Abstracts for

36th biennial congress of the Nordic Society of Nephrology in Odense, 4th-7th of May 2022

Poster presentations

P7

Far Infrared Radiation on the Arteriovenous Fistula changes plasma VCAM and ICAM in Patients on Hemodialysis

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Introduction: There is a substantial risk of stenosis in the arteriovenous fistula (AVF) in hemodialysis patients. Far infrared radiation (FIR) is a non-invasive intervention with a potentially beneficial effect on AVF patency. The mechanism is not clear. The aim of this study was to investigate the effect of a single FIR treatment on inflammatory, vasodilatory and endothelial dysfunction factors in the AVF.

Methods: Forty hemodialysis patients with an AVF were included in the study. Patients were randomized to receive either FIR (FIR group) or no FIR (control group). Blood samples were drawn from the AVF arm and the non-AVF arm before (T0) and after (T40) treatment in both groups at the start of a hemodialysis session. The changes (median [interquatile range]) in several factors during FIR were explored.

Results: Nineteen patients in the FIR and 21 patients in the control group were included. After one FIR treatment, Vascular Cell adhesion molecule (VCAM) and Intercellular adhesion molecule (ICAM) changed, although the change was significantly lower in the AVF arm compared to the control group. sVCAM: -31.55(-54.33;22.1) vs. -89.87(-121.55;-29.31), p=0.005 and sICAM: -24.19(-43.53;25.26) vs. -49(-79.91;-11.58), p=0.02. Other factors, such as interleukins, nitric oxide and tumor-necrosis-factor 1 also declined, but with no significant differences related to FIR.

Conclusion: One FIR treatment attenuated the decrease in sVCAM and sICAM in the AVF arm compared to a control group. These findings do not support the hypothesis of FIRs beneficial effects on the endothelium, though the long term effects of FIR on these factors are unknown.

P10

Thymoglobulin reduces regulatory T cell specific forkhead box P3 (FOXP3) transcripts in kidney transplant recipients

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Background: The expression of the forkhead box P3 (FOXP3) protein is essential for the differentiation of T regulatory cells, which are major regulators of immune tolerance and immunologic activity. Determination of FOXP3 transcripts in peripheral blood mononuclear cells may indicate the level of tolerance in kidney transplant recipients. Now, we evaluated the effect of different induction therapies on FOXP3 transcripts on the first postoperative day.

Methods: Blood samples were collected the first day after transplantation from incident adult kidney transplant recipients. Data concerning induction therapies were collected from medical record review. Ribonucleic acid was extracted from peripheral blood mononuclear cells and used in quantitative reverse transcription polymerase chain reaction. Levels of FOXP3 were normalized to the reference gene β-actin, transformed to a logarithmic scale, and correlated to variables using a Bonferroni corrected Spearman's correlation.

Results: 538 patients were included, of which 70 were recipients of ABO-incompatible donor kidneys, 172 ABO-compatible donor kidneys, and 296 deceased donor kidneys. Kidney transplant recipients receiving thymoglobulin had significantly lower levels of FOXP3 (log scale, median (IQR)): ABO-incompatible, other, -7.8 (-8.5 to -7.2) vs thymoglobulin, -10.7 (-11.3 to -10.1); p<0.001; ABO-compatible, -8.0 (-8.5 to -7.5) vs -10.1 (-11.1 to -9.8); p<0.001; and deceased donors, -8.0 (-8.4 to -7.4) vs -10.8 (-11.5 to -9.7); p<0.001. Levels of FOXP3 correlated positively with the lymphocyte counts (r=0.4: p<0.01) and negatively with number of previous transplantations (r=- 0.2; p<0.01).

Conclusion: Treatment with thymoglobulin significantly reduces FOXP3 transcripts compared to the reference gene in peripheral blood mononuclear cells.

P19

Altered glucagon receptor signaling has a direct effect on albuminuria and renal hemodynamics

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The main risk factor for chronic kidney disease is diabetes, which develops in ~40% of the patients. Increased plasma glucagon concentrations are characteristically observed in type 2 diabetes, and might contribute to the pathophysiology of diabetic kidney disease. Glucagon is associated with glomerular hyperfiltration and urinary excretion of β2-macroglobulin, urea, sodium, and potassium. Patients with end-stage renal disease have elevated plasma levels of glucagon. Whether altered glucagon receptor (GCGR) signaling contributes to the development of renal disease in patients with diabetes remains unknown. We investigated the effects of long-term GCGR inhibition and activation on renal function in C57Bl/6JRj mice with a long-acting GCGR antagonist (REGN1193, Regeneron) or a long-acting glucagon analogue (NNC9204-0043, Novo Nordisk). Eight weeks of treatment with the GCGR antagonist significantly increased kidney weight with no sign of albuminuria, whereas treatment with the GCGR analogue increased urinary albumin/creatinine ratio by 100%. Glomerular matrix expansion, thickening of the glomerular basement membrane and tubulointerstitial fibrosis are currently being assessed via histological examination. We also investigated the acute renal effect of glucagon before and after inhibiting the GCGR with a GCGR antagonist (25-2648, Novo Nordisk) in healthy rats. Glucagon acutely increased renal blood flow, urinary excretion and excretion of sodium and urea. These effects were mainly mediated through the GCGR. Our study suggests that long-term GCGR activation is associated with albuminuria, whereas inhibiting the GCGR increases the kidney weight in mice. Further, our acute studies in healthy rats suggest that glucagon has a direct effect on renal excretory function and hemodynamics.

P22

Chronic kidney disease in primary care and the risk of cardiovascular comorbidity and mortality

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Background: Prevalence of CKD is increasing. Early diagnosis may be important. We determined the prevalence and outcome of CKD in a Danish primary care cohort.

Methods: Observational data from individuals above age 40 followed in primary care in Copenhagen (2000–2015) was linked to Danish health registries. Outcomes were stroke, myocardial infarction (MI), heart failure, peripheral artery disease (PAD), cardiovascular (CV) mortality and all-cause mortality. Conventional CKD classification were used with CKD stage 1 and 2 as reference. We used Cox proportional hazards to calculate hazard ratios for outcomes according to CKD class. We explored associations between kidney function and outcomes using eGFR as a continuous variable with penalised splines. All models were adjusted for age, gender, diabetes, hypertension, existing CVD, LDL cholesterol and antihypertensive treatment.

Results: We included a population of 171,133 individuals. As expected, the majority (n=157,002) was in CKD 1+2 at index date, and only small proportion (0.05%) was in CKD stage 5. In general, event rates were low in CKD 1+2 and rose with higher stages of CKD. In the adjusted analyses we observed a stepwise increase in hazard rates for every outcome with every increment in CKD stage confirmed by the continuous analyses. Compared to CKD 1+2, individuals in CKD4 had approximately double the hazard rate of PAD, MI, CV and all-cause mortality.

Conclusion: Our data from a large primary care cohort demonstrate an increase in risk of outcome at CKD3. This underlines the importance of studying early intervention in primary care.

P24

Experiences of being a living kidney donor-perceived stress levels before and after kidney donation

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Background and Aims: To donate a kidney is a life-changing experience, and there is a diverse spectrum of emotions connected to this process. This study aimed to investigate kidney donors' perceived and measured stress levels before and after donation.

Method: A prospective observational study including 83 patients (46 ±10.9 years, 63 % women), who donated a kidney at Sahlgrenska University Hospital, Gothenburg, during 2009-2010. Three self-rating surveys concerning stress

(*Everyday Life Stress Scale)*, vital exhaustion (*Maastricht Questionnaire of vital exhaustion)*, and depressive symptoms (*Depressive Mood Scale)* were answered on the day before surgery, and then two and six months after kidney donation.

Results: Kidney donors generally scored low in self-rating stress mean 15.5 and depression symptom scales mean 10.8 pre-donation. The Maastricht's questionnaire showed a trend toward significant gender difference at two months; women mean score was 32.1±9.3 and men 35.8±6.9, p =0.092. At six months there was a significant gender difference in self-reported vital exhaustion, where women scored higher 36.9±7.1 than men 30.7±11.6; p=0.037 and a near significant difference on the Depressive Mood Scale, 12.2±12.5 vs 6.4±8.2 at six months; p=0.058. No significant difference over time in experienced wellbeing (Everyday Life Stress Scale) was found, 15.6±8.2 vs 14.3±7.6, p=0.554.

Conclusion: Kidney donors self-reported stress level and depressive symptoms did not change pre-donation to six months after donation. Women reported more feelings of exhaustion and stress than men did at six months post-donation.

P25

Cardiovascular mortality among persons with advanced chronic kidney disease: a matched cohort study

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Background: Chronic kidney disease (CKD) and diabetes are both well-established risk factors for cardiovascular mortality. However, the risk of cardiovascular mortality and the impact of diabetes for those who have already reached advanced CKD are poorly examined. The aim of this study was to examine the risk of cardiovascular mortality among persons with advanced CKD with and without diabetes.

Methods: In a nationwide registry-based retrospective matched cohort study, we identified all Danish persons aged ≥ 18 years with advanced CKD between 2002 and 2018. Non-exposed persons with eGFR ≥ 30 mL/min/1.73m^2 were matched on birthyear and sex. Multiple outcome-specific Cox regression was performed to calculate standardized absolute risk of cardiovascular mortality adjusted for age, sex, and cardiovascular disease.

Results: We included 135,824 persons with advanced CKD. Overall, 52% were women and the mean age was 76 years. 31,991 (23.6%) had diabetes with a mean duration of 9.7 years. For persons with diabetes, the standardized absolute risk (95% CI) of cardiovascular mortality was 9.6% (9.3-9.8) after 1 year and 28.4% (27.9-29.0) after 5 years. Compared to age- and sex matched persons, the corresponding relative risk (95% CI) was 3.1 (3.0-3.1) and 2.2 (2.2-2.3), respectively. Among persons without diabetes, the standardized absolute 1- and 5-year risk was 7.7 (7.6-7.8) and 23.7 (23.4-23.9), respectively. The corresponding relative risk was 2.5 (2.4-2.5) and 1.9 (1.8-1.9).

Conclusions: Persons with advanced CKD had a two- to three-fold increased risk of cardiovascular mortality compared to the background population, with the greatest risk among persons with concomitant diabetes.

P26

Designing The PRIMETIME1 (PRecIsion MEdicine based on renal TIssue Molecular interrogation in diabetic nEphropathy) cohort, a retrospective nationwide cohort study

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Background: Diabetic kidney disease (DKD) is a common and serious complication to diabetes. DKD is often diagnosed based on clinical characteristics, although only a kidney biopsy can give an accurate diagnosis. This leads to a gap in knowledge on the distribution of renal impairment caused by diabetic nephropathy and non-diabetic nephropathy, in individuals with diabetes. Long-standing tradition of national population registration in Nordic countries offers a unique possibility of working with high quality registry data and a long follow up period. We aimed to create a large national retrospective cohort of individuals with diabetes and kidney disease comprising a wide range of data – the PRIMETIM1 cohort.

Methods: All adult individuals with diabetes who previously had a kidney biopsy performed were included. The population were identified by connecting The Steno Diabetes Center Copenhagen Diabetes Register (including all

Danish adults with diabetes) with The Danish Pathology Register (including national data on results from the microscopical, pathological examination of kidney biopsies). Following, data from eleven nationwide registries and databases was assembled and stored at Statistics Denmark.

Preliminary results and perspectives: 6590 individuals with diabetes, diagnosed between 1996 and May 2020, had a previosly performed kidney biopsy. A variety of demographic-, socioeconomic-, clinical- and prognostic- variables was gathered. Data analysis is ongoing.

The PRIMETIME1 cohort will provide studies on epidemiologic data, predictive value of clinical variables on disease course, prognostic value of findings in kidney biopsies, and investigation on how to guide practitioners in risk stratification of individuals suffering diabetes and kidney disease.

P28

Hepatic Steatosis in Patients with Type 2 Diabetes and Chronic Kidney Disease

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Background: Non-alcoholic fatty liver disease (NAFLD) is suggested as being a risk factor for chronic kidney disease (CKD). The incidence of NAFLD is rising globally parallel to the increasing incidences of obesity and type 2 diabetes. As diabetes remains the leading cause of CKD the co-existence of NAFLD, CKD and type 2 diabetes needs to be explored. Our primary aim was to determine the prevalence of hepatic steatosis in patients with type 2 diabetes with and without CKD.

Methods: This study included 50 patients with type 2 diabetes and CKD Stages 3–5, and 50 patients with type 2 diabetes without CKD. Liver fat content was estimated by proton magnetic resonance spectroscopy (^{1}H-MRS) and magnetic resonance imaging proton density fat fraction (MRI-PDFF) in a 3 Tesla full body scanner. Hepatic steatosis was defined as ≥5.56% liver fat. Further, continuous glucose monitoring (CGM) was performed for four days.

Results: Hepatic steatosis was identified in 22 (44%) patients with CKD and 19 (38%) patients without CKD (P=0.68). Median (IQR) values of percentage liver fat were 4.7% (3–8.5) and 4.1% (2.9–7.7) in patients with and without CKD, respectively, corresponding to 5.3 (95% CI: -23%–45%, P=0.75) higher levels of hepatic fat percentage in patients with CKD. Mean sensor glucose from CGM was 9.0 ± 1.6 mmol/ L and 8.7 ± 1.8 mmol/ L in patients with and without CKD, respectively (p=0.47).

Conclusions: These findings do not support any association between hepatic steatosis and CKD Stages 3–5 in patients with type 2 diabetes.

P30

Characterization of adipocyte size and glucose uptake in adipose tissue with focus on perirenal fat depots

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Background: Characteristics of adipocytes regulating adipose tissue function may be of importance for renal function and disease.

Aim: To characterize adipocyte size and glucose uptake in human perirenal, renal sinus and paranephric adipose tissue.

Subjects and methods: Perirenal, renal sinus, paranephric, omental and subcutaneous adipose tissue were collected from 25 healthy kidney donors (50% men, age 48±11 years and BMI 25.7±3.1 kg/m^2). Adipocyte diameter, basal glucose uptake (no insulin) and insulin-stimulated glucose uptake (25 and 1000 µU/mL) were measured in isolated adipocytes from the different tissues.

Results: The mean adipocyte cell diameter from perirenal, renal sinus and paranephric were smaller than those from omental and subcutaneous adipose tissue (mean±sd; 69.3±15.5, 65.5±13.5 and 75.9±16.5 vs. 80.3±20.5 and 85.5±16.7 µm, respectively, and differed significantly between all adipose tissue depots except for subcutaneous vs. omental (p=0.07), omental vs. paranephric (p=0.17) and perirenal vs. renal sinus (p=0.06). There were no significant gender

differences in the cell size. Insulin-stimulated glucose uptake was significantly higher in adipocytes from paranephric (n=18; $p<0.01$), perirenal (n= 21; $p< 0.01$) and subcutaneous depots (n=6; $p< 0.05$) compared to basal, but not omental (n=3; $p>0.05$) or renal sinus (n=4; $p>0.05$). Basal glucose uptake and insulin-fold effect were significantly higher in renal sinus than omental adipocytes ($p<0.001$).

Conclusions: This study in healthy subjects indicate differences between different fat depots surrounding the kidney that may be of importance. The fat depot in the renal sinus is of specific interest. Furthermore, detailed metabolic characterization of the fat depots is ongoing.

P31

Parathyroid-specific knockout of core circadian clock gene Bmal1 increase proliferation of the parathyroid gland in CKD

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Background: Proper rhythms in metabolism, hormone secretion and activity are maintained by a molecular circadian clock. We have previously shown that an internal circadian clock operates in the parathyroid gland (PTG) and that it is disturbed in CKD. Here, we investigated the transcriptome of wildtype-mice over 24h and we construct a PTG-specific *Bmal1* knockdown mouse to investigate the role of the PTG clock in health and in CKD.

Methods: Blood samples and PTGs were harvested at 4h-interval and 24h gene-expression was examined by RNAseq. PTG-specific knockdown of *Bmal1* was generated by crossing *PTHcre*-mice with *Bmal1*$^{flox/flox}$-mice(WT) creating *PTHcre*;*Bmal1*$^{flox/flox}$-mice(KD). CKD induced by adenine-high-phosphate-diet and proliferation examined by Ki-67 labeling. Circadian rhythmicity was assessed by cosinor analysis and JTK_CYCLE algorithm.

Results: 6.85% of all expressed genes were significantly rhythmic in the wildtype PTG, including parathyroid signature genes *Casr*, *Vdr,* and *Fgfr1*. KD mice had global dampening of PTG circadian clock gene rhythmicity and parathyroid signature genes. Plasma-PTH was significantly rhythmic in both KD and WT mice. PTG *Bmal1* knockdown resulted in downregulation of genes involved in mitochondrial function and ATP synthesis. In CKD, KD mice had significantly reduced compensatory PTH secretion, hypocalcemia and significantly increased PTG KI-67 labeling index (9.3% vs. 2.2%, p=0.018).

Conclusion: Dampened rhythm of PTG circadian clock genes downregulated genes involved in ATP synthesis, and reduced rhythmicity of parathyroid signature genes. When superimposed by uremia, PTH secretion was inadequate to maintain normocalcemia and markedly increased proliferation was found, indicating a key role of the circadian clock in regulating PTG proliferation.

P34

Increased Risk of Coronary Revascularization, Heart Failure, Atrial- and Ventricular Arrhythmias among patients with ANCA-Associated Vasculitis

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Background: ANCA-Associated vasculitis (AAV) are autoimmune diseases, with cardiovascular disease being the leading cause of death. Current literature has described increased risk of venous thrombosis, stroke and myocardial infarction (MI) while studies examining adverse cardiovascular outcomes i.e. use of coronary procedures, atrial- and ventricular arrhythmias/use of implantable-cardioverter-defibrillators (ICD) and heart failure (HF) are limited.

Methods: Using Danish nationwide registries, we examined AAV patients from 1996-2018 in a validated cohort (PPV 97%), with ≥2 consecutive hospital encounters registered as polyangiitis with granulomatosis [ICD-10:DM313] or microscopic polyangiitis [ICD-10:DM317]. AAV patients were matched 1:3 with controls from the general population on age and gender. We computed adjusted hazard ratios (HRs) with 95% CI for each cardiovascular outcome, with all-cause mortality accounted for as competing risk.

Results: 2306 AAV patients (median age: 62.9yrs, 52.6% male) were matched with 6918 controls. Median study follow-up was 9.5yrs (IQR 5.3-15.8yrs). Compared with controls, AAV patients had a higher rate of ischemic heart disease (HR 1.67 [95% CI, 1.45-1.95]), MI (HR 1.43 [95% CI, 1.11 to 1.83]), CAG (HR 1.51[95% CI, 1.27 to 1.80), PCI (HR 1.42 [1.11-

1.88]), and ventricular arrhythmia/ICD-implantation (HR 2.03 [1.17-3.55]). Secondarily, AAV patients also had an increased rate of additional adverse cardiovascular events compared with controls: HF (HR 1.77 [1.48-2.11]), deep vein thrombosis (HR 2.89 [95% CI, 2.24-3.72]), pulmonary embolism (HR 3.59 [2.74-4.72]), AFLI (HR 1.73 [1.51-1.98]), ischemic stroke (HR 1.34 [1.12-1.61]) and in-hospital cardiac arrest (HR 1.97 [1.29-2.99])

Conclusions: AAV patients are at increased risk of coronary revascularization, heart failure and atrial-/ventricular arrhythmias.

P36

Increased fluid intake disseminates infections in a murine model of ascending urinary tract infection

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Urinary tract infections (UTIs) are the second most common type of infection after respiratory infections. Usually, the infection is localised to the bladder, however, in severe cases UTIs can ascend to the kidneys causing pyelonephritis and potentially life-threatening urosepsis. General treatment is antibiotics, but patients are also encouraged to increase their fluid intake to clear current infection and prevent reinfection. However, it is not known whether extensive fluid intake does promote bacterial clearance and reduces risk of severe disease. Here, we investigated whether increased fluid intake aids clearance of bacteria in a mouse model of ascending UTI.

Uropathogenic *Escherichia coli* were installed directly in the urinary bladder of female Balb/c mice randomised to receive either regular food or gel-food (70% water). After 24 hours the kidneys were removed and plated on LB-agar to assess the degree of pyelonephritis.

Mice receiving gel-food had, over the 24-hour observation period, a 4-fold increase in urine production ($p<0.05$) and a 2-fold reduction in urine osmolarity (668.7±81 mOsm) compared to control (1439±221.5 mOsm, $p<0.0001$). Surprisingly, we found that the mice with an increased fluid intake presented with more bacterial colonies in their kidneys ($p<0.01$) and more gel-food mice developed pyelonephritis compared to control mice (87.50% vs 43.75% respectively).

In conclusion, our results demonstrate that increased urinary flow alone does not clear bacteria from the urinary tract. On the contrary, increased urinary flow seemed to promote dissemination of the infection with increased invasion of the kidneys, which may question current recommendations regarding fluid intake during UTIs.

P40

A novel AQP2 sequence variant causes intracellular aquaporin-2 retention and autosomal dominant nephrogenic diabetes insipidus

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Background: Congenital nephrogenic diabetes insipidus (NDI), a rare disease, may be caused by dysfunction of the water channel aquaporin-2 (AQP2), which facilitates arginine-vasopressin (AVP)-induced water reabsorption in the principal cells of the collecting ducts.

Methods: We found a novel sequence variation in the *AQP2* gene in a proband. We characterized the clinical phenotype, explored the response to treatment with high doses of the AVP analogue desmopressin, and investigated the consequences of the mutation on the localization and glycosylation of AQP2.

Results: The proband displayed polyuria (24 h urine volume 10-13 L/day) and polydipsia and a NDI phenotype with reduced urine concentrating ability upon water deprivation (urine osmolality from 111 mmol/kg to 398 mmol/kg). The pedigree indicated autosomal dominant inherence. Treatment with incremental doses of desmopressin (60 µgx1/day to 240 µgx3/day) reduced 24 h urinary volume to 6.8 L/day. Gene sequencing of *AQP2* revealed a heterozygous sequence variant: c.799_800del; p.(Arg267Glyfs*12), causing the substitution of arginine 267 for glycine in the C terminus of the AQP2 protein and a frameshift with a new, by 6 amino acids extended sequence beyond Gly267. Consistent with the phenotype, mutant AQP2 accumulated in the intermediate compartment between Golgi and Endoplasmatic reticulum,

ERGIC, which was associated with increased glycosylation. Despite stimulation of cAMP, mutant AQP2 was resistant to redistribution to plasma membrane.

Conclusion The novel sequence variant in *AQP2* encoding AQP2-R267G causes autosomal dominant NDI due to retention of AQP2 in the ERGIC. Administration of desmopressin induced partial recovery of the water reabsorpion in the patient.

P42

Can glucose uptake during peritoneal dialysis be blocked by SGLT2-inhibitor treatment? Results from a proof of concept clinical trial

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Introduction: Exposure to glucose in peritoneal fluid during peritoneal dialysis causes local inflammation, which over time causes fibrosis. The capacity of water- and waste product exchange is limited by fibrosis and is the most commonly reason for termination of peritoneal dialysis.

SGLT2-channels are identified in peritoneal mesothelial in humans. An *in vitro* model of human peritoneal mesothelial cells incubated with the SGLT2-inhibitor significantly decreased the glucose uptake.

We aim to test whether treatment with oral SGLT2-inhibitor can reduce peritoneal uptake of glucose during peritoneal dialysis.

Method: In a phase 2a single center clinical trial ten participants in chronic peritoneal dialysis are open label assigned to treatment with 10 mg dapagliflocin for three consecutive days. Standardized peritoneal dialysis is conducted before and after treatment. Peritoneal fluid glucose levels are analyzed every 30 minutes during four hours dialysis with intraperitoneal infusion of 2000 ml 2.27 % glucose.

Results: The first two enrolled participants are age 70 and 77 years with a duration of peritoneal dialysis of 2 and 25 month, respectively. The mean peritoneal glucose level was 98.5 mmol/L at the start of the peritoneal dialysis both prior to and after three days of treatment. The mean glucose level in the peritoneal fluid, at the end of peritoneal dialysis, was 41.5 and 40.0 mmol/L, prior to and on day three of treatment, respectively. No adverse events were observed.

Conclusion: Preliminary results of the first two participants on SGLTT2-inhibitor treatment show no effect in blockade of peritoneal glucose up-take.

P44

Rationale and protocol for a prospective, clinical trial of biopsy-proven diabetic nephropathy in people with type 2 diabetes – The PRIMETIME2 study

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Background: Diabetic kidney disease (DKD) is a severe complication of diabetes. The diagnosis is based on clinical characteristics; persistent macroalbuminuria, hypertension, and decline in kidney function, although this method is subject to significant uncertainty. The only way to secure an accurate diagnosis, diabetic nephropathy (DN), is via kidney biopsy.

The clinical presentation of DN can be associated with a heterogeneous range of histological features, including glomerulosclerosis, tubulointerstitial fibrosis, tubular atrophy, and arteriolar hyalinosis, demonstrating the condition's complexity. Current treatment plans aim to slow the condition's progression, with little focus on underlying and individual pathological processes.

Methods: We will prospectively collect research biopsies from an unselected cohort of eligible participants with type2 diabetes(T2DM), severe albuminuria (≥ 700 g/d), and an eGFR > 30 mL/min/1.73 m2. The kidney tissue, blood, urine, feces, and saliva samples will be thoroughly investigated with cutting-edge molecular technologies for comprehensive profiling and associated with disease course and clinical outcome with annual follow-up for 20 years. We will use the tissue for a precise histological diagnosis and next-generation sequencing to provide a new understanding of the

molecular features of DN. Proteomic and metabolomic profiles will be made from urine and plasma. Lastly, we plan to profile the whole genome and microbiome.

Discussion: This study will investigate the prevalence of DN in individuals with T2DM with albuminuria. The deep characterization of the biopsy material and biological biospecimen may lead to a better understanding of the pathological processes involved and reveal new targets for individualized treatment and improve diagnostic accuracy.

P45

ACE-2 and TRMPSS-2 in human kidney tissue and urine extracellular vesicles from patients with critical Covid-19 disease

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Background: SARS-CoV-2 virus requires ACE-2 and TMPRSS-2 for cell entry. Aging and male sex are risk factors for severe disease. It was hypothesized that ACE-2 and TRMPSS-2 are more abundant in kidney from men and in aging and, furthermore, that during Covid-19 disease, ACE-2 and TRMPSS-2 are shed from men in larger quantities.

Methods: Human kidney cortices were from 4 groups of patients (n=6 in each) subjected to nephrectomy due to cancer without Covid-19: (<50years, >75y, male, female). Tissue was used for immunoblotting. Urine was collected from 22 patients (n=10 male) hospitalized with critical Covid-19 illness. Urine from healthy young men (n=10) served as control. Urine extracellular vesicles (uEVs) were used for immunoblotting. ACE-2 was measured by ELISA in urine.

Results: ACE-2 and TRMPSS protein abundances in kidney cortex were not changed with age. ACE-2 was more abundant in kidney cortex of females. ACE-2 was elevated in uEVs from patients compared to healthy controls. TRMPSS2 was more abundant in uEVs from males than females, was cleaved proteolytically in males, and was not changed in patients with Covid-19 compared with healthy males. ELISA showed no gender difference in soluble ACE-2 in urine but level was 271-times higher in spot urine normalized for creatinine from patients with Covid-19 than controls.

Conclusion: ACE-2 and TRMPSS2 abundances in the kidney are not elevated with age or male sex. ACE-2 is shedded in EVs in urine from patients with Covid-19. Loss of kidney ACE-2 could impact kidney function and systemic blood pressure in Covid-19.

P46

Aortic calcification increases central blood pressure relative to brachial blood pressure in CKD patients – a study in patients undergoing elective coronary angiography

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Objective: This study examined the impact of aortic calcification on central systolic blood pressure (cSBP) relative to brachial systolic blood pressure (bSBP) in patients with chronic kidney disease (CKD).

Design and methods: Patients with and without CKD undergoing elective coronary angiography (CAG) at Aarhus University Hospital were considered for inclusion in this cross-sectional study. During CAG, cSBP was measured in the ascending aorta with a fluid-filled catheter while bSBP was measured with an oscillometric device using a cuff. Furthermore, patients underwent a non-contrast computed tomography (CT) scan of the entire aortawith subsequent blinded Agatston-scoring of the aorta. Data are presented as mean □ standard deviation. Statistical comparisons were made using Wilcoxon rank sum test and Bonferroni-adjusted Kruskal-Wallis test.

Results: 149 patients were included in the study. Of these, 134 patients had a CT-scan of sufficient quality to allow analysis. Agatston-score was higher in CKD patients (n=110) as compared to patients with normal kidney function (n=24, *P*<0.001). bSBP was 6.5 □ 13.1 mmHg higher than cSBP in patients categorized into the first tertile of Agatston-scores. This difference was reduced to 3.3 □ 11.0 mmHg in the second tertile (p=0.31, compared to first tertile) and -2.6 □ 16.8 mmHg in the third tertile (p<0.01, compared to first tertile).

Conclusion: Patients with CKD undergoing CAG have a higher degree of aortic calcification. Furthermore, patients with a high degree of aortic calcification have a higher invasively measured cSBP as compared to the bSBP measured with an ordinary oscillometric BP device.

P48

Vitamin K supplementation and bone mineral density in dialysis: results of the double-blind, randomized, placebo-controlled RenaKvit trial

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Background Patients with chronic kidney disease (CKD) suffer from bone disease contributing to low bone mineral density (BMD) associated with bone fractures, increased morbidity and mortality.

Vitamin K deficiency is highly prevalent in patients on dialysis and may contribute to the low bone mineral density (BMD). This study investigated the effect of vitamin K2 (menaquinone-7 (MK-7)) supplementation on BMD in patients on dialysis.

Methods In a 2-year multicenter double-blind placebo-controlled intervention trial, 123 patients on chronic dialysis were randomized to an oral, daily supplement of either 360 µg MK-7 or placebo. BMD of the distal radius (1/3, mid, ultra-distal, and total), femoral neck, lumbar spine (L1-L4), and whole body was assessed by Dual-energy X-ray Absorptiometry. Vitamin K status was assessed by serum levels of vitamin K1 and MK-7, plasma levels of total osteocalcin, dephosphorylated-uncarboxylated matrix Gla protein, and Protein Induced by Vitamin K Absence-II.

Results After 2 years, BMD of the 1/3 distal radius decreased around 3% and BMD of the lumbar spine increased around 5% with MK-7 supplementation compared with placebo (mean difference of changes between groups -0.023 (95% CI (-0.039;-0.008)) g/cm2 and 0.050 (95% CI (0.015;0.085)) g/cm2, respectively). No significant effects were observed at the remaining investigated skeletal sites. Vitamin K status strongly improved in MK-7 supplemented participants.

Conclusions Two years of MK-7 supplementation caused a decrease in BMD of the 1/3 distal radius and an increase in lumbar spine BMD. The clinical implications of these opposite effects on BMD in patients on chronic dialysis are unknown.

P49

Natriuretic peptide receptor A knockout downregulates gene products associated with podocyte protection

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Background: Atrial natriuretic peptide (ANP) and Brain natriuretic peptide (BNP) are endogenous peptides that are secreted in response to increased atrial and ventricular volume and promote vasodilation and natriuresis. ANP and BNP bind to the natriuretic peptide receptor A (NPRA) leading to an increase in cGMP. In the kidney, natriuretic peptides can increase renal blood flow and GFR. NPRA is found in human intrarenal arteries and podocytes. NPRA deletion in podocytes leads to amplified renal injury in disease models suggesting a protective role.

Objective: The study was conducted to map signaling pathways initiated by the NP/NPRA interaction in podocytes in vivo.

Methods: A discovery-based approach was used by transcriptome analysis of isolated GFP^+ podocytes from mice (n=6) with a functional deletion of the *NPR1* gene encoding NPRA and mice (n=6) with an intact functional *NPR1* to compare gene expression patterns. The podocytes were isolated by Fluorescence-activated Cell Sorting (FACS) and used for RNA-sequencing.

Results: The transcriptome analysis of mice with- and without NPRA revealed that mice without NPRA had significantly downregulated transcripts associated with podocyte protection and upregulated RNA transcripts that have previously been associated with kidney damage. Protein S, Semaphorin 3G, and Sulfatase 2 are examples of transcripts that were downregulated by NPRA deletion and with established podocyte-protective properties. Osteoglycin was upregulated and is known to be associated with chronic kidney disease.

Conclusion: Endogenous levels of natriuretic peptides in mice exert multiple protective effects directly at glomerular podocytes. In vivo natriuretic peptide changes could directly affect the filtration barrier.

P51

A Multi-Center, Randomized, Double-Blind, Placebo Controlled, Parallel Roup, Phase III Study to Evaluate the Efficacy and Safety of LNP023 in Primary IGA Nephropathy Patients

Poster presented on behalf of the authors by Per Ramløv Ivarsen, Aarhus University Hospital
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Background: IgAN is characterized by deposition of IgA1-containing immune complexes in the glomerular mesangium, leading to inflammation and glomerular injury.[1]

There is histologic evidence of the involvement of the alternative complement pathway (AP) in ~90% of patients[2]. Co-deposition of C3, properdin and FH with immune complexes in the mesangium is common.[2]

Iptacopan (LNP023) is an oral, highly potent, selective inhibitor of factor B (FB), a key protease of the AP.[3,4]

Iptacopan binds FB to suppress the activity of C3 convertase, preventing downstream generation of the C5 convertase complex, opsonization and formation of C5a anaphylatoxins and membrane attack complex (MAC). [3,4]

Methods: This is a multicenter, randomized, double-blind, placebo controlled parallel group study. The purpose is to evaluate the efficacy and safety of iptacopan compared to placebo on proteinuria reduction and slowing disease progression in primary IgAN patients.[5]

Patient population: Biopsy-confirmed IgAN patients with elevated proteinuria (UPCR ≥1 g/g) despite being on stable doses of ACEi/ARB for at least 90 days.[5]

Primary objectives: Interim analysis: Assess superiority of iptacopan versus placebo in reduction of proteinuria (UPCR from 24-h urine collection) at 9 months.[5]

Final analysis: Assess superiority of iptacopan versus placebo in slowing progression of IgAN measured by annualized total slope of eGFR decline over 24 months.[5]

Sample size: Main cohort (eGFR ≥30 mL/min/1.73 m2): ~430 patients. Severe renal impairment cohort (eGFR 20–29 mL/min/1.73 m2): ~20 patients (not included in the primary analysis).[5]

Results: Recruitment started in Q1 2021.[5]

Conclusion: This trial will evaluate the efficacy of iptacopan, a new therapy for IgAN, in reducing proteinuria and slowing loss of kidney function over 2 years.[5]

P52

Implications of cardiac biomarkers in patients with renal insufficiency on probability of coronary angiography and subsequent cardiovascular outcomes

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Background: Renal insufficiency is associated with an increased risk of cardiovascular morbidity and mortality. Although cardiac troponin remains essential markers for diagnosis of myocardial injury in general population, the diagnostic utility remains uncertain in patients with renal insufficiency.

Methods: Based on data from multiple Danish nationwide health care registries, all hospitalized patients with elevated troponin I or T were identified between 2000 and 2021. Renal function was calculated based on preceding plasma creatinine. The probability of being referred for coronary angiography was computed across strata of renal insufficiency based on multiple Cox regression calculating hazard ratios for 30-day likelihood of coronary angiography, with subsequent comparison of cumulative risk and hazard ratios for myocardial infarction using the Aalen-Johansen estimator and multiple Cox regression, respectively.

Results: In total 57,044 patients were included in the study. Hazard ratios for 30-day likelihood of coronary angiography were 1.26 (95% IC 1.10-1.44) for eGFR 15-29 mL/min/1.73m^2, 2.00 (95% IC 1.77-2.25) for eGFR 30-44 mL/min/1.73m^2 and 2.95 (95% IC 2.63-3.31) for eGFR 45-59 ml/min/1.73m^2, using eGFR <15 as reference. Hazard ratios for risk of myocardial infarction were 0.86 (95% IC 0.71-1.03) for eGFR 15-29 mL/min/1.73m^2, 0.58 (95% IC 0.49-0.69) for eGFR 30-44 mL/min/1.73m^2 and 0.49 (95% IC 0.42-0.58) for eGFR 45-59 mL/min/1.73m^2, using eGFR <15 as reference.

Conclusion: In patients with elevated troponin levels, renal insufficiency is associated with incrementally decreased probability of coronary angiography despite a graded proportional increase in risk of subsequent myocardial infarction.

P54

Impact of renal insufficiency on choice of rhythm or rate control in atrial fibrillation and subsequent effects on cardiovascular outcomes

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Background: Atrial fibrillation remains the most common sustained arrythmia in the general population, with prevalence inversely correlated with renal function. Management of atrial fibrillation relies on either rhythm or rate control, however the choice of treatment in patients with renal insufficiency remains contentious. Accordingly, we examined clinical practice and subsequent cardiovascular outcomes.

Method: Based on nationwide healthcare registers, all patients with atrial fibrillation were identified between 2000 and 2021. Patients were stratified into rhythm or rate control and baseline renal function was calculated using the CKD-EPI equation. The probability of rhythm vs rate control stratified on eGFR (>90ml/min/1.73m^2, 60-90 mL/min/1.73m^2 , 30-60 mL/min/1.73m^2 , <30 mL/min/1.73m^2) was estimated using odds ratios based on multiple logistic regression with subsequent appraisal of risk of cardiovascular outcomes based on the Aalen-Johansen estimator and multiple Cox regression.

Results: A total of 37,920 patients were included. eGFR-stratified odds ratios were 0.91 (95% CI 0.84-1.0) for eGFR 60-90 mL/min/1.73m^2, 0.85 (0.75-0.96) for eGFR 30-60 mL/min/1.73m^2 and 0.77 (0.61-0.98) for eGFR <30 mL/min/1.73m^2 compared to patients with eGFR >90 mL/min/1.73m^2 .

Referencing rate control, hazard ratios for subsequent cardiovascular outcomes were 1.51 (95% CI 1.40-1.62) for eGFR >90 mL/min/1.73m^2, 1.53 (1.45-1.62) for eGFR 60-90 mL/min/1.73m^2, 1.86 (1.68-2.05) for eGFR 30-60 mL/min/1.73m^2 and 1.88 (1.47-2.41) for eGFR <30 mL/min/1.73 m^2.

Conclusions: Rhythm control was less likely employed and was associated with progressivly increased risk of cardiovascular outcomes in patient with renal insufficiency compared to rate control; thus, supporting clinical practice in greater choice of rate control.

P55

Dynamics of complement split-products in allograft rejection in kidney transplant recipients. An observational explorative study

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Complement activation is thought to be an important contributor to allograft injury in kidney transplantation. While dynamics of complement proteins reflect complement activation, monitoring of complement could be a biomarker of ongoing immunological activity and rejection. Therefore, we hypothesized that P-C3d, P-C3a, P-C4a, P-C5a, U-C3dg, and U-sC5b-9 increase in rejecting kidney transplant recipients.

We measured P-C3d, P-C3a, P-C4a, P-C5a, U-C3dg, and U-sC5b-9 at time of rejection and at time of stability in 15 patients with rejection and 15 patients without rejection. Furthermore, we explored possible confounders and adjusted results accordingly.

Data were extracted from our research biobank (OPEN_219). P-C3d analyzed with double-decker rocket immunoelectrophoresis, P-C3a, P-C4a and P-C5a with flow-cytometry, and U-C3dg and U-sC5b-9 with ELISA.

In plasma, there was no significant difference in C3d and C3a between the rejection and the control group. In the rejection group, C3d and C3a increased significantly at time of rejection compared to time of stability ($p<0.01$). When adjusting for pre-transplant C3d, steroids, and delayed graft function, P-C3d was significantly higher in the rejection group at time of rejection compared to the control group ($p=0.04$). We found no significant changes in C4a and C5a.

In urine, C3dg/creatinine and sC5b-9/creatinine did not differ significantly between the rejection and the control group. At time of rejection, C3dg/creatinine increased significantly in both groups; sC5b-9/creatinine increased in the rejection group.

P-C3d and P-C3a increase at time of rejection in kidney transplant patients. Dynamics of P-C3d and P-C3a might reflect ongoing rejection, which a larger prospective study could clarify.

P56

Presence of Gastrointestinal Symptoms in IgA Nephropathy

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Background: Gastrointestinal (GI) symptoms are common in end-stage kidney disease. The intestine seems to play an important role in the pathogenesis of IgA nephropathy (IgAN). No studies exist about the obvious question; do patients with IgAN suffer from GI symptoms.

Methods: Presence of GI symptoms was studied among 104 kidney biopsy-verified IgAN patients by the validated Gastrointestinal Symptom Rating Scale (GSRS) questionnaire. The results were compared with 147 healthy controls. A person was regarded to suffer from 'increased GI symptoms' if his/her GSRS score exceeded plus 1 standard deviation (SD) of the mean of the corresponding score in the healthy controls. The study was conducted at Tampere University Hospital and Tampere University, Finland.

Results: IgAN patients had more GI symptoms than healthy controls based on the GSRS total score (2.0 vs. 1.7, $p=0.001$). Female IgAN patients had higher GSRS total score than male IgAN patients (2.2 vs. 1.7, $p<0.001$). More IgAN patients with preserved kidney function (eGFR >60ml/min/1.73m^2) suffered from increased symptoms of diarrhoea (76 vs. 25%, $p=0.028$), constipation (81 vs. 19%, $p=0.046$), and reflux (85 vs. 15%, $p=0.004$), than did IgAN patients with reduced kidney function (eGFR <60ml/min/1.73m^2).

Conclusions: IgAN patients experienced more GI symptoms compared to healthy people. The idea of GI symptoms being apparent only with declining kidney function was challenged. Systematic enquiry of GI symptoms might increase the standard of care among IgAN patients. GI symptoms may provide clues for future studies aiming to reveal the pathophysiology of IgAN.

P58

Mineralocorticoid receptor antagonist treatment in patients with renal insufficiency and the associated risk of hyperkalemia

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Background: Mineralocorticoid receptor antagonists (MRA) is kidney protective but not recommended in patients with advanced renal failure due to perceived risk of hyperkalemia and death. The aim of the present study was to examine the impact of MRA treatment in progressive chronic kidney disease on risk of hyperkalemia and to evaluate subsequent attributable mortality.

Methods: Rates of hyperkalemia were compared across strata of eGFR and MRA treatment using a nested case–control framework with 1:4 matching of patients with hyperkalemia > 6.0 mmol with controls from the Danish general population on age, gender, diabetes and hypertension. Risk of subsequent death was assessed in a cohort study with comparisons across strata of eGFR and MRA using multiple Cox regression models.

Results: In total 34.442 cases with hyperkalemia were matched with 131.410 controls. MRA treatment was associated with increased rate of hyperkalemia with hazard ratios (HR) of 8.32 (95%CI:7.82-8.85), 4.55 (95%CI:4.26-4.86) and 2.00 (95%:CI:1.71-2.32) for eGFR >60ml/min/1.73m2, 30-60ml/min/1.73m2, and <30ml/min/1.73m2, respectively (reference= Non-MRA treatment). In 34.439 patients with hyperkalemia, MRA treatment was associated with lower rate of subsequent death; HR 0.84 (95%CI:0.78-0.90, p<0.001), 0.67(95%CI:0.62-0.73, p<0.001) and 0.98 (95% CI:0.86-1.12, p=0.77) for eGFR >60ml/min/1.73m2, 30-60ml/min/1.73m2 and <30ml/min/1.73m2, respectively (reference= Non-MRA treatment).

Conclusions: Although mineralocorticoid receptor antagonist treatment was associated with increased risk of hyperkalemia in all stages of kidney impairment, the attributable subsequent 30-day mortality was however lower compared with patients with corresponding kidney function without mineralocorticoid receptor antagonist treatment.

P65

Evaluation of the survival in patients with diabetes mellitus operated for renal cell carcinoma

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Purpose: To investigate the role diabetes mellitus (DM) has on overall survival (OS) in renal cell carcinoma (RCC) patients operated with nephrectomy, and whether other treatments should be considered in this patient group.

Methods: This observational, retrospective register-based cohort study identified 2,752 RCC patients from Danish national registers who had a nephrectomy between 2000-2010. They were distributed in two groups depending on DM-status. OS was investigated with a cox-regression analysis.

The analyses were conducted using Stata Software (version 15.1) with the significance-level set at p<0.05.

Results: Total 2,752 RCC patients were included, 2,277 (82.7 %) were non-DM and 475 (17.3 %) were DM patients. The hazard ratio (HR) was 1.191 (p=0.056) and 1.437 (p=0.007) for 0-10 years and >10 years duration of DM, respectively, thereby exhibiting a lower OS for DM patients.

Other significant variables were age (HR 60-70 years 1.222 (p=0.013), HR70-80 years 1.870 (p<0.001), HR>80 years 2.856 (p<0.001), compared to <60 years), sex (HR male 1.205 (p=0.005), compared to being female), T-stage (HR T2 1.395 (p<0.001), HR≥T3 2.063 (p<0.001), HR Tx 1.344 (p=0.035), compared to T1-stage), N-stage (HR N+ 1.846 (p<0.001), compared to N0-Nx-stage) and M-stage (HR M+ 2.963 (p<0.001), compared to M0-stage).

Conclusion: The study indicates that DM significantly affects the OS in RCC patients operated with a nephrectomy. Future studies should examine whether the impact of DM on OS after nephrectomy exceeds that of DM in general.

P67

Can low-energy extracorporeal shockwave therapy (ESWT) improve the function of kidney allografts?

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Background: Low-energy extracorporeal shockwave therapy (LE-ESWT) has shown therapeutic potential for multiple conditions. Recent studies indicate, that LE-ESWT improves renal function after ischemic injury and in diabetic nephropathy. Our objectives were to study glomerular filtration rate (GFR) and albuminuria in kidney transplant recipients before and after treatment with LE-ESWT and determine possible side effects of the treatments.

Methods: A total of 16 kidney allograft recipients were recruited for this prospective, single-arm clinical study. The patients were treated with six sessions of LE-SWT during a 3-week period. Follow-up visits were performed at 1 and 3 months after final ESWT session.

Results: In general, the treatment was well tolerated, as 89% did not experience any side effects. Reported side effects were mild and included tenderness or mild pain at the side of treatment, fatigue, and increased diuresis. LE-ESWT showed no positive effect on GFR and albuminuria. At baseline, median GFR was 38.0 mL/min/1.73 m2 compared with 29.0 mL/min/1.73 m2 at 3 months follow-up. Median albuminuria was 914 mg/24 hour at baseline and tended to increase to 1256 mg/24 hour 3 months after treatments, and proteinuria showed a similar tendency with a median of 1.55 g/24 hour at baseline and 1.79 g/24 hour at 3-month follow-up. Only the change in GFR shoved statistical difference between baseline and follow-up results.

Conclusions: LE-ESWT is a well-tolerated treatment. Inclusion of more patients is needed to determine whether LE-ESWT can improve renal functional outcome in kidney transplant recipients.

P69

A new venous chamber for haemodialysis (Emboless™) reduces microbubbles of air more efficient than other tested systems. In vitro studies.

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Haemodialysis (HD) induce microbubbles (MBs) of air within the extracorporeal circuit (ECC). Venous chambers (VC) are inserted in the ECC to eliminate contamination of air that may cause emboli in the patient.

The study investigated the efficacy of VC in clinical use and a preclinical VC (Emboless™) to limit MB into the return line of the patient.

Method: An in vitro setting of an ECC with a FX10 dialyzer was recirculated with a dextran-albumin solution to mimic blood viscosity. The Emboless™ and the VC for HD-machines AK98, Artis, 5008 and 6008 were all placed parallel in the same closed system.

A Gampt BCC200 device measured extent and diameter of MBs (20-500µm) and percentage change from inlet to outlet of the VC. Reduction percentage was calculated as = 100*(outlet-inlet)/inlet for each size of MB. Bloodflow (Qb) was 200 and 300 ml/min, respectively. Statistical analyses: Wilcoxon paired test.

Results: At Qb 200 a median change in % was with: Emboless -58%, AK98 -24%, Fresenius5008 -23%, Artis -8% and least with Fresenius 6008 ±0%.

At Qb 300 median change was: Emboless -36%, AK98 ±0%, Fresenius5008 ±0%, Artis +25%, Fresenius6008 +21%. The Emboless reduction was superior to other VC both at Qb200 and Qb300 ($p<0.001$). Qb300 with Emboless™ still eliminated more MBs than all the other VC with Qb200 ($p\leq0.003$).

Conclusion: The choice of VC and Qb are important to limit exposure of MB that enter the patient and may cause microemboli in lung, brain and heart. Emboless™ showed best reduction capacity.

Acknowledgements: Medtech4health

P70

A clinical Ph1-2 trial of orellanine as potential curative therapy for patients with metastatic renal cancer and dialysis treatment

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The medical need remains high for patients with metastatic renal cancer (RC) with complete remission rates of ~15%. The kidney-specific effects observed after accidental intake of mushrooms of the *Cortinarius* family are well-known to nephrologists. The active substance, orellanine, selectively enters proximal tubular cells through transporters seemingly conserved in the RC derived from these cells. Orellanine has demonstrated targeted, organ-specific, and potent anti-

tumor effects on human RC *in vivo* and *in vitro*. Studies confirm the unique kidney-specific action of orellanine, with no safety signals from other organs.

In 2021, the Swedish Medical Products Agency (MPA) approved a clinical phase 1/2 trial (ONC001-CL-001) with the primary objective to study safety and tolerability of orellanine. The trial starts at a single site at Karolinska with Dr. Yachnin as PI. Eligible patients are those with metastatic clear cell or papillary RC requiring dialysis and fulfilling other inclusion criteria. Colleagues in the Nordic countries, France, and Germany are invited to refer patients that might benefit from this treatment. A concierge service will be provided to bring patients to Stockholm for monthly treatment and tumor assessment by computer tomography (CT) scan. The clinical protocol allows for repeated dose escalations every cycle, and to increase the start dose for the next patient (if tolerated). After positive proof of concept, the trial will continue with a dose expansion phase.

If you have a potentially eligible patient, please contact Dr Yashnin (jeffrey.yachnin@regionstockholm.se).

P71

Dialysis initiation according to classic criteria is associated with improved renal survival in critically ill AKI patients receiving continuous veno-venous hemodialysis

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Introduction: Data on the association between timing of dialysis initiation and renal outcomes in acute kidney injury (AKI) patients have been inconsistent in previous studies. We explored the effect of starting dialysis according to classic dialysis initiation criteria (CDIC) on renal survival in critically-ill AKI patients treated in the intensive care unit (ICU) in this retrospective study.

Methods: The study cohort comprised 191 critically-ill AKI patients receiving continuous veno-venous hemodialysis (CVVHD) at the research ICU between 2010 and 2019. CDIC was defined as pH ≤7.2 or bicarbonate ≤12mmol/l or potassium ≥6mmol/l or ratio of fluid balance (in liters) and body weight ≥10% at dialysis initiation.

Results: Median age was 64 (53-70) years, 52 (27.2%) were female and median baseline eGFR was 79 (51-99) ml/min/1.73m^2. Median ICU care and CVVHD duration was 9 (4-16) and 5 (3-11) days, respectively, and median sequential organ failure assessment (SOFA) score was 11 (9-13) at dialysis initiation indicating high disease severity. At 90 days follow-up median eGFR was 57 (38-88) ml/min/1.73m^2 in survivors and 22 (11.5%) were on maintenance dialysis. CVVHD start according to CDIC was positively associated with eGFR at 90 days follow-up in univariate linear regression analysis (β 0.215, p=0.003) and the association remained significant in the multivariable linear regression analysis after adjusting for age, sex, baseline eGFR, ICU disease severity markers, hypertension and diabetes (β 0.139, p=0.030).

Conclusions: CVVHD initiation according to the CDIC appears to be associated with improved renal outcomes in critically-ill AKI patients.

P74

Risk factors for development of de novo post transplantation diabetes mellitus from 8 weeks after kidney transplantation

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Background: PTDM is a major risk factor for cardiovascular events and death in kidney transplant recipients. In a retrospective single-center cohort study we investigated risk factors for development of *de novo* PTDM from eight weeks after kidney transplantation.

Methods: Inclusion criteria were kidney transplantation, age > 18 years, no known diabetes prior to, or at the eight-week control after transplantation and with at least one year of follow up. *De novo* PTDM was diagnosed at OGTT performed routinely at the one-year visit, or as at least two registered dispensations of glucose lowering medication in the Norwegian Prescription Database.

Results: In total 632 patients with a median follow-up of 2.7 years [1-4] were included of which 54 (8.5%) developed *de novo* PTDM (31 diagnosed by the OGTT at 1 year and 23 identified by glucose lowering dispensation). *De novo* PTDM

patients were older than non-PTDM patients at transplantation (median age 63 vs 52 years) and were more often males (81 % vs 61%).

In multiple logistic regression analysis, significant associated factors of PTDM were age (years), OR 1.04 (CI 95%: 1.01;1.06), triglycerides (mmol/L), OR 1.42 (CI 95%: 1.10;1.81) and tacrolimus (µg/L) OR 1.23 (CI 95%: 1.03;1.46) concentrations measured at the one-year control visits, and D+/R- CMV serostatus, OR 2.12 (CI 95%: 1.04;4.28). Plasma magnesium, gender, BMI and plasma creatinine were not associated with development of PTDM.

Conclusion: Development of *de novo* PTDM from eight weeks after kidney transplantation was associated with increased age, higher triglycerides, higher tacrolimus concentrations and D+/R- CMV-serostatus.

P75

Prediction of CKD progression and cardiovascular events using pulse wave velocity and albuminuria

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Background: Chronic kidney disease (CKD) is associated with increased risk of cardiovascular disease (CVD) and death. We compared the ability of carotid-femoral pulse wave velocity (PWV) and urine albumin-creatinine (UAC) ratio to predict CKD progression, cardiovascular events (myocardial infarction or stroke), and mortality in a cohort of CKD patients.

Methods: In stage CKD stage 3—4 patients PWV and UAC were measured at baseline. The endpoint of CKD progression was defined as 50% decline in estimated glomerular filtration rate (eGFR), initiation of dialysis or renal transplantation. The composite endpoint was defined as the CKD progression endpoint, myocardial infarction, stroke or death. Endpoints were analyzed in Cox regression analysis adjusted for age, gender, blood pressure, baseline eGFR, BMI and including both PWV and UAC.

Results: We included 182 patients (median age 69 [IQR 60-75] years, 68% males) with a mean eGFR 37±12 ml/min/1.73 m^2 and UAC 52 [5-453] mg/g. Mean PWV was 10.6 m/s. Median follow-up until first event was 4 [3-6] years with 44 and 89 patients reaching the CKD progression and the composite endpoints, respectively. UAC (mg/g) significantly predicted both the CKD endpoint (HR 1.0005 [1.0002;1.0008]) and composite endpoint (HR 1.0004 [1.0001;1.0007]) in adjusted cox regression. In contrast, PWV (m/s) was not associated with the CKD endpoint (HR 0.99 [0.84;1.18]) nor the composite endpoint (HR 1.03 [0.92;1.15]).

Conclusions: In an ageing CKD population, UAC predicted both CKD progression and a composite endpoint of CKD progression, cardiovascular events, or death, while PWV at baseline did not.

P76

Physical function trajectories predict patient survival in older recipients of deceased donor kidneys

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Background: Health-related quality of life (HRQOL) has been positively associated with post-transplant survival and poor outcomes may indicate risk for clinical deterioration. We aimed to prospectively evaluate if, in older recipients of deceased brain-dead donor (DBD) kidneys, HRQOL development during the 1st year post-transplantation differed between survivor and non-survivors.

Methods: The Kidney Disease Quality of Life Short Form version 1.3 was used to assess HRQOL prior to KT, at 10 weeks, 6 months and 12 months post-KT. A mixed-effect model was used to examine the development of HRQOL in survivors versus non-survivors. Trajectories for each HRQOL domain were identified using a group-based trajectory modelling and their association with patient survival was assessed using a Cox proportional hazard regression.

Results: Among 289 included KT candidates aged ≥ 65 years, 192 received a DBD kidney. Mean age at KT was 72 (4.1) years. During a median observation time of 4.6 (3.2, 6.3) years post-KT, 66 recipients died. In survivors, all the generic and kidney-specific HRQOL domains substantially improved during the 1st year post-KT, whereas in non-survivors HRQOL deteriorated. Three developmental HRQOL trajectories, describing poor, fair, and good outcomes were identified. Recipients perceiving poor physical development during the 1st post-transplant year had 2.5-times higher

mortality risk, while recipients with fair physical development had 1.4-times higher mortality risk, compared to recipients with good physical development.

Conclusion: In elderly KT recipients poor post-transplant physical function trajectory may indicate impaired survival. The systematic HRQOL monitoring following KT may identify high-risk patients, and guide therapeutic decisions.

P77

Protective effect of LCZ696 on kidney function after partial nephrectomy

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Introduction: The frequent use of imaging methods leads to increasing incidental diagnosis of small renal tumors (<7 cm). Partial nephrectomy is the preferred surgical treatment that often requires warm ischemia with increased risk of AKI and a higher cumulative risk of CKD. We hypothesized that treatment with the combined AT1 receptor and neprilysin blocker (LCZ696) protects kidney function after partial nephrectomy. To test the hypothesis a pig model was employed.

Material and methods: 20 landrace pigs with a mean weight of 33kg (27-38) were enrolled and divided into 4 groups:

1) Partial nephrectomy+ LCZ696 49/51mg/day (N=6); 2), partial Nephrectomy+vehicle (N=6); 3) Control+ LCZ696(N=4); 4) Control+vehicle (N=4). Removal of 1/3 of the right kidney with 60min warm ischemia was performed in each surgery group.

99^{m} Tc-DTPA GFR was measured at baseline and after 15 days. Urinary output and 99^{m} Tc-DPTA clearance was measured during 4 hours at termination. Urine was collected form bladder at baseline and from right and left ureters at termination. Data were analyzed by two-way ANOVA with Tukey's correction using GraphPad 9.

Results: Mean difference in clearance of 99^{m} Tc-DPTA after surgery and LCZ696 or vehicle was 24 ml/min (p=<0,05).in the group undergoing right partial nephrectomy and vehicle as there was an increase in proteinuria from the injured kidney and albuminuria from both kidneys, while such increase were not reported in the group undergoing partial nephrectomy and treated with LCZ6969

Conclusions: Treatment with LCZ696 improved total 99^{m} Tc-DPTA clearance, and protected kidney filtration barrier after ischemia-reperfusion insult.

P78

Orellanine selectively elicits hyperacute chemical nephrectomy with no other organs affected

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It is well known that 5-14 days after accidental intake of certain mushrooms (*Cortinarius rubellus*), patients develop severe uremia and require dialysis for their survival. Clinical experience indicates that the active substance, orellanine, is highly kidney specific. However, the severe uremic syndrome could mask effects on other organs, at least theoretically.

Methods: To elucidate the acute effects of high doses of orellanine, we decided to study three groups of anesthetized rats (n=24), monitoring ECG, blood pressure, and blood chemistry including electrolytes, liver enzymes and 23 cytokines. Group A. Infusion of 5+20 mg/kg of orellanine, B. Infusion of orellanine and calcium, and C. Orellanine or saline in nephrectomized animals.

Results: A. Within 30 minutes of start of orellanine infusion, dramatic elevations were observed in potassium, phosphate, creatinine, and BUN blood levels. Lethal levels of hyperkalemia (>8 mM) were reached within 4 hours, causing changes in ECG, and reduction of blood pressure to pre-shock levels. B. Infusion of calcium reduced the cardiotoxic effects of hyperkalemia, prevented acidosis, and restored blood pressure in most animals. C. In nephrectomized rats, all parameters were similar after orellanine or saline.

Conclusion: The hyperacute kidney injury elicited by orellanine can only be mimicked by surgical removal of both kidneys, i.e., chemical nephrectomy, indicative of almost instantaneous loss of function. Due to the high metabolic rate of rodents, lethal potassium levels are reached within 4 hours. The cardiotoxic effects can partially be prevented by calcium infusions. Finally, orellanine is extremely organ-specific, with no detectable extra-renal effects.

P79

Baseline physical endurance and muscular strength in the lower limbs associated with better survival in non-dialysis dependent patients in stages CKD 3-5

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Background: The purpose of this study was to investigate the effects of baseline physical function and 12 months of self-administered exercise training on survival in patients with non-dialysis dependent chronic kidney disease (CKD) stages 3-5.

Methods: This is an observational study comprising patients from the RENEXC-trial. Physical function was assessed with the 6-Minute Walk test (6MWT), Sit-to-Stand 30 seconds (30s-STS), handgrip strength (HGS), Functional Reach (FR) and quadriceps strength (IQS) at baseline and after 12 months. Survival analyses were performed with Cox regression analyses adjusted for age, sex, co-morbidity, eGFR, time in dialysis and time as transplanted

Results: 151 patients were included, 65 % men, mean age 66 ± 14 years, median follow-up 60 months. 112 patients completed 12 months of exercise. 40 % started dialysis, 12 % were transplanted during follow-up and 40 % died by the end of follow-up.

6MWT at baseline was associated with a significantly better survival (HR 0.996; 95% CI 0.993 - 0.998) as was 30s-STS (HR 0.943 CI 0.893 - 0.995).

Patients who improved HGS had a significantly better survival compared with patients who deteriorated (HGS right (HR 2.655; 95% CI 1.070 – 6.591); HGS left (HR 2.990; 95% CI 1.108 – 8.070).

Conclusion: Physical function was independently associated with survival in patients with CKD stages 3-5. Patients who improved HGS had a better survival compared with patients who deteriorated.

P82

Amiloride decreases plasma Tumor Necrosis Factor and Interleukin-6 but not Interleukin-17A in patients with treatment resistant hypertension and type 2 diabetes

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Introduction: Deficiency of the pro-inflammatory cytokine interleukin-17A (IL-17A) is protective against hypertension in animals. Dendritic cells are salt-sensitive and depend on the epithelial sodium channel (ENaC) for activation and to promote Th-17 conversion. We hypothesized that anti-hypertensive treatment with the ENaC blocker, amiloride, and the consequent increase in plasma potassium, reduce plasma IL-17A and other T-helper and macrophage-derived cytokines in patients with diabetes and resistant hypertension (RHTN).

Methods: Cytokines (IL-17A, IFN-γ, TNF, IL-6, IL-1β and IL-10) were determined by multiplex immunoassays in paired plasma samples, before/after amiloride treatment, from patients with type 2 diabetes mellitus (T2DM) and treatment-RHTN included in an interventional, open-label, non-randomized, study (n=60, amiloride 5-10 mg/day, 8 weeks). Sensitivity of LPS-stimulated THP-1 macrophages to amiloride and benzamil was determined *in vitro*.

Results: In patients with T2DM and RHTN, mean arterial blood pressure and diastolic blood pressure correlated positively to plasma IL-1β at baseline. Systolic blood pressure correlated positively with IL-17A at baseline. Urine albumin creatinine ratios correlated positively with plasma IL-17A, IL-6, IL-1β and TNF at baseline. Amiloride reduced plasma TNF and IL-6 in the T2DM patients. In THP-1 macrophages, amiloride decreased LPS-induced IL-6, IL-10, and IL-1β but not TNF (P=0.07 at 1-100 nmol/L). The more selective ENaC blocker, benzamil, reduced all 4 cytokines (TNF, IL-6, IL-10, and IL-1β) at 1 nmol/L.

Conclusion: Thus, ENaC inhibitors lower macrophage-derived cytokines (TNF and IL-6) *in vitro* and *in vivo* in patients with T2DM and treatment-RHTN. In conclusion, amiloride exerts anti-inflammatory actions *in vivo* relevant for organ protection and hypertension.

P84

Congenital Anomalies of the Kidney and Urinary Tract at the Second Trimester Screening – Sibling Recurrence Risk

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Background: Congenital anomalies of the kidney and urinary tract (CAKUT) are an important cause of chronic kidney disease in children and do together with inherited kidney disease account for close to half of all childhood cases of end-stage renal disease. Thus, these anomalies have a great impact on child morbidity and quality of life.

A growing number of monogenic causes of congenital anomalies of the kidney and urinary tract (CAKUT) are discovered, each however accounting for only a minority of cases. Furthermore, many underlying genetic causes have shown reduced penetrance and variable expressivity. Also, environmental factors seem to have an influence on the risk of CAKUT in a fetus. Drug exposure but also maternal obesity and diabetes have been shown to increase the risk. As it is the case here complex causal factors of a given trait often hamper the estimation of recurrence risk in an individual family. In these situations, genetic counseling benefits from empirical estimates of sibling recurrence risk.

Method: This is a nation-wide population-based cohort study. The study period is 2008-2019. We will estimate to what extent having a fetus diagnosed with CAKUT in the second trimester influences a subsequent second trimester fetus' risk of being diagnosed with CAKUT. Data is drawn from the Danish Fetal Medicine Database, the Astraia Databases and the Prescription Database. Sibling pairs is linked by the identification number of the mother.

Results: Statistical analysis are soon to be initiated and results are expected to be ready before May 2022.

Conclusion:

P85

Outbreak of nephropathia epidemica in Jutland, Denmark

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In Denmark most cases of nephropathia epidemica (NE) occur in the island of Funen and are caused by the transmission of Puumala Hantavirus to humans from the bank vole.

During 2020-21 we have seen a growing number of cases of NE occurring in close vicinity to Silkeborg, Jutland, where the disease is not usually seen. This is a case report of 4 of the cases. The case report was earlier published in Ugeskrift for Læger.

NE is characterized by increased vascular permeability and patients present with general symptoms progressing to acute kidney injury. When NE occurs in areas where it has not traditionally been endemic, awareness of the disease is important to ensure proper diagnosis.

P86

Defining New Reference Intervals for Serum Free Light Chains in Individuals With Impaired Kidney Function: Results of the Population- Based Iceland Screens, Treats, or Prevents Multiple Myeloma (iStopMM) Study

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Background: Serum free light chain (FLC) concentration, a cornerstone in diagnosis and follow-up of monoclonal gammopathies, is greatly affected by kidney function. In this population based study we aimed to determine a kidney reference interval for absolute FLCs and FLC ratio.

Methods: A total of 75 422 participants of the Iceland Screens, Treats or Prevents Multiple Myeloma (iStopMM) study were screened with serum FLC (FREELITE®), serum protein electrophoresis (SPEP), and immunofixation (IFE). Serum creatinine (SCr)-based CKD-EPI-calculated eGFR closest to screening was used to estimate kidney function. Participants with M-protein, eGFR ≥60 mL/min/1.73 m^2, or no SCr measurement <1 year from screening were excluded. Central 95% reference intervals were determined, and 95% CI calculated.

Results: Serum FLCs were measured in 6 503 (12%) qualifying participants with eGFR <60 mL/min/1.73 m^2. Median (IQR) kappa level was 21.7 mg/L (16.6-29.4), lambda level 19.0 mg/L (14.8-25.0), and FLC ratio 1.16 (0.97-1.39). Using current reference intervals, 60% and 21% of persons had abnormal values for kappa and lambda, respectively. The FLC ratio was outside the standard reference interval (0.26–1.65) in 9% and the current kidney reference interval (0.37–3.10) in 0.7% of participants. New reference intervals for FLC and FLC ratio were established for patients with eGFR of 45–59, 30–44, and <30 mL/min/1.73 m^2.

Conclusions: Current reference intervals for FLC and FLC ratio are inaccurate for patients with decreased kidney function. We propose that new reference intervals for FLC and FLC ratio be implemented in patients with impaired kidney function.

P88

Vascular access in Octogenerians. Mortality and Outcome of Placed Fistulas among Men and Women. A Seven Year National Registry Follow-up

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Background: The number of elderly patients requiring hemodialysis is increasing, and the choice of vascular access is a challange. The aim of this audit was to evaluate the survival after fistula placement and fistula outcome separated by sex.

Method: All placed fistulas among men and women ≥80 years registrered in the Swedish Renal Registry between 2011-2017 were retrospectively reviewed. The cumulative incidence was calculated for mortality, and reinterventions and abandonment in different fistula types separated by sex. A Cox proportional-hazard regression model was used to explore factors for fistula outcome.

Results: Among registered fistulas were 11%(n=675) at age≥80 years with a male dominace (70%). A forearm fistula was more common n=430 (64%), upper arm 155 (23%), arteriovenous graft (AVG) 90 (13%). All cause mortality among men and women at one, two and three years was 16／14, 30／25, 41／36 %, with detriment for men. Men were more intervened in upper arm and AVG fistulas as compared to women

p<0.05, who in turn had a higher frequency of abandonment p < 0.001. Age was associated with interventions of forearm fistulas but no association was found for any fistula abandonment (Hazard ratio 1.11 ⟨1.06–1.15⟩) p<0.001.

Conclusion: Age alone should not disqualify patients for fistula surgery. However were mortality rates, the burden of interventions and rate of fistula abandonment high with differences among sex. This needs to be taken into account when planning for a vascular access.

P89

Microbubbles are deposited in the lung, brain and heart in hemodialysis and ALS patients

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Objectives: Microbubbles of air (MB) develop in the extracorporeal circuit during hemodialysis (HD). The aim of the study was to investigate if MB remained in circulation to be verified post-mortem in the lungs, brain and heart.

Methods: Tissue sections from 46 autopsied patients were investigated for MB. One group consisted of 25 patients on HD (HD-group), and another group included 19 patients who died from amyotrophic lateral sclerosis (ALS-group). To discriminate between MB caused by artificial contamination during autopsy versus MB deposited in vivo, tissues were stained with a polyclonal fluorescent antibody against fibrinogen, fibrin and fragments E and D. Fluorescence visible MB were counted within 25 microscopic fields (600 x) of each tissue preparation. Only one tissue preparation was used for each available organ.

Results: The HD-group had a higher median of MB than the ALS-group for the lung (6 vs 3, p=0.007), heart (2.5 vs 1, p=0.013) and brain (7.5 vs 2, p=0.001). For the HD-group, a correlation existed between the vintage of HD and MB in the lungs. There were significantly more MBs/tissue sections in the lungs versus the heart or brain.

Discussion: MBs can be verified at autopsy as microembolies (ME) in lung, heart and brain. Most findings were in the lungs and indicate that air exposure by MBs in return blood during HD or by injections or infusion through the veins is the main route.

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P90

The effect of SARS Cov-2 vaccination in a hemodialysis population in the Region of Southern Denmark

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Background: Patients receiving hemodialysis represent a high-risk, immune compromised population. Therefore, it would be expected that the vaccine against SARS Cov-2 have a reduced efficacy in this group of patients. The mortality in SARS-Cov2 infection among hemodialysis patients is high.

Methods: In this prospective observational study performed on three dialysis facilities in the Region of Southern Denmark (Kolding Hospital, Odense University Hospital and Sydvestjysk Hospital) in the period February 2021 to December 2021. SARS Cov-2 Spike glykoprotein IgG was measured in bloodsamples collected one, two and five months after the second vaccination and one month after the third vaccination. All hemodialysis patients received the mRNA vaccine Comirnaty/Pfizer-BioNTech.

Results: Preliminary data shows a significant increase in the antibody level after the third booster vaccination with a large variation (n= 65 mean = 2333 SEM ±250) compared to four weeks after the second (n=85 mean = 672 SEM ±149). 22% did not respond (antibodies below 50) after the second vaccination. This was reduced to 4.6% after the third vaccination. Data for over 200 hemodialysis patients will be presented at the conference.

Conclusion: The preliminary data showed that the third booster vaccination resulted in a significantly rise in the antibody levels and reduced the group of non-responders. Furthermore, the longevity of the immune response to the third booster vaccination is not known. In this study, we plan to measure antibodies up to two years after the first vaccination. We hope this study will give at better insight in predicting high-risk patients and non-responders.

P93

Chronic kidney disease stages 3-5 among patients treated with lithium

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Background: The association between lithium use and chronic kidney disease (CKD) is not well understood, and the impact of comorbid diseases remains unknown. The aim of this study was to examine the risk of developing CKD stages 3-5 among individuals using lithium.

Methods: This was a retrospective cohort study of all patients in Iceland treated with lithium in the years 2008–2018. A control group comprised patients with affective disorders (ICD-10 codes F30-F39) who attended the outpatient clinics of the Landspitali–The National University Hospital Mental Health Services in 2014–2016 and had not been prescribed lithium. CKD 3-5 was defined as eGFR <60 ml/min/1.73 m^2; eGFR was calculated from serum creatinine (SCr) using the CKD-EPI equation. Individuals with CKD 3-5 prior to 2008 and those with fewer than 2 SCr measurements during the study period were excluded. Multivariable logistic regression was used to assess risk.

Results: A total of 2682 persons had received lithium treatment, of whom 2051 (76.5%) were included in the study. Of those 221 (10.8%) developed CKD 3-5. Of the 1426 persons in the control group, 1010 (70.8%) were included, of whom 29 (2.9%) developed CKD 3-5. Lithium use was significantly associated with CKD development (OR 1.94, 95% CI 1.25–3.11) after adjusting for sex, age, and comorbid diseases.

Conclusion: Lithium treatment is a highly significant independent risk factor for the development of CKD in individuals with affective disorders. Kidney function of these patients should be carefully monitored.

P95

Prevalence and incidence of chronic kidney disease using age-adapted GFR criteria

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Background: Age-adapted GFR criteria for definition of chronic kidney disease (CKD) have been proposed. The aim of this study was to determine the prevalence and incidence of CKD stages 1-5 based on age-adapted GFR criteria compared with GFR cut-off of 60 mL/min/1.73 m^2.

Methods: We obtained all serum creatinine (SCr) and urine protein measurements from all laboratories in Iceland in 2008-2016. Clinical information was retrieved from electronic medical records. Estimated GFR (eGFR) was calculated using the CKD-EPI equation. CKD was defined as presence of kidney damage (proteinuria or kidney-specific diagnoses) or reduced eGFR (<60 mL/min/1.73 m^2) for ≥3 months. The age-adapted eGFR definition was <75 mL/min/1.73 m^2 for age <40 years, <60 mL/min/1.73 m^2 for 40-65 years and <45 mL/min/1.73 m^2 for age ≥65 years.

Results: We obtained 2,120,147 SCr values for 218,437 individuals. The median age was 46 (range, 18-107) years; 47% were men. A total of 25,996 individuals met the KDIGO criteria for CKD compared with 17,593 using the age-adapted criteria. Annual age-standardized prevalence per 100,000 overall, for men and women was 5940, 5130 and 6750, respectively, with KDIGO criteria and 3640, 3270 and 4010 using age-adapted GFR criteria. Annual age-standardized incidence of CKD per 100,000 overall, for men and women was 671, 649 and 694 with KDIGO criteria, and 501, 480 and 522 using age-adapted criteria.

Conclusion: This nationwide study comprising data from the majority of the Icelandic population demonstrates markedly lower prevalence and incidence when age-adapted GFR thresholds are used compared with the standard KDIGO criteria.

P97

Detection and diagnosis of acute kidney injury in the emergency department

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Background: Recently, new definitions of acute kidney injury (AKI) based on changes in serum creatinine (SCr) have gained acceptance, but awareness by primary care and emergency physicians may still be limited. We studied the documentation of AKI diagnosis among patients presenting to the emergency department (ED)

Method: In this prospective study, SCr of all individuals who presented to the University Hospital's ED from January 1, 2020 to May 1, 2021 (with intermissions due to Covid-19), were examined for the presence of AKI. All patients fulfilling the KDIGO criteria for AKI were invited to participate. ICD-10-CM codes N17 and N19 at discharge from the ED were considered indicative of AKI diagnosis.

Results: A total of 527 cases of AKI were identified, 445 (84%) of whom participated. Their mean (±SD) age was 67.2±16.8; 47% were female. AKI diagnosis was assigned to 104 (23.4%) participants, with no difference between women and men, 20.9% and 23.9% (p=0.85), respectively, or between age groups (18-49 years, 23.9%; 50-69 years, 21.7%; and >70 years, 21.7%; p= 0.84). Thirty-nine (8.7%) participants carried a pre-existing diagnosis of CKD and were significantly more likely to receive an AKI diagnosis than those without CKD. Among the participants with a diagnosis of AKI, 48.0% had stage 3 AKI, 25.2% stage 2 AKI and 15.1% stage 1 AKI.

Conclusion: These results may indicate lack of awareness of recent guidelines among emergency physicians. Measures should be taken to improve the diagnosis and documentation of AKI in the ED.

P98

Risk of all-cause mortality according to eGFR and proteinuria in the elderly: results from a nationwide study in Iceland

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Background: The aim of this study was to estimate the risk of all-cause mortality according to eGFR category and proteinuria in individuals aged >65 years in the general population.

Methods: We obtained all serum creatinine (SCr) and urine protein measurements from all laboratories in Iceland in 2008-2016. Clinical information was retrieved from electronic medical records. Estimated GFR (eGFR) was calculated using the CKD-EPI equation. CKD was defined as presence of kidney damage (proteinuria or kidney-specific diagnosis) or reduced eGFR (<60 mL/min/1.73 m^2) for ≥3 months. A multiple imputation method was used to account for missing urine protein measurement data. A joint model using repeated measurements was used to assess mortality and simultaneously account for decline in eGFR over time, adjusting for age as a continuous variable, sex and multiple comorbid conditions.

Results: We obtained 782,995 SCr values for 37,937 individuals aged >65 years, of whom 23,344 (62%) had information on proteinuria. The median age was 75 (range, 66-106) years and 46% were men. Adjusted hazard ratios for all-cause mortality are demonstrated in the table.

Table. Adjusted hazard ratios (95%CI) according to eGFR and proteinuria

eGFR (mL/min/1.73 m2) No Proteinuria Proteinuria

>104 6.39 (4.73-8.63) 8.02 (3.02-21.3)

90-104 1.56 (1.43-1.71) 1.92 (1.52-2.43)

75-89 1.09 (1.04-1.16) 1.27 (1.12-1.43)

60-74 Reference 1.33 (1.16-1.51)

45-59 1.05 (0.99-1.11) 1.28 (1.12-1.46)

30-44 1.18 (1.10-1.27) 1.40 (1.22-1.61)

0-29 1.58 (1.42-1.77) 1.89 (1.63-2.19)

Conclusion: Among elderly individuals, eGFR >104 carries a high mortality risk, whereas eGFR of 45-59 without proteinuria is not associated with increase in mortality risk.

P99

Acute kidney injury in the emergency department: a prospective case-control study

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Background: The aim of this study was to examine the incidence and causes of AKI among patients presenting to the emergency department (ED).

Methods: This was a prospective case-control study in which serum creatinine (SCr) of all individuals visiting the University Hospital's ED were examined for the presence of AKI. All patients who met the KDIGO criteria for AKI were invited to participate, as well as randomly selected controls (1:2). Participants answered questions about their medical history and use of medications, including over-the-counter (OTC) drugs. Factors associating with AKI were assessed by logistic regression.

Results: A total of 372 AKI cases were identified, 315 (85%) of whom participated. The mean (±SD) age of AKI cases and controls was 66.6±16.1 years and 66.3±16.2 years, respectively; 46% of cases and controls were female. AKI cases were significantly more likely than controls to have used non-steroidal anti-inflammatory drugs (NSAIDs) (31.1% vs

22.2%, p=0.003) in the week preceding the ED visit, particularly OTC NSAIDs (24.7% vs 16.2%, p=0.001). AKI was associated with vomiting (OR 2.40, 95%CI 1.74-3.35), diarrhea (OR 1.35, 95%CI 1.00-1.84), diabetes (OR 1.66, 95%CI 1.17-2.35) and NSAID use (OR 1.60, 95%CI 1.18-2.23), but not with use of ACE inhibitors/angiotensin receptor blockers or diuretics, or a history of hypertension, vascular disease or chronic kidney disease.

Conclusion: These results suggest that volume depletion and use of NSAIDs play a major role in the development of AKI in the community setting. Frequent use of OTC NSAIDs is a concern in light of serious adverse effects.

P105

AKI Risk Stratification and Early Optimization of Renal Risk Medications among Older Patients in the Emergency Department: Are suPAR and/or NGAL useful?

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Background: Diagnosis of acute kidney injury (AKI) based on plasma creatinine often lags behind actual changes in renal function. Here, we investigated early detection of AKI using the plasma soluble urokinase plasminogen activator receptor (suPAR) and neutrophil gelatinase-sssociated lipocalin (NGAL) and observed the impact of early detection on prescribing recommendations for renally-eliminated medications. This study is a secondary analysis of data from the DISABLMENT cohort on acutely admitted older (>65 years) medical patients (n = 339).

Methods: Presence of AKI according to kidney disease: improving global outcomes (KDIGO) criteria was identified from inclusion to 48 h after inclusion. Discriminatory power of suPAR and NGAL was determined by receiveroperating characteristic (ROC). Selected medications that are contraindicated in AKI were identified in Renbase®.

Results: A total of 33 (9.7%) patients developed AKI. Discriminatory power for suPAR and NGAL was 0.69 and 0.78, respectively, at a cutoff of 4.26 ng/mL and 139.5 ng/mL, respectively. The interaction of suPAR and NGAL yielded a discriminatory power of 0.80, which was significantly higher than for suPAR alone (p = 0.0059). Among patients with AKI, 22 (60.6%) used at least one medication that should be avoided in AKI.

Conclusions: Overall, suPAR and NGAL levels were independently associated with incident AKI and their combination yielded excellent discriminatory power for risk determination of AKI.

P107

Hyperkalemia and the use of new Potassium Binders in clinical practice in outpatient clinic- A single center experience from Vestfold Norway (The PotBind study)

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Introduction: Hyperkalemia (HK) is a common complication of CKD. CKD patients +/- CHF counts for 48,0% of HK. HK is associated with serious adverse events. HK treatment has been limited to diet, diuretic therapy, managing metabolic acidosis, and lowering RAASi. New potassium-binders (PBs) Patiromer and Zirconium Cyclosilicate for treatment of HK is developed with promising results on outcomes of HK.

Study objective: Aim was to prevent HK to maintain RAASi treatment in CKD patients.

Materials and methods: Retrospective study in users of PB for chronic HK in CKD.

Patient's characteristics: Mean age 65 years. 67.3% males. CKD stage 3, 47.3%, CKD stage 4, 21.8%, CKD stage 5, 9.1%, dialysis 20%.

Results: 55 (100%) received PB. Treatment time was 2.7-167 weeks, mean 8.4 weeks. Lokelma users 76%. 12.7% had admission for HK 12 months prior to starting PB. 30% of these with prior HK received hemodialysis. Hospital admission for HK 3.8 times higher in dialysis compared with non-dialysis. No admission for HK after initiation of PB during study. Lower rate of un-planed dialysis in PB users.

Mean otassium values was significantly lower after PB. Non-significant changes in s-bicarbonate, eGFR and concomitant medication before and after PB treatment. RAASi treatment raised significantly with 10% by PB treatment (P < 0.000).

Conclusions: HK is important complication of CKD. In our experience use of the new PB in practice is easy task and safe treatment with few side effects and good tolerability in CKD with significant lower risk for hyperkalemia on maintained RAASi.

P109

Prevalence of thromboembolic complications in dialysis patients with new-onset atrial fibrillation - results from the nationwide FinACAF study

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Background: The incidence and prevalence of atrial fibrillation (AF) in end-stage renal disease (ESRD) is higher than in general population and AF in ESRD is associated with greater mortality and morbidity. The Finnish AntiCoagulation in Atrial Fibrillation (FinACAF) is a nationwide study among AF patients conducted as a retrospective register-based linkage study combining data from several Finnish health care registers. We studied prevalence of thromboembolic complications in dialysis patients with new-onset AF.

Methods: FinACAF includes data from 411 000 patients covering all Finnish AF patients from 1 January 2004 to 31 December 2018. All patients 20 years or older with a new-onset AF diagnosis between January 2010 and December 2018 and a measured estimated glomerular filtration rate (eGFR) within the proximity of the AF diagnosis were included (n=124 926).

Results: Percentage of any form of dialysis was 0.3 % (318 patients) including 220 hemodialysis (HD) and 90 peritoneal dialysis (PD) patients, 8 patients had no information on the type of dialysis. Mean age of HD and PD patients was 70 and 69 years, respectively (p=0.492). Percentage of male patients was 69.1 % and 74.4 %, respectively (p=0.347). Before the cohort entry 0.9 % of HD and 3.3 % of PD patients had had pulmonary embolism (p=0.124), 12.3 % and 6.7 % other venous thromboembolism (p=0.146) and 15.5 % and 17.8 % ischemic stroke or TIA (p=0.614).

Conclusion: Prevalence of thromboembolic complications did not differ significantly between HD and PD patients with new-onset AF.

P110

Eight weeks of Treatment with Mineralocorticoid Receptor blockade Does Not Alter Vascular Function in Individuals with Type 2 Diabetes

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Background: Individuals with type 2 diabetes have an increased risk of endothelial dysfunction and vascular disease. Plasma aldosterone has been suggested to be implicated by reactive oxygen species dependent mechanisms. We aimed to investigate the effect of acute antioxidant infusion and of 8-weeks mineralocorticoid receptor blockade (Eplerenone) on endothelial function in individuals with type 2 diabetes compared to healthy controls.

Methods: In a case-control design, 12 individuals with type 2 diabetes and 14 controls were included. Measurements of leg hemodynamics were performed at baseline and during femoral arterial infusion of acetylcholine (10, 25 and 100 µg min^{-1} [L leg volume]$^{-1}$) and sodium nitroprusside (0.2, 2 and 5 µg min^{-1} [L leg volume]$^{-1}$), with and without concomitant n-acetylcysteine (antioxidant; 125 mg·kg^{-1} $hour^{-1}$ for 20 min. followed by 25 mg·kg^{-1} $hour^{-1}$), before and during mineralocorticoid receptor blockade after 8-weeks of treatment.

Results: No difference was detected in leg blood flow or vascular conductance before, or at the end of treatment with mineralocorticoid blockade, in the individual groups or between the individuals with type 2 diabetes and the control group. Infusion of n-acetylcysteine increased baseline blood flow and vascular conductance, but did not change the vascular response to acetylcholine or sodium nitroprusside before or during mineralocorticoid receptor blockade.

Conclusions: No beneficial effect of mineralocorticoid blockade was found on endothelial function in individuals with type 2 diabetes. The included participants did not have known complications of diabetes thus, these results may not apply to individuals with already developed vasculopathy of diabetic origin.

P111

Marked beneficial short-term effects of the New Nordic Renal Diet on urine excretion of uremic toxins and metabolic acidosis in patients with chronic kidney disease stages 3 and 4

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Background: Chronic kidney disease (CKD) is increasingly prevalent worldwide and obesity is an emerging cause. CKD increases uremic toxins like Indoxyl sulphate (IS) and p-cresyl sulphate (PCS) and causes chronic metabolic acidosis, both associated with increased mortality and morbidity. We designed a new food concept, the New Nordic Renal Diet (NNRD) based on fresh, organic foods, with a phosphorus content of 850 mg/day and investigated its effect on metabolic acidosis and urinary excretion of IS and PCS in moderate CKD compared to the habitual Danish diet.

Methods: Plasma total CO2, urine pH and urinary excretion of ammonium, titratable acids, bicarbonate, IS and PCS were measured in 24h urine collections acquired at day 1, 4, and 7 in 18 patients with CKD stages 3 and 4. Data were acquired from a randomized controlled crossover trial comparing 1-week period of a Danish habitual diet with 1-week period of the NNRD.

Results: Plasma total CO2 increased with 10% ($P = 0.02$), urine pH increased 25% ($P < 0.0001$), 24h urine excretion of ammonium and bicarbonate decreased 34% ($P < 0.0009$) and increased 680% ($P < 0.0001$), respectively in the NNRD period. 24h net acid excretion decreased 80% ($P < 0.0001$), during the NNRD period. 24h urine excretion of PCS and IS was reduced in the NNRD period by 36% ($P=0.013$) and 38% ($P=0.008$), respectively.

Conclusion: NNRD has an obviously positive effect on reducing metabolic acidosis and urinary excretion of uremic toxins in moderate CKD.

P112

Efficiency of treatment with reduced prednisolone and activated vitamin D compared to standard treatment in minimal change nephropathy – preliminary data

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Background: International guidelines for treatment of minimal change nephropathy (MCN) in adults recommend prednisolone at 1 mg/kg/day, a dose that is empirically based.

This study examines if treatment with reduced dose of prednisolone in combination with active vitamin D is as efficient as standard dose prednisolone in patients with MCN, but with fewer adverse events.

Methods: A non-inferior, open label, randomized, controlled multicenter study aiming to include 96 patients with primary MCN. Patients are randomized to standard dose (1 mg/kg/day) or reduced prednisolone (0.5mg/kg/day) in combination with alfacalcidol 0.5µg/day and followed until first relapse of MCN or for one year after remission. The primary endpoints are rate and time to remission. Secondary endpoints are rate and time to relapse and adverse events to treatment.

Results: Forty-four patients have been included (24 male) with a median age of 51 (range 18-82). Of those included for more than 30 days (n=42), 36/38 (95%) have attained remission with a median time from diagnosis to remission of 32.5 days (range 11-105). Four patients were excluded before attaining remission due to adverse effects (n=1), revised diagnosis (n=1), or protocol violation (n=2). One patient never attained remission and one patient is still in active therapy. Two patients were excluded after remission due to pregnancy or adverse events. Median follow-time after remission is 236 days and relapse has been identified in 10/36 (28%) patients at a median time of 168 days (range 83-283) after remission.

Conclusions: Our preliminary data are comparable to previous published data on MCN.

P113

Plasma kallikrein cleaved H-kininogen (cHK): An end-point marker for contact activation in vitro and ex vivo

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Objectives: Patients with end-stage renal disease undergoing hemodialysis (HD) are burdened with high mortality rates due to cardiovascular complications and bloodstream infections. During HD the immune system, including the contact system, is activated due to contact with foreign materials during the process of HD, which could lead to decreased immunoactivity. To reveal the effect of HD on the contact system a specific marker of contact activation is needed. Plasma kallikrein (PKa) cleaved H-kininogen (cHK) is an end-point marker of contact activation. Presently, we developed a specific and precise enzyme-linked immunosorbent assay (ELISA) for determination of cHK *in vitro* and *ex vivo.*

Methods: cHK specific mouse monoclonal antibodies (mAbs) were generated using a peptide corresponding to the PKa cleavage site on HK as immunogen. ELISA, surface plasmon resonance analysis, and immunoprecipitation established the specificity of the mAbs. The cHK-specific mAb was subsequently used in an ELISA. The analytical imprecision and the concentration of cHK in a reference population were determined. cHK was assessed *in vitro* in plasma exposed to biomaterials: polytetrafluoroethylene, silicone, and glass.

Results: The cHK-specific mAb showed excellent specificity towards cHK. The intra-assay and inter-assay CV of the ELISA were 3.6% and 6.0%, respectively. A reference interval of 0.82 – 2.56 µg/mL was established. cHK was elevated in plasma exposed to polytetrafluoroethylene, $p=0.001$, and glass, $p<0.0001$.

Conclusions: The cHK-specific antibody and the ELISA could be promising tools for assessment of contact activation in HD patients and for *in vitro* investigations of the plasma compatibility of hemodialysis membranes.

P114

Role of urokinase for kidney injury in DOCA-salt murine model

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Background: In proteinuria, aberrant filtration of urokinase and plasminogen leads to intratubular activation of plasmin with potential proteolytic activation of ENaC. Deletion of plasmin protects against kidney fibrosis. Role for urokinase-type plasminogen activator (uPA) is not resolved.

Objective: The hypothesis was tested that urokinase activates plasminogen to cause kidney injury and hypertension in DOCA-salt murine model.

Methods: FVB/uPA wildtype (WT) and gene-targeted (KO) mice were subjected to unilateral nephrectomy and insertion of DOCA pellet combined with high dietary Na (4% NaCl) for 21 days. In metabolic cages, urine was collected to determine electrolytes, albumin, and plasmin. At termination, organs and blood were collected to determine electrolytes and urea.

Results: Diuresis, water intake, food intake and Na^+ but not K^+ excretions were significantly elevated in the DOCA-salt mice with no difference between KO and WT. DOCA-salt mice displayed significant ~15-fold increase in albumin excretion. Urine subjected to SDS-PAGE showed glomerular proteinuria with no genotype difference. Immunoblotting showed significant and similar urine plasminogen excretion from DOCA-salt treated mice. Active plasmin was absent in urine from DOCA-salt KO. DOCA-salt increased kidney and heart/body weight ratios ($p<0.0001$) with no difference between genotypes. Plasma urea was significantly higher in male compared to female WT DOCA-salt-treated mice ($p=0.02$) with no genotype difference. DOCA-salt leads to proteinuria, urine plasmin activation, albuminuria, cardiac and renal hypertrophy but maintained kidney function.

Conclusion: In proteinuria, uPA is the activator of plasminogen in urine. Urokinase does not contribute to albuminuria and cardiac and renal hypertrophy in DOCA-salt murine kidney injury model.

P115

Patients with dialysis dependent chronic kidney disease have normal myocardial perfusion reserve

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Background: Uraemia is associated with cardiac microvascular disease. However, epicardial coronary artery disease (CAD) makes estimation of impact of microvessels on myocardial perfusion (MP) difficult. In this study we measured MP in patients with dialysis dependent chronic kidney disease (CKD) without significant coronary artery disease (CAD).

Methods: Basal MP and adenosine stimulated stress MP were measured in 13 patients with dialysis dependent CKD on kidney waiting list and in 10 healthy controls by [^{15}O]H_2O positron emission tomography (PET). Myocardial perfusion reserve (MPR) was calculated dividing stress MP by basal MP. Basal MP was corrected (basal MP_{corr}) by cardiac workload (rate pressure product, RPP = heart rate x systolic blood pressure) according to formula: (basal MP/own RPP) x average RPP of controls. Coronary computed tomography (CCT) was performed and left ventricular mass index (LVMI) was assessed by Doppler echo.

Results: 9/13 patients had no CAD in CTT. 4/13 patients had mild CAD. There was a statistically significant difference in basal MP between the patients and the healthy [1.4 (1.1 – 1.5) and 0.9 (0.8 – 1.1) $ml \cdot g^{(-1)} \cdot min^{(-1)}$, p=0.009, respectively], which disappeared after correction of basal MP by cardiac workload [1.1 (0.9 – 1.1) and 1.0 (0.8 – 1.0) $ml \cdot g^{(-1)} \cdot min^{(-1)}$, p=0.64, respectively]. Stress MP, MPR and MPR_{corr} (stress MP/basal MP_{corr}) were the same in both groups (p=NS). 10/13 patients had normal LVMI.

Conclusion: This is the first study to measure MP by quantitative PET method in patients with dialysis dependent CKD without significant CAD. Uraemia seems not to have influence on MP.

P119

Recurrent AA Amyloid After Kidney Transplantation

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Background: Kidney transplantation (KTX) in amyloidosis has been controversial, mainly due to concern for poor graft outcome.

Methods: We report outcomes from the Norwegian Renal Registry of all patients with AA-amyloidosis in Norway receiving a first kidney (only) transplant from 1988 through 2017 (AAMY, n=109) with follow-up until January 2022. KTX recipients with diabetic nephropathy (DIA, n=1000) and polycystic kidney disease (ADPKD, n=763) in the same time period served as controls. We calculated patient-, graft- and death-censored graft survival using the Kaplan-Meier method.

Results: Inflammatory rheumatic and bowel diseases were dominating causes of AA-amyloidosis in AAMY recipients. Mean age (SD) at KTX was 50.2 (14) years for AAMY, 48.2 (12) years for DIA and 55.2 (11) years for ADPKD. The 1-5-10 year patient survival after KTX was 92%-72%-45% in AAMY, 95%-82%-64% in DIA and 97%-89%-73% in ADKPD; whereas death-censored graft survival was 97%-89%-71% in AAMY, 95%-90%-83% in DIA and 99%-93%-88% in ADKPD.

Death-censored graft survival was similar between groups the first six years after KTX, but significantly different over the entire study period. The cause of graft losses in AAMY were recurrent amyloid in 17/36 and rejection in 17/36 recipients. In the DIA group recurrent diabetes was the cause of graft loss in 6/192 and rejection in 150/192 patients. In the ADPKD group, 101/129 lost their graft due to rejection.

Conclusions: Recurrent AA-amyloidosis in kidney graft is a major cause of graft loss in AAMY that needs attention in care of these patients.