-0.31 and p=0.021). There were no correlations between the PaCO2 levels and the Total Body Water as well as the overall hyperhydration.
Conclusions: The Obesity Hypoventilation Syndrome is characterized by obesity and hypercapnea and frequently leads to Sleep-Apnea syndrome with increased morbidity and mortality. Even though the BMI of our patients was below 35 kg/m2, there was a correlation with fat tissue markers and PaCO2. Bioimpedance spectroscopy is a useful technique for the early identification of patients at risk for the development of OHS so that we can target our therapy to weight reduction.

MP298 WHEN IS A RENAL BIOPSY PERFORMED ON A PATIENT WITH DIABETES MELLITUS?

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Introduction and Aims: Approximately 30-40 % of patients with diabetes develop diabetic nephropathy (DN) and is the most common cause of entry into renal replacement therapy in Spain. The agreement between retinopathy and diabetic nephropathy in type I diabetes is 95%. However, in type II diabetic association is not so narrow (about 60%) so the absence of retinopathy does not exclude the probability that out diabetic nephropathy . The prevalence of non-diabetic nephropathy (NND) in type II diabetics is unknown and varies between 1-80% depending on the study and criteria used by the authors.
Methods: We retrospectively reviewed renal biopsies of diabetic patients,performed at our center in the last 10 years(2002-2012)
Results: Of the 49 diabetic patients biopsied. 38men and 11women .Their mean age was 63±13 years.The duration of diabetes was 9±7.6years.ADO took 24 at the time of diagnosis, 18 insulin, 1 Insulin+ADO , 6controlled diet. 41 did not have diabetic retinopathy and 8 if they had retinopathy , 2 had polyneuropathy. 44 were hypertensive The average BP was 151±21/78±10.9mmHg. BMI was 31±4.7kg/m2. Crp average upon performance of biopsy was 3.7±3.1mg/dl. Crp clearance 24h urine was 40±36ml/min and GFR calculated by MDRD 32±27ml/min/1.73m2.Albuminuria 1677±1508mg/day, and proteinuria was 4.3±3.2g/24h. Glycosylated hemoglobin of 6.9±1.2%. IgA levels were normal except in 10 cases with a mean age of 451ng/ml.In another 8 cases showed positive ANCAP, 7 ANA ,3 ANA + ENAs,1 AMBG.In 12 cases the diagnosis was ND and in 11 case was ND + NAE(Nephroangioesclerosis),8 extracapillary GN,5 acute interstitial,4 focal segmental GN,2 NAE,2 membranous,2 IgA, 1 Chronicles GN, 1 lupus, 1 amyloidosis. The number of glomeruli per sample analyzed was 17.5±8.4. In 15 cases, the indication of the biopsy was FRA , 11 new onset nephrotic syndrome , 10 suspected systemic disease , 5 nephrotic range proteinuria, glomerular suspected pathology, 6 rapidly progressive renal disease.In 19 cases had nephrotic syndrome.32 had alterations in the sediment. The average renal size by ultrasound was 10.6 ± 1.5 cm.15 patients required dialysis income renal biopsy was performed.When we conducted analyzes comparing subrupos NND vs ND not find differences with BMI , duration of DM , age, Ta , nephrotic syndrome, glycosylated hemoglobin, IgA levels , the number of glomeruli examined by the pathologist , or kidney size . We observed significant differences from the MDRD (ml/min/m2) NND25 vs ND35 p<0.05, crp (mg/dl) NND4.2 vs ND3.1 p<0.05, ie the NND had worse renal function, proteinuria (g/24h)NND4.8 vs ND3.9 p<0.05 ie NDD had higher proteinuria, with respect to age 57 years old NND vs ND 67 p<0.05 ie NND were older.When we analyzed taking insulin vs ADO front NND vs ND we note that the NND is more frequent use of ADO (63% of cases) and the ND is more frequent use of insulin (64% of cases), both pathological and normal sediment were distributed equally in both groups NND vs ND, and 8 ANCAP + one went in ND and 7 NND , ie that marker is clearly related to the NND . Of the 41 cases without RD (18ND and NND 23) and 8 patients with RD (5 with ND and 3 with NND)is saying a similiar distribution in both groups.
Conclusions: IgA levels , immunological markers ANA , ENA , and alterations in the sediment were not useful to us when differentiating a ND vs NND.Although not significant using ADO orient to the possibility that they were a NND.And use insulin more oriented to the possibility that it is a ND.The presence of ARF with ancap+ oriented with a high probability that it is a NND.

MP299 ASSESSMENT OF THE EFFECT OF FLUVASTATIN ON VASCULAR ENDOTHELIAL GROWTH FACTOR-A, ANGIOPOIETIN- 2 AND URINARY ALBUMIN EXCRETION RATE IN PATIENTS WITH TYPE 2 DIABETES

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Introduction and Aims: Diabetic nephropathy (DN), the commonest cause of end-stage renal disease is characterized by abnormal angiogenesis. Increased vascular endothelial growth factor (VEGF)-A and angiopoietin (ang) - 2 in glomeruli during the initial phases of diabetes lead to destabilization of blood vessels, excessive angiogenesis, glomerular injury and increased urinary albumin excretion. Statins have a biphasic dose-dependent effect on angiogenesis characterized by a proangiogenic effect at low doses and antiangiogenic effect at high doses. This study aimed at assessing the effect of a high dose of fluvastatin on VEGF -A, ang -2 and urinary albumin excretion rate (AER) in type 2 diabetic patients.
Methods: This study was conducted on forty five subjects, group 1 included fifteen healthy subjects as controls, group II included fifteen type 2 diabetic patients with normal albumin excretion rate (AER) and group III included fifteen type 2 diabetic patients with increased AER. To all studied participants, complete clinical assessment and laboratory investigations included: Estimation of fasting serum levels of glucose (FBG), creatinine, urea, cholesterol (total, HDL-C and LDL-C), triglycerides (TG), serum aminotransferases (AST and ALT), creatine kinase (CK), glycated hemoglobin (HbA1c) and 2 hours postprandial serum glucose. Estimation of urinary albumin/creatinine ratio (ACR) and determination of serum levels of VEGF- A and ang -2 were done. All diabetic patients received 80 mg fluvastatin once in the evening daily for 10 weeks. ALT, AST and CK assays were repeated after 4 weeks of treatment and all laboratory investigations were repeated after 10 weeks.
Results: Before starting fluvastatin therapy: VEGF-A level was significantly higher in all diabetic patients and in diabetic patients with increased AER compared to controls and was correlated with ACR. Ang -2 level tended to increase in diabetic patients with normal AER, and was significantly higher in diabetic patients with increased AER compared to controls . Ang -2 was correlated with FBG. Following fluvastatin therapy, there were significant reductions in levels of ACR, VEGF-A and ang -2 in both groups of diabetic patients compared to their corresponding values before treatment.

Conclusions: VEGF-A and ang -2 were increased in patients with increased AER, so they can be used as risk markers of renal disease in diabetic patients. The use of high dose fluvastatin demonstrated significant reductions in VEGF-A, ang -2 and ACR and may protect against DN. Fluvastatin therapy should be considered for patients with DN particularly in the early stages of their diseases.

MP300 FGF-23 AND MAGNESIUM AS PREDICTORS OF VALVULAR CALCIFICATIONS IN TYPE 2 DIABETIC PATIENTS WITH 3 AND 4 STAGES OF CHRONIC KIDNEY DISEASE

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Introduction and Aims: Vascular (VC) and mitral valve calcification are common complications observed in CKD patients and have been implicated with the high cardiovascular mortality incidence observed. In the present study we intended to investigate the implication of serum levels of magnesium and FGF-23 with mitral valve calcification in diabetic patients with CKD.
Methods: Prospective, observational study that included 150 diabetic patients, divided into 4 groups according to Wilkins Score' grades, with 38 patients allocated to Grade 1 group, 47 on Grade 2, 29 on Grade 3 and 36 patients on Grade 4 Group. Descriptive statistics were used as well as ANOVA test for comparison between groups. Multiple linear regression were applied in order to identify risk factors and receiver operating characteristic (ROC) curve was drawn to determine a cut point for the serum levels of FGF-23 and Magnesium for predicting mitral valve calcification.
Results: The mean age of these patients was 66.6±9.7 years (40-85) and 35.3% (53) were female. The grade 4 group patients presented higher levels of serum creatinine (p=0.001), phosphorus (p=0.050), PTH (p=0.0001), IL6 (p=0.005) and FGF-23 (p=0.0001), as well as lower values of eGFR (p=0.007), Vitamin D (p=0.001) and Magnesium (p=0.0001). Furthermore, Magnesium levels seem to decrease as the calcification grade worsens, and an inverse relationship was observed for FGF-23, with its serum values increasing with poorer calcification grades. In multiple linear regression FGF-23 (r=0.468, p=0.0001) and Magnesium (r=- 0.469, p= 0.0001) are independent risk factors of mitral valve calcification. ROC curve analysis showed that FGF-23 (AUC=0.997 , P<0.001) and magnesium (AUC= 0.916, p= 0.001), are de predictors of mitral valve calcification in type 2 diabetic in early stages of chronic kidney disease . The mean cut-off value obtained for FGF-23 was 117 RU/mL and for Magnesium the mean cut-off value was 1.7 mg/dL.
Conclusions: Hypomagnesemia and high FGF-23 levels are independent predictors of mitral valve calcification in type 2 diabetic with 3 and 4 stages chronic kidney disease. They might be used diagnostic/therapeutic targets in order to better manage the currently high cardiovascular risk in CKD patients entering dialysis.

MP301 LIPID DEPOSITS THE KIDNEYS OF PATIENTS WITH UNHEALTHY OBESITY OR DIABETES.

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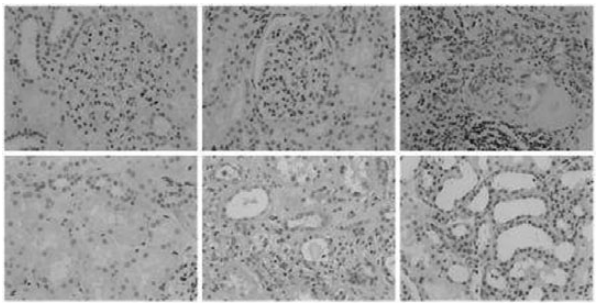
Introduction and Aims: The pandemia of obesity and type 2 diabetes mellitus (T2DM) may have consequences in renal medicine. Metabolically unhealthy obesity is related with risk factors for renal disease i.e. hyperglycaemia, hypertension, dyslipidemia, insulin resistance, sub-clinical inflammation, which are also present in T2DM. Early renal alterations, glomerular hyperfiltration and albuminuria are frequent in both diseases. Thus, T2DM and obesity may a common pathway in the induction renal dysfunction. Dislipidemia may be involved in obesity/diabetes induced renal disease. Renal-lipotoxicity has been proposed as a trigger of glomerular damage, interstitial inflammation and fibrosis. However, in humans, little evidence of its relevance is available. The aim of this study is to evaluate the lipid deposits in human kidneys in patients with or without T2DM or unhealthy obesity.
Methods: We analyzed 16 patients who underwent a nephrectomy due to cancer. Patients with other causes of renal disease were excluded. Subjects were classified in (a) T2DM (ADA criteria), (b) unhealthy obesity: obese subjects (BMI >30 kg/m^2) with metabolic syndrome (MS: ATPIII criteria) and (c) patients without MS.The non-neoplastic kidney tissue was analyzed with the adipophilin staining. Adipophilin immunohistochemistry visualizes small lipid droplets that are not visible by conventional light microscopy. We analyzed the presence of positive adipophilin stain in tubular epithelial cells and in glomeruli. The intensity of the stain was empirically divided in 0=absence, 1:< 25%, 2= 25-75% and 3: < 75%. The pathologists (RR, ES) were blinded for the clinical characteristic of the patients.
Results: Six cases had T2DM, 4 were unhealthy obese and 6 have no MS.The 6 biopsies of T2DM subjects were positive for adipophilin in tubular cells (<25%) in the basal side and in the whole cytoplasm. Also, 5/6 cases were positive in glomeruli (<25 or 25-75%). The 4 biopsies of unhealthy obese were positive for adipophilin in tubular cells (<25%), mainly in the basal side. Only 1 was positive in the glomeruli (<25%). The 6 biopsies of patients without MS were negative for adipophilin in the glomeruli and only 1 was positive in tubular cells (<25%). Two patients without MS were obese. Figure 1 shows three cases. Left: obese without MS, no stain is observed in the glomeruli (up) or tubuli (down). Middle: unhealthy obese, mild lipid droplets in epithelial cells in the glomeruli (up) and in the epithelial cells (down); Right: T2DM, more intense lipid droplets in glomeruli (up) and epithelial cells (down).
Conclusions: In this preliminary study, we observed that lipid droplets are intense in the renal tissue of diabetic patients, mild in obese with MS and rare in patients without MS. Further research is needed to evaluate the clinical relevance of this technique. This study is an initiative of the DIABESITY working group, which is nested in the ERA-EDTA.



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MP302 RENOPROTECTIVE EFFECTS OF COMBINING RAS BLOCKADE DRUGS WITH SPIRONOLACTONE IN PATIENTS WITH DIABETIC MEPHROPATHY AND OVERT ALBUMINURIA

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Introduction and Aims: Several studies have demonstrated that spironolactone has anti-albuminuric function in diabetic nephropathy. But it has been also known that spironolactone often induces the increase creatinine levels with lowering blood pressure. We therefore aimed to evaluate if this anti-albuminuric function of spironolactone is independent of hemodynamic alterations when spironolactone was added on conservative treatment with renin angiotensin system (RAS) blocking drugs.
Methods: Fifty-four Japanese patients with diabetic nephropathy and albuminuria (from100 mg/gCr to 2000 mg/gCr) using RAS-blocking treatment were enrolled in prospective, randomized, open-labelled study. Patients were treated with additional spironolactone 25mg once daily and compared with matched controls for 8 weeks.
Results: Albuminuria was reduced by 33% (95%CI 22-54; P=0.0002) during treatment with spironolactone. When adjusted by systolic blood pressure and eGFR, treatment of spironolactone still showed significant effect on reduction of albuminuria in a linear mixed model (coefficient ± SE; 514.4 ± 137.6 mg/gCr, P<0.0005). Spironolactone treatment also induced significant decrease in urinary excretion of β2-microglobulin, N-acetyl-beta-D-glucosaminidase and angiotensinogen by 2.3±6.5 U/gCr, 1026.9 ± 3174.6 μg/gCr and 156.7 ± 466 μg/gCr compared to group C (P=0.0304, 0.029 and 0.0004), respectively.
Conclusions: Our study suggests that spironolactone has anti-albuminuric effects to be independent of hemodynamic alterations and also plays a role in improving tubule-interstitial injuries and controlling local RAS activity in the kidney.

MP303 REMOVAL OF GLUCOREGULATORY HORMONES DURING HAEMODIALYSIS AND HAEMODIAFILTRATION

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Introduction and Aims: Patients with end-stage renal disease have increased fasting concentrations and disturbed postprandial responses of several glucoregulatory hormones. These findings constitute current or potential targets in the treatment of

diabetes. The aim of the present study was to evaluate removal of glucoregulatory peptide hormones during high-flux haemodialysis (HD) and high-volume haemodiafiltration (HDF).
Methods: 10 non-diabetic patients receiving chronic haemodialysis were examined with a standardised liquid mixed meal test one hour into an HD and an HDF. On a third, optional, examination day, the meal test was performed without concurrent dialysis treatment. Plasma and dialysate samples for measurement of insulin, glucagon and the two gut-derived incretin hormones glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) were collected repeatedly during the examinations. Removal fraction, clearance and the fractional appearance in dialysate were calculated. Results are expressed as mean or geometric mean with confidence intervals (CI).
Results: 10 participants with mean fasting plasma glucose of 4.6 (CI: 4.3-4.9) mmol/l completed the meal test during HD, 8 completed the meal test during HDF and 4 the optional meal test without dialysis. Average dialysis blood flow was 334 (CI: 314-354) ml/min with no detectable recirculation. HDF treatments were all high-volume with an ultrafiltration exceeding 20 l/dialysis. All plasma hormone concentrations declined during the first fasting hour for both dialysis modalities ranging from 24.8 to 47.0% (P<0.043). A significant removal fraction was detected for the hormones except GLP-1. All hormones had a significant clearance ranging from 44.3 to 136.5 ml/min (P<0.013). The fractional appearance of hormone entering the utilised dialysate ranged from 16.6 to 60.0%. A tendency towards higher clearance during HDF was observed for all peptides, significant for GIP (P<0.022). The average hormone concentrations following the meal test were lower during dialysis treatments (P<0.038).
Conclusions: Haemodialysis and haemodiafiltration significantly remove glucoregulatory peptide hormones in non-diabetic dialysis patients. These findings may affect the prescribed dose of present and future antidiabetic treatments in dialysis patients.

MP304 COMPARATIVE ANALYSIS OF GLYCEMIC VARIABILITY PARAMETERS IN PATIENTS WITH CHRONIC KIDNEY DISEASE IN PREDIALYSIS vs PERITONEAL DIALYSIS

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Introduction and Aims: There are many factors that influence the glycemic control in uremic diabetic patients both in predialysis and undergoing replacement therapies.Aim of study is the comparative analysis of glycemic variability in patients with chronic kidney disease (CKD) and type 2 diabetes mellitus (T2DM) vs peritoneal dialysis (PD) diabetic patients using continuous glucose monitoring system (CGMS).
Methods: The study included 15 patients with CKD stage 3-4 and T2DM (7M/8F, 66.8 ±7.8 years) and 11 uremic diabetic patients undergoing PD (3M/8F, 65.8±10.2 years) which were monitorised with CGMS for 72 hours. Parameters analyzed: interstitial glucose, HbA1c, MAGE (Mean Amplitude of Glycemic Excursion), MODD (Mean of Daily Differences), fractal dimension (FD), the percentage of time that were recorded blood glucose higher than 180 mg/dl, the percentage of time that patients had blood glucose lower than 70 mg/dl. All PD patients were adequately dialyzed with Kt /V>1.7.
Results: In diabetic CKD patients, mean interstitial glucose was higher than peritoneal dialysis patients (187,7±52,2 vs 150.6±15.1, p=0,05). The percentage of time glucose values> 180 mg / dl, was significantly increased in CKD patients compared to the diabetic PD patients (51.8±37.2 vs 16.9±11.6, p=0,04). MAGE was higher in patients with CKD in predialysis compared to patients with peritoneal dialysis, however, the differences being not statistically significant (126.3±46.1 vs 100.08±39.5, p=0,2). Also MODD was significantly higher in diabetic CKD patients compared with peritoneal dialysis patients (48,36±10,4 vs 35.2±14.5, p=0,02). However, FD was significantly higher in peritoneal dialysis patients compared to diabetic patients with CKD stages 3-4 (1.2±0.04 vs 1.5±0.08, p=0,001).
Conclusions: Peritoneal dialysis improves glycemic control in uremic diabetic patients probably by decreasing insulinresistance in these patients. Diabetic PD patients had more low amplitude and high frequency glycemic oscillations (FD) but a lower inter day glycemic variability (MODD) compared to diabetic CKD patients.

MP305 THE UTILITY OF BIOIMPEDANCE SPECTROSCOPY IN DIABETIC PATIENTS WITH CHRONIC KIDNEY DISEASE

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Introduction and Aims: Cardiovascular events remain the primary form of mortality and morbidity in diabetic patients with Chronic Kidney Disease (CKD). The abnormal hydration state has been related to arterial hypertension and other symptoms and signs including pulmonary and peripheral edema, heart failure, left ventricular hypertrophy and other adverse cardiovascular sequelae. To determine the hydration status, clinical surrogate parameters are used such as weight gain and blood pressure. However, clinical findings are not always conclusive and sometimes are contradictory. Bioimpedance spectroscopy (BCM-Body Composition Monitor) based on the principle of a vector sum of reactance and resistance seems to be a valid method for assessing and monitoring hydration and nutritional status. The aim of this study was to evaluate the hydration status of diabetic patients with CKD using the BCM.
Methods: This is a single center cohort study of 87 patients with DMT2 and CKD (46m, 41f) with mean values of age 70.08±9.01 years, body weight 86.77±21.01 Kg, serum creatinine 1.68±0.6 mg/dl, eGFR 50.76±22.3 ml/min/1.73m2, serum albumin 4.28±0.40 g/dl, CRP 0.53±0.08 mg/dl, Urine protein to creatinine ratio (P/Cr) 0.92 ±0.19, Systolic Blood Pressure (SBP) 154.5±18.5 mmHg, Diastolic Blood Pressure 79.1 ±11.7mmHg and BMI 32.06±5.56 kg/m2. The patients' hydration status and body composition(OH-overhydration, ECW-extracellular water, ICW-intracellular water) were estimated by using bioimpedance spectroscopy technique with mean values for OH 0.53±0.17 Kg. The scope of the study was to investigate the possible correlation between BCM measurements with clinical and biochemical parameters.
Results: In this study, overhydration was statistically significant correlated (Spearman's correlation) with serum creatinine (r=0.32,p=0.002), with urine protein to creatinine ratio(r=0.44,p<0.001), with SBP (r=0.23,p=0.027) and DBP (r=0.22,p=0.034). Additionally OH was negatively statistically significant correlated with eGFR (r=-0.22, p=0.033) and serum albumin (r=-0.24,p=0.023). The increase of TBW and ECW was statistically significant correlated with diastolic blood pressure increase (r=0.22, p=0.035 & r=0.22, p=0.033 respectively). CRP was statistically significant correlated with P/Cr ratio (r=0.25,p=0.02) but there was no overall correlation with patients' hydration status
Conclusions: Overhydration was statistically significant correlated with the deterioration of renal function (eGFR, proteinuria) with an increase of Blood Pressure and with the decrease of albumin values (nutrition marker). Diabetic patients with CKD are more exposed to expansion of extracellular volume and overhydration (predictors of mortality and morbidity). Bioimpedance spectroscopy technique is a potentially useful method for identifying and treating patients with subclinical or clinical overhydration.

MP306 RELIABILITY OF POINT GLUCOSE MONITORING IN HAEMODIALYSIS PATIENTS: ARE NEW INTERNATIONAL GUIDELINES BEING MET?

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Introduction and Aims: Intermittent blood glucose monitoring (BGM) is still the most routinely used method for monitoring glucose in haemodialysis patients as continuous methods are still under evaluation and regulatory review. However we have previously reported that many endogenous factors modified by haemodialysis can affect the accuracy of BGM devices. The use of inaccurate BGM's may be more widespread than anticipated and as such may increase the risk of poor glycaemic control in haemodialysis patients. Recently new international guidelines (ISO15197 2013 and CLSI POCT12-A3:2013) have been published defining new accuracy requirements that BGM's should achieve. The aim of this study was assess the reliability of two BGMs commonly used in Japan in order to determine concordance to the new international guidelines.
Methods: Venous whole blood specimens were obtained from 44 patients just prior to and upon completion of haemodialysis. Glucose values were measured using two different commonly used glucose meters (StatStrip and Glutest). Following this a plasma sample was prepared from the whole blood specimen and analyzed in the central laboratory using a glucose hexokinase method run on a JCA-BM2250 analyzer (reference method). The bias of each glucose meter measurement compared to the reference method was determined and evaluated according to acceptance criteria in the new international guidelines. Glucose values were also analyzed using Consensus Error Grid which were defined in the new SMBG guideline, ISO 15197:2013.

Table

Accuracy comparison of POCT and SMBG meter based on new POCT12-A3 guideline

Pre-dialysis

Required % of Measurements Meeting Error Limit		95	95	98	98
Deveice	N	Glu < 100 mg/dL Within +/- 12mg/dL	Glu >= 100 mg/dL Within +/- 12.5%	Glu < 75 mg/dL Within +/- 15mg/dL	Glu >= 75 mg/dL Within +/- 20%
StatStrip	157	91.3 % (21/23)	98.5 % (132/134)	N/A	100 % (157/157)
Glutest	157	73.9 % (17/23)	84.3 % (113/134)	N/A	97.5% (153/157)

Post-dialysis

Required % of Measurements Meeting Error Limit		95	95	98	98
Deveice	N	Glu < 100 mg/dL Within +/- 12mg/dL	Glu >= 100 mg/dL Within +/- 12.5%	Glu < 75 mg/dL Within +/- 15mg/dL	Glu >= 75 mg/dL Within +/- 20%
StatStrip	148	100% (30/30)	99.2 % (117/118)	N/A	99.2 % (147/148)
Glutest	148	3.3 % (1/30)	25.4 % (30/118)	N/A	60.8 % (90/148)

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Results: There was a difference in the accuracy and reliability of the two meters in meeting the acceptance criteria of the new guidelines.StatStrip Glucose meter achieved the accuracy criteria. Compared to the target criteria of 95%, StatStrip Glucose achieved 100% (n = 30) for glucose concentrations < 100 mg/dL and 99.2% (n = 118) for glucose concentrations more than 100 mg/dL .Glutest meter did not achieve the accuracy criteria. Compared to the target criteria of 95%, Glutest achieved 3.3% (n = 30) for glucose concentrations < 100 mg/dL and 25.4% (n = 118) for glucose concentrations more than 100 mg/dLUsig Consensus Error Grid Analysis with reference method, all 157 data (100%) for pre-dialysis from StatStrip fell in Zone A which is considered to be accurate or acceptable. Only 1 data (0.6%) for post-dialysis fell in Zone B which might lead to altered clinical action.All measurements by StatStrip glucose meter falleexceeded clinically relevant accuracy expectation defined in the guideline. 154 Data (98.1%) for pre-dialysis from Glutest fell in Zone A, however, 50 data (31.8%) for post-dialysis fell in Zone B.
Conclusions: One of the two commonly used PGM's failed to meet the acceptance criteria for new international guidelines for glucose accuracy. This raises concern about now reliable glucose monitoring and the management of glycaemic control is in haemodialysis patients.

MP307 SERUM 25-HYDROXYVITAMIN D INVERSELY CORRELATES WITH PULSE WAVE VELOCITY (PWV) IN NON-DIALYSIS DIABETIC CHRONIC KIDNEY DISEASE (CKD) PATIENTS

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Introduction and Aims: Cardiovascular disease is common in CKD patients and considered to be one of the most common causes of death. Diabetic CKD patients are at especially high risk for cardiovascular mortality. PWV assesses arterial stiffness and is a predictor of both mortality and cardiovascular outcomes. Some studies suggest that vascular injury is so advanced at the dialysis stage that the response to some interventions, like statin treatments is quite poor.To identify predictors of PWV in a prospective cohort of diabetic non-dialysis CKD patients.
Methods: This is a cross-sectional analysis of a prospective cohort of forty seven diabetic CKD patients (31 males, mean age 63.4±14.3 years). 40 laboratory parameters potentially related to cardiovascular risk and carotid-femoral PWV (SphygmoCor) were prospectively assessed. CKD stage distribution was 7 (14%) stage 1, 16 (34%) stage 2, 10 (21%) stage 3A, 12. (25%) stage 3B and 1 (4%) stage 4. Albuminuria 1000 in 5 patients (11%). Data were analyzed by JMP9 ©2012 SAS Institute Inc statistical package.
Results: Mean carotid femoral PWV was 12.47 ± 4.1 m/sec. Higher than expected for age values were observed in 23 (51%) patients. A univariate analysis showed that three variables were associated with PWV with a p<0.1: PWV had a significant positive correlation with age (p=0.0047), but a negative correlation with serum 25 hydroxyvitamin D (p=0.0860) and serum phosphorus (p=0.0664). A multivariate analysis using those three variables yielded a model with an r2 =0.234. Both age (t ratio 2.57, p=0.029) and serum 25 hydroxyvitamin D (t ratio -2.14, p=0.0378) significantly and independently contributed to predict PWV in this model. The contribution of serum phosphate to the model was not statistically significant.
Conclusions: To our knowledge, it is the first study to show that low 25 hydroxyvitamin D values are associated with high PWV; indicating higher vascular stiffness, in early CKD diabetic patients. Prospective studies should explore whether nutritional vitamin D supplementation improves arterial stiffness in this context.

MP308 SURVIVAL OF DIABETIC AND NON DIABETIC PATIENTS ON HEMODIALYSIS IS SIMILAR: REASONS FOR ANOTHER (FRENCH)PARADOX

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Introduction and Aims: Globally the survival of diabetic patients (DP), compared to non-diabetic patients (NDP) with ESRD and undergoing hemodialysis (HD) is significantly lower. This is often assigned to the increased organ damage associated with the diabetes. However, we have not noted a similar pattern and have analysed our data with the aim to identify possible explanations to this paradox which may help in the optimal management of DP with ESRD.
Methods: During the last decade, 408 patients (pts) were treated by HD in our unit. Pts were assigned to the DP cohort when, diabetic nephropathy was the primary cause of ESRD. Diabetes mellitus (DM) as comorbidity was recorded in the NDP group. Analysed mortality risk factors included: age, sex, co-morbidity (Charlson Index [CI]), hospitalisation, anemia management, biological parameters, causes of mortality, and in the DP group relations with HbA1c, and the patient-doctor contact (PDC). Modalities of treatment were similar: dialysis 3 times a week; if necessary, IV erythropoietin-stimulating agents (ESA)(mostly darbepoetin alfa [DA]) was administered every two weeks and IV iron (mostly iron sucrose) once a week. Data were presented as mean±standard deviation (SD). The Student t-test was used for comparison between both groups, and survival curves were constructed using the Kaplan-Meier method.
Results: Out of 408 pts, 101 were DP, and 307 were NDP (including 26pts [8.5%] with DM as comorbidity). In DP 19 pts were type I and 82 pts type II. Causes of ESRD for NDP were nephrosclerosis (24%), glomerulopathy (38%), interstitial nephropathy (27.5%) polycystic kidney disease (10.5%).Survival for DP and NDP at 1, 3 and 5 years was similar: 95.8, 81.7, 65.3% and 95, 85.2, 67.2% respectively, despite the DP being older, having more intensive co-morbidities and requiring more frequent hospitalisation. Mean HbA1c level was 7.4±1.2% for DP and no difference in survival was seen for values higher or lower than 7.5%. Cardiovascular mortality was more frequent in DP (66%) than in NDP (43%) p<0.05. Reasons for equivalent mortality may be: similar Hb level, ESA dosing, serum albumin, CRP levels, a PDC program with visits at least twice a week, and for DP, a regular program, every two weeks, of foot inspection. Conversely, the sample size may be insufficient, however these findings do warrant further investigation.
Conclusions: It may be possible to obtain similar survival rates for DP and NDP on HD. Additional monitoring and care is required for DP especially in relation to cardiovascular diseases and foot examination.

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Parameters	Diabetic Patients	Non-Diabetic Patients	p value
Number of Pts	101	307	
Sex: M /F %	63 / 37	65 / 35	NS
Age: years (SD)	60.2 (12.5)	53.5 (17.2)	0.0001
Charlson Index(SD)	11.2 (2.7)	7.0 (3.3)	0.00001
Hemoglobin:g/dL (SD)	11.41 (0.89)	11.31 (0.92)	0.31
DA:µg/kg/week(SD)	0.51 (0.51)	0.53 (0.39)	0.52
Albumin: g/L (SD)	38.1 (3.4)	38.7 (3.4)	0.12
CRP: mg/L (SD)	11.3 (11.7)	10.9 (16.4)	0.18
Hospitalisation: % pts All pts(days/pt/y)	52 5.52 10.5	43 3.14 7.3	0.05 0.05
Hospitalised pts (days/y)			0.24

MP309 STUDY OF ASSOCIATION OF ANGIOTENSIN CONVERTING ENZYME GENE POLYMORPHISMS AND TARGET ORGAN DAMAGE IN TYPE 2 DIABETES MELLITUS

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Introduction and Aims: Diabetes mellitus is a global health problem. Insertion/deletion (I/D) polymorphisms of angiotensin converting enzyme(ACE) gene are associated with ACE levels and increased risk of coronary heart disease but their association with other complications of diabetes mellitus has not been fully understood with conflicting results in various studies. We studied distribution of ACE gene polymorphisms and their relation to target organ damage in Type 2 Diabetes mellitus in our population.
Methods: After ethics committee clearance, we prospectively did ACE gene polymorphism analysis by polymerase chain reaction, restriction fragment length polymorphism and DNA sequencing in patients of type 2 diabetes mellitus attending our nephrology clinic over 6 months. Clinical, demographic and biochemical data were collected. Association of various polymorphisms with complications of diabetes mellitus such as proteinuria, retinopathy, dyslipidemia, ischemic heart disease, peripheral neuropathy, hypertension and decline in glomerular filtration rate(GFR) were studied. Analysis was done on SPSS version 15 using using Pearsons Chi Square Test for comparing categorical variables and one way Anova to compare continuous variables.

MP309 Table 1: Distribution of complications of Type 2 Diabetes mellitus among ACE gene polymorphisms

Complications	ACE D/D n=16	ACE I/D n= 76	ACE I/I n=38	p-value
Retinopathy	14	58	30	0.61
Hypertension	15	65	31	0.51
Neuropathy	5	22	8	0.61
Proteinuria	13	53	23	0.30
Total Cholesterol (mg/dl)	168.16 ± 82	162.33 ± 47	178.64 ±47	0.41
Triglycerides (mg/dl)	134.5 ± 54	190.7 ± 23	179.57 ±29	0.80
HDL Cholesterol(mg/dl)	35.5 ± 12	35.37 ± 10	31.57 ±12	0.40
Non HDL Cholesterol(mg/dl)	109.83 ± 59	126.06 ± 51	138.63 ±40	0.41
LDL cholesterol(mg/dl)	87.56 ± 50.4	90.68 ± 36.15	97.65 ±35.2	0.75
Ischemic heart disease	5	16	10	0.62
Systolic dysfunction	4	13	8	0.69
Diastolic dysfunction	7	37	15	0.64
Left ventricular hypertrophy	12	49	25	0.72
Ejection Fraction (%)	62.72 ±10	65.73 ± 8	66.03 ± 9	0.51

Results: Of 130 patients, 103 were males (79%), mean age 53.88 ± 9 years, average GFR of the study group was 53.88 ml/min/1.73 m2. The genotype distribution was I/D 58.5%, I/I 29.2% and DD 12.3%. None of the ACE gene polymorphisms were significantly associated with hypertension, proteinuria, retinopathy, peripheral neuropathy, dyslipidemia, ischemic heart disease, left ventricular systolic dysfunction; diastolic dysfunction, left ventricular hypertrophy and left ventricular ejection fraction (table 1). On follow up in 69 patients over 28.5 months interquartile range (IR) (12 to 44.7) the median GFR fall/month was not significantly different among the genotypes (table 2).
Conclusions: ACE I/D gene polymorphisms are not associated with complications of diabetes mellitus and progression of diabetic nephropathy.

MP309 Table 2: Average fall in GFR in ml/min/month (n =69)

ACE D/Dn = 7	ACE I/Dn = 42	ACE I/In = 20	P value
0.4 (IR 0 to 0.7)	0.4 (IR 0 to 0.8)	0.2 (IR 0 to 1.2)	0.96

MP310 THE HETEROGENEITY OF RENAL DAMAGE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Introduction and Aims: Renal pathology and structural-functional relationships of diabetic nephropathy (DN) have been less well studied in type 2 versus type 1 diabetic patients. Although renal damage in type 1 and type 2 diabetic patients shares many similarities, a high incidence of non-diabetic lesions has been reported in clinical biopsies from proteinuric type 2 diabetic patients. As far as diabetic patients undergo renal biopsy only in cases of DN atypical clinical presentation, this heterogeneity could be explained mainly by the coexistences of diabetes (DM) and other kidney disease.The aim of the study was to analyze the nature of kidney damage in patients with type 2 diabetic patients, who had clinical indications for kidney biopsies.
Methods: The retrospective analysis was performed in 58 patients with DM type 2 (31 men, 27 women, mean age 61 ± 9.2). The median of duration of DM was 96 (36; 156) months. In all patients renal biopsy was performed for diagnostic purposes and evaluated by light microscopy and immunofluorescence. All patients had proteinuria above 1,0 g/d, 43% of them had nephrotic syndrome, 80% of patients were hypertensive. Microhematuria was found in 56% patients. Serum creatinine levels were 173 (120; 364) μmol/l.Medians, 25 and 75 percentiles were calculated, statistical significant difference were determined using Mann-Witny method.
Results: According to patterns of renal injury, the patients were divided into 3 groups. The 1-st group (G1) consisted of 29 patients (50%), who had typical changes of DN. In 12 patients (21%, G2) the patterns of DN combined with the signs of other kidney disease. In 17 patients (G3, 29%) no signs of DN were found, and other kidney disease was diagnosed. Non-diabetic patterns were found in total in 29 patients. They included: FGS (8 pts), IgA nephropathy (4 pts), MGN (4 pts), MCD (3 pts), RPGN (4 pts), cryoglobulinemic GN (2 pts), SLE (1pt), tubulo-interstitial nephritis (1 pt), ATI (2 pt). There were no significant difference in basic demographic and clinical parameters between groups (table)
Conclusions: Our data show that about 50% of proteinuric patients with type 2 DM mellitus could have non-diabetic renal lesions, which are accounted for by both the developing of different than DN kidney disease or the combination of latter with DN. We recommend the kidney biopsy in all the patients with atypical clinical course of type 2 diabetes mellitus.

MP311 FGF-23, MAGNESIUM AND ADROPIN AS NEW RISK FACTORS OF SUBCLINICAL ATHEROSCLEROSIS IN TYPE 2 DIABETIC WITH 3 AND 4 STAGES CHRONIC KIDNEY DISEASE

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Introduction and Aims: The carotid intima media thickness (cIMT) is an early marker of atheromatous disease and a strong predictor of cardiovascular morbidity and mortality in the renal population. The abnormalities of the mineral metabolism are apparent early in the course of chronic kidney disease (CKD) and are also associated with cardiovascular events in non-dialyzed patients with CKD. In the present study we intended to investigate the association of serum levels of magnesium, FGF-23 and a new regulator of endothelial function (adropin) with cIMT in diabetic patients with CKD.
Methods: In a cross sectional study we included 150 diabetic patients, divided into 2 groups according to cIMT: G-1 (n=76) - cIMT<0,9mm) and G-2 (n=74) - cIMT≥ 0.9 mm. Descriptive statistics were used as well as Student's t-test for comparison between groups. Single and multiple linear regressions were applied in order to find independent risk factors of carotid intima media thickness.
Results: The mean age of the patients was 66.6±9.7 years (40-85) and 35.3% (53) were female. The G-2 group patients presented higher levels of serum phosphorus (3.8 *vs* 3.5 mg/dL p=0.003), PTH (179.5 *vs* 112.6 μg/mL p=0.0001), FGF-23 (151.6 *vs* 74.4 RU/mL p=0.0001) and IL6 (8.7 *vs* 5.8 pg/mL p=0.0001), as well as lower values of $1.25(OH)_2D3$ (17.6 *vs* 24.5 pg/mL p=0.0001), adropin (5.2 *vs* 9.7 ng/mL p=0.0001) and magnesium (1.2 *vs* 2.1 mg/dL p=0.0001). In multiple linear regression, FGF-23 (r=0.566, p=0.0001), magnesium (r=- 0.490, p= 0.0001) and adropin (r=-0.345 p= 0.030) independently influenced the carotid intima media thickness.
Conclusions: Hypomagnesemia, hypo-adropin and high FGF-23 levels are independent predictors of carotid intima media thickness in type 2 diabetic with 3 and 4 stages chronic kidney disease. Further studies are needed to validate the clinical significance of these new markers in the pathogenesis of atherosclerosis.

MP312 MAY SERUM CYSTATIN C BE A USEFUL SCREENING MARKER OF NEPHROPATHY IN PATIENTS WITH TYPE 2 DIABETES?

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Introduction and Aims: An increased rate of urinary albumin excretion is an important diagnostic and prognostic marker for renal disease in diabetic patients. Multiple studies have demonstrated that serum and urinary Cystatin C could be a reliable marker of GFR in diabetic patients with mild to moderate kidney functions. In this study, we analyzed the use of serum Cystatin C as a marker of early renal impairment in patients with diabetes. We evaluated the relationship of albuminuria, creatinemia and serum cystatin C in diabetic patients to determine whether there is an association with the decline of GFR.
Methods: The study was carried out in 82 type 2 diabetic patients with normoalbuminuria (n = 39), microalbuminuria (n = 15) and macroalbuminuria (n = 28). Serum Cystatin C was measured by Elisa method while microalbuminuria by immunoturdimetric assay. The eGFR level was calculated using the Modification of Diet in Renal Disease (MDRD) formula.
Results: The study showed that serum Cystatin C increased with increasing degree of albuminuria and become statistically significant in patients with macroalbuminuria 2.57 ±0.71 ($p<0.001$). In difference from other studies we did not found a difference in serum Cystatin C levels between patients with normoalbuminuria and microalbuminuria (0.68 ±0.4mg/ml vs. 0.85±0.40mg/l; $p > 0.05$). The serum Cystatin C level was higher in patients with eGFR < 60 mL/min/1.73 m^2 (2.80±0.43 mg/l versus 1.28±0.69 mg/l, $p<0.001$). We found a linear increase of Cystatin C levels with creatinine levels, but the difference was not statistically different in patients with stage 2 and 3 of renal disease according to eGFR level (0.76±0.39 mg/l versus 1.28±0.69 mg/l, $p>0.05$).
Conclusions: Serum Cystatin C could be an alternative to urinary albumin excretion and serum creatine in screening for renal impairement in type 2 diabetic patients. It is a practical and non-invasive method for the evaluation of renal impairment among diabetic patients especially in normoalbuminuric patients but maybe further studies with a larger sample size could be useful to confirm the potential application of Cystatin C as a new biomarker for early detection of diabetic nephropathy.

MP313 CAROTID ATHEROSCLEROSIS IS ASSOCIATED WITH DETERIORATION OF KIDNEY DISEASE IN PATIENTS WITH DIABETES MELLITUS TYPE 2

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Introduction and Aims: The presence of albumin in the urine (albuminuria) and the progression of Chronic Kidney Disease (CKD) are traditional risk factors for

MP310 Basic demographic and clinical parameters in groups of patients with type 2 DM

Croup	Age	Duration of diabetes (month's)	Mean BPmm Hg	Protein excretiong/24 hrs	Serum creatinineμmol/l	Serum proteing/dl
1	61.057.3;65.0	72.024.0;153.0	122104;138	4.02.8;8.1	210.0140.5;433.0	5.855.3;6.8
2	60.056.0;65.0	120.087.0;210.0	10093; 107	3.01.4;.4.2	148.0115.5;379.0	6.465.3;5.73
3	61.060.7;68.0	72.048.0;192.0	11098;127	4.02.5;6.0	139.0109.0;230.0	5.294.47;6.65

cardiovascular disease (CVD) and all-cause mortality. A good predictor of the incidence of CVD is found to be carotid atherosclerosis, which is being evaluated by the Intima-Media-Thickness of the carotid artery wall (cIMT). The aim of the study was to examine the relationship between the cIMT and the stage of CKD based on the estimated Glomerular Filtration Rate (eGFR) as well as the presence of diabetic nephropathy graded by the urinary albumin excretion in patients with type 2 diabetes mellitus.
Methods: In this study 151 Diabetes Mellitus type 2 patients (79 males and 72 females) with mean age of 68±9 years and 15.5±13 years of diabetes duration were included. Traditional risk factors (Body Mass Index, blood pressure, smoking, serum lipids) as well as more recent (cIMT measurements using B-mode ultrasonography) were assessed and correlated to the stage of CKD and the presence of albuminuria. Associations between cIMT, albuminuria and eGFR and between albuminuria and lipid values were determined by Spearman's nonparametric correlation analysis.
Results: The median carotid IMT in stages 1, 2, 3, 4 and 5 was 0.76mm (0.55-1.61), 0.905mm (0.63-1.61), 0.93mm (0.66-1.78), 0.95mm (0.66-1.66) and 0.98mm (0.60-1.60) respectively, and in 35% of the patients the presence of a carotid plaque was revealed. The carotid IMT was significantly elevated as the stage of CKD was progressing ($p<0.001$, Kruskal-Wallis test) and was significantly correlated to the eGFR ($r=-258$, $p=0.002$) and the presence of albuminuria ($r=301$, $p=0.004$). However, it was not significantly correlated to the glycemic control (assessed by HbA1c). Additionally, hypertriglyceridemia was significantly negatively correlated to the deterioration of eGFR ($r=-282$, $p=0.001$) and positively correlated to the presence of albumin in the urine ($r=373$, $p<0.001$).
Conclusions: Increased levels of urinary albumin excretion and reduced eGFR are associated with atherosclerosis of the carotid artery and elevated serum triglyceride levels in type 2 diabetic patients.This study attenuates the importance of ultrasonography of the carotid Intima-Media Thickness as a way of recognition and prediction of eGFR's deterioration besides a classic indicator of vascular calcification.

MP314 GLYCATED ALBUMIN AND HEMOGLOBIN A_{1C} IN DIABETIC PATIENTS WITH PRE-DIALYSIS CHRONIC KIDNEY DISEASE

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Introduction and Aims: Glycated albumin (GA), compared with hemoglobin A_{1c} (HbA_{1c}), is thought to be more accurate indicator of glycemic control in dialysis dependent patients. However, the significance of these assays has not been evaluated in patients with pre-dialysis chronic kidney disease (CKD).
Methods: GA and HbA_{1c} were measured simultaneously in 132 diabetic patients. According to the estimated glomerular filtration rate (eGFR), the subjects were categorized into pre-dialysis CKD (eGFR< 60 ml/min/1.73 m^2, n=83) and control group (eGFR $\geq$ 60 ml/min/1.73 m^2, n=49).
Results: GA tended to be higher and HbA_{1c} tended to be lower in pre-dialysis CKD group compared with control group. However, there was no significant difference in GA (20.4% ± 5.0% vs 18.9% ± 6.8%, P = 0.193) and HbA_{1c} (7.4% ± 2.0% vs 7.7% ± 2.5%, P = 0.530) between 2 groups. GA/HbA_{1c} ratio was significantly higher in CKD group compared with control group (2.76 ± 0.38 vs 2.46 ± 0.30; P < 0.001). GA/ HbA_{1c} ratio was inversely correlated with eGFR only in CKD patients. (r = -0.57, P < 0.001). In all patients, multiple regression analysis showed pre-dialysis CKD group was the significant predictor for GA/ HbA_{1c} ratio after adjustment of age, sex, smoking status, hemoglobin, albumin, and random glucose (β = 0.29, P = 0.009).
Conclusions: Our results show HbA_{1c} significantly underestimates glycemic control while GA more accurately reflects glycemic control in diabetic patients with pre-dialysis CKD.

MP315 THE ANTIPROTEINURIC EFFECT OF SITAGLIPTIN IN PATIENTS WITH DIABETIC NEPHROPATHY

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Introduction and Aims: Proteinuria is an important risk factor for progression of chronic kidney disease. It has been shown that sitagliptin has some favourable effects beyond its glucose lowering effect. However, little is known about the effect of sitagliptin on urinary protein excretion. The aim of the study was to investigate antiproteinuric effect of sitagliptin in patients with diabetes nephropathy.
Methods: This study was performed in 50 (29 female and 21 male) patients with diabetic nephropathy. Body mass index (BMI), systolic and diastolic blood pressure (BP) and biochemical tests including fasting and postprandial blood glucose (FBG and PBG respectively), hemoglobin A1c (HbA1c), high-sensitivity C-reactive protein (hsCRP), lipid profile, 24-h urinary protein excretion were obtained at the beginning of the study. Glomerular filtration rate (GFR) was calculated according to the abbreviated modification of diet in renal disease (MDRD) formula. Patients received sitagliptin (100 mg/d) for 12 weeks.
Results: Systolic and diastolic BP were significantly decreased (P=0.005 and P=0.001). There were significant reductions in FBG, PBG, HbA1c, and hs-CRP (P<0.001; P<0.001; P<0.001; P<0.001, respectively). Proteinuria was significantly decreased with sitagliptin (P<0.001). However, no correlation was detected between the reduction in proteinuria and reductions in other variables.
Conclusions: We found that sitagliptin significantly reduces urinary protein excretion. Furthermore, it exerts antihypertensive and antiinflammatory properties in addition to its antidiabetic effect.

MP316 SELENIUM STATUS IN DIABETIC HEMODIALYSIS PATIENTS

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Introduction and Aims: Selenium(SE) is a trace element with antioxidant activity, cardioprotective effect and immunostimulatory properties. SE deficiency is known to be present in hemodialysis(HD) patients. However, in more recent studies normal pre-dialysis serum SE levels have been reported but with no distinction between presence and absence of diabetes. In this study SE status was investigated in diabetic HD patients.
Methods: We studied 34 hemodialysis patients, 22 males and 12 females, 67(25-85) years old, dialyzed for 62(16-307) months, treated with standard HD (S HD) using polysulfone membranes. Group A included 14 patients with diabetes mellitus, group B consisted of 20 non diabetic patients and a third group C included 16 gender and age-matched healthy subjects. SE was measured by atomic absorption spectrometry in blood drawn before and after dialysis session and in effluent dialysate collected at the beginning, the end and every hour during session.
Results: In the total of patients, pre-dialysis serum SE levels were lower than those in healthy controls (93,7±41,4 vs 129,9±46,2μg/L -p=0,01) but only group A patients had lower pre-dialysis serum SE levels (80,6±37μg/L) compared both with group C (p=0,001) and group B patients (114,1±42,8μg/L -p=0,01). Compared with serum SE levels in healthy subjects, pre-dialysis serum SE levels in non diabetic patients did not show any statistical difference. In spite of hemoconcentration, post-dialysis serum SE levels were unchanged in groups A and B, which is compatible rather with an intradialytic SE loss that was similar in both groups. Actually, there was no difference between patient groups in the excreted SE mass into dialysis fluid during sessions. Compared to group B, group A patients had higher serum glucose (146±81 vs 83 ±18mg/dl -p=0,001) and γGT levels (51±32 vs 26±10U/L -p=0,01) and lower magnesium (1,9±0,4 vs 2,4±0,5mg/dl -p=0,001), sodium (136±2,5 vs 138±2,8mmol/L -p=0,01) and hemoglobin levels (11,1±1,1 vs 12±0,9g/dl -p=0,01). In group A pre-dialysis serum SE levels showed a direct correlation with serum potassium levels (R=0,55 -p=0,04) and in group B a negative correlation with serum glucose levels (R=-0,46 -p=0,03).
Conclusions: In conclusion, there was a similar SE loss in effluent dialysate during session in diabetic and non diabetic patients. SE deficiency was present only in diabetic HD patients, it does not seem to be related with SE loss through dialysis membrane pores but rather to metabolic factors and nutritional status. However, this issue needs further investigation.

MP317 ASSOCIATION OF CIRCULATING SERUM LEVELS OF GELATINASE-B AND VASCULAR ENDOTHELIAL GROWTH FACTOR-A WITH VASCULAR ULTRASOUND DETERMINANTS OF DEMENTIA IN PATIENTS WITH TYPE 2 DIABETIC NEPHROPATHY IN EARLY STAGES

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Introduction and Aims: Gelatinase-B, reported also as matrix metalloproteinase-9 (MMP-9), is the main enzyme that degrades collagen type-IV (col-IV) and has been implicated in chronic kidney disease (CKD) and cardiovascular disease (CVD). Col-IV is the major collagenous component of extracellular matrix (ECM) which constitutes the architectural structure of the vessels' basement membrane (BM) and the glomerular BM (GBM). It remains controversial the mechanism by which vascular endothelial growth factor-A (VEGF-A) works in the kidney, as well as in vessels at least in the early stages of diabetic nephropathy (DN) and CKD. Whether VEGF-A is detrimental in early stages of DN or other renal conditions has not yet been clearly answered. Recent evidence supports that combined findings of carotid ultrasound and lower limp Doppler studies denoting atherosclerosis are associated with dementia. Matrix metalloproteinases (MMPs) may play a role in the pathophysiology of Vascular Dementia (VD). MMP-9 and tissue inhibitors of metalloproteinases (TIMPs) are elevated in postmortem brain tissue of VD patients. MMPs and TIMPs are found in neurons, microglia, vascular endothelial cells and leukocytes. The aim of the present

study was to determine the serum levels of MMP-9 and VEGF-A and to investigate their potential correlation with the atherosclerotic markers and albuminuria and VD in early stages of type 2 DN.
Methods: CKD patients of stages 1 and 2 with type II DN (n=50) were included. As controls, there were two groups, patients with diabetes type II without CKD (n=40) and healthy individuals (n=40). Clearance of creatinine (Clcr) and albumin excretion were examined in the 24h urine. VEGF-A and MMP-9 levels were measured by an ELISA method. Intima media thickness of carotid and femoral arteries and atheromatic plaque were evaluated by a high resolution ultrasonography. Analysis of atherosclerosis markers involved imaging by duplex of carotid and femoral arteries in all patients in longitudinal fashion, to detect the presence of plaque and to assess the intima-media thickness (IMT). Each artery was assigned a score (presence of plaque=1, absence of plaque=0, IMT<0.8mm= 1, IMT<0.8mm=0) and the total score of the 4 vessels (2 carotid and 2 common femoral) was calculated per patient (atherosclerotic ultrasonic score - ATHUS). Subsequently, the mini-mental score examination (MMSE) of every patient was evaluated. Brain CT scans were performed to exclude other reasons for the intellectual decline of patients. Statistical analysis was performed with the use of a SPSS system.
Results: There was a statistically significance between VEGF-A ($p<0.001$) and MMP-9 ($p<0.0001$) levels in each of the groups. MMP-9 serum levels were strongly correlated with VEGF-A serum levels in the group of DN (pearson correlation 0.520, $p<0.0001$). There was a statistically significant correlation between levels of VEGF-A, MMP-9 and albuminuria ($p<0.0001$). Further, VEGF-A and MMP-9 levels were independently correlated with IMT and atheromatic plaque ($p<0.0001$) and MMSE score in DN patients.
Conclusions: Our study suggests that serum levels of VEGF-A and MMP-9 might present independent risk factors of atherosclerosis, albuminuria and vascular dementia at least in the early stages of type II diabetic nephropathy to the progression of CKD.

MP318 SERUM FERRITIN LEVEL IS POSITIVELY ASSOCIATED WITH MICROALBUMINURIA IN TYPE 2 DIABETES OF TAIWAN

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Introduction and Aims: Serum ferritin has been found closely related with diabetes and glucose metabolism, but its impacts on diabetic nephropathy remains unknown. This study aimed to explore the association between serum ferritin and microalbuminuria in type 2 diabetes.
Methods: Eight hundred and fifty one type 2 diabetes subjects were selected from a cohort participating in a glycemic control study in Taiwan in 2008. We used urine albumin-to-creatinine ratio to define microalbuminuria; serum ferritin was divided into quartiles for analysis. Logistic regression and trend tests were used to delineate the association between serum ferritin and microalbuminuria.
Results: Diabetes subjects with higher ferritin tended to have earlier diabetes onset, more metabolic disorders, higher high-sensitivity C-reactive protein (hsCRP), and higher prevalence of microalbuminuria. Compared with those in the lowest quartile, diabetes subjects in the highest ferritin quartile were 53% (P=0.032) more likely to develop microalbuminuria. After controlling for demographics, metabolic profiles, and other inflammatory markers, the effect of serum ferritin levels on microalbuminuria remained significant (P for trend < 0.001). This independent relationship was not changed either for those who had better glycemic control or those who had not used an angiotensin converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB).
Conclusions: The current study shows an independent dose-response effect of serum ferritin on microalbuminuria in type 2 diabetes patients.

MP319 GAS CHROMATOGRAPHY IS NEW OPPORTUNITY OF RENAL DISEASES AND DIABETES NEPHROPATHY DIAGNOSTICS

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Introduction and Aims: Diabetic nephropathy is the main cause of renal replacement therapy. Breath tests seem to be a promising diagnostic device offering early non-invasive disease detection. Trimethylamine (TMA), dimethyl sulfide (DMS), carbon disulfide (CS2) are mentioned in literature as potential markers of chronic kidney disease (CKD) and diabetic nephropathy.The aim of our study was to determine breath composition in persons suffering from CKD.
Methods: Breath samples were collected from 14 CKD patients (6 with type 2 diabetes) and 7 healthy volunteers (control group - CG). Exhaled air samples were analyzed by gas chromatography equipped with mass spectrometer (GC-MS). Samples were enriched using solid phase microextraction (SPME).
Results: The mean age in whole group was 64.6 ± 15.8 years. eGFR in the study group averaged 37.4 ± 18.9 ml/min/1.73 m2 and significant albuminuria daily average of about 700 mg. Diabetic patients characterized significantly higher serum glucose, fibrinogen and CRP level, lover albumin and total cholesterol level than other patients with CKD ($p<0.05$). Trimethylamine (TMA) was detected in case of 11 patients and none in control group. TMA values in exhaled air were 0.19 to 4.03 nmol/l (4.78 - 98.61 ppb). Among breath components were detected: sulfur compounds: dimethyl sulfide (DMS), carbon disulfide (CS2), aceton and also potential markers of oxidative stress: propane, butane, pentane, 2-methylpentane, hexane. Interesting results were obtained also for sulfur compounds. In the control group DMS concentrations ranged from 0.05 to 0.39 nmol/l (1.26 - 9.00 ppb), in patients from 0.01 to 1.02 nmol/l (0.26 - 24, 85 ppb) - $p<0.05$. In the control group, 4 out of 7 cases detected the presence of CS2 in the concentration range from 0.01 to 0.02 nmol/l (0.25 - 0.58 ppb). Carbon disulphide was detected in all patients, and its concentration ranged from 0.009 to 0.15 nmol/l (0.24 - 3.80 ppb) - $p<0.05$. Diabetic patients characterized significantly higher TMA and ACETON level in breath samples than other patients ($p<0.05$). TMA significantly correlated with glucose ($r=0.06$ $p=0.02$) and fibrinogen ($r=0.33$ $p=0.02$) in examined patients.
Conclusions: The elaboration of quick, noninvasive diagnostic method is specially important in case of asymptomatic diseases. Chronic kidney disease (CKD) belongs to a group of diseases which are often diagnosed too late, while the complications of associated diseases are sensible. Unfortunately the explanation of correlation between metabolic processes and the respective compounds indicated in breath is difficult. Hopefully, presented project of researches will be helpful for the breath profile's description of patients suffering from CKD. These studies should allow to elaborate the breath test that is useful for early diagnosis of CKD. Correlation of breath composition with biochemical blood analysis should supplement information about metabolic origin of detected substances in breath. In the future, current diagnostic procedures (blood and urine tests, kidney biopsy) may be supplemented by detection of TMA, DMA and CS2 concentration in human breath.