Abstracts for

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Oral presentations

O1

The risk of renal co-morbidities in celiac disease patients depends on the phenotype of celiac disease

Rakel Nurmi [1], Camilla Pasternack [2], Teea Salmi [3], Kaisa Hervonen [4], Inka Koskinen [5], Jutta Järvelin [6], Heini Huhtala [7], Pekka Collin [2], Jukka Mustonen [8], Katri Kaukinen [2], Satu Mäkelä [9]
[1] Tampere University, Celiac Disease Research Center, Tampere, Finland, [2] Tampere University, Celiac Disease Research Center, Tampere , Finland, [3] Tampere University Hospital, Department of Dermatology, Tampere , Finland, [4] Tampere University Hospital, Department of Dermatology, Tampere, Finland, [5] Central Finland Health Care District, Department of Internal Medicine, Jyväskylä, Finland, [6] Finnish Institute for Health and Welfare, Helsinki, Finland, [7] Tampere University, Faculty of Social Sciences, Tampere, Finland, [8] Tampere University, Faculty of Medicine and Health Technology, Tampere, Finland, [9] Tampere University Hospital, Department of Internal Medicine, Tampere, Finland

Background: Albeit the association between renal disorders and celiac disease is still somewhat contradictory, an elevated risk of kidney diseases in patients with celiac disease has been shown. Only case reports have described the link between glomerulonephritis and dermatitis herpetiformis, a cutaneous manifestation of celiac disease. This study aimed to evaluate whether patients with various phenotypes of celiac disease have an increased risk of renal co-morbidities compared with matched references.

Methods: The diagnoses of glomerulonephritides, diabetic nephropathy, interstitial nephritis, and end-stage renal disease were collected from the Finnish National Hospital Discharge Register from 1970 to 2015 among 1440 celiac disease patients and 4296 age- and sex-matched references. Further, patients were divided into two cohorts, dermatitis herpetiformis and any other phenotype of celiac disease. We used Cox proportional-hazards model to compare the risk of renal co-morbidities between patients and reference individuals.

Results: Celiac disease was positively associated with renal disorders even after adjusting for type 1 diabetes (HR 1.81, 95% CI 1.18-2.76). 3-fold and 12-fold risk increases were seen for glomerulonephritis and IgA nephropathy, respectively. Furthermore, the risk of co-morbidities was less obvious in patients with dermatitis herpetiformis than in patients with any other phenotype of celiac disease.

O2

The Effect of Magnesium Supplementation on Vascular Calcification in Chronic Kidney Disease - A Randomised Clinical Trial (MAGiCAL-CKD)

Iain Bressendorff,
Herlev and Gentofte Hospital, Herlev, Denmark

Background: Higher levels of serum magnesium (Mg) are associated with lower risk of cardiovascular (CV) events in patients with CKD and Mg prevents vascular calcification (VC) in animal models of CKD. We hypothesized that oral Mg supplementation would slow the progression of VC in CKD.

Methods: In a randomised, double-blind, placebo-controlled, parallel group, clinical trial we recruited 148 patients with an eGFR between 15 and 45 mL/min and randomised them to oral Mg hydroxide 15 mmol twice daily or matching placebo for 12 months. We excluded kidney transplant recipients.

Results: Seventy-five subjects were randomised to Mg and 73 to placebo. eGFR was 25 mL/min at baseline. Mg treatment significantly increased plasma Mg ($p < 0.001$). CAC scores were not significantly different between the two groups after 12 months (mean difference 0.01%, 95% CI –13.5% to 15.6%; $p = 0.991$). A prespecified subgroup analysis of subjects with CAC > 0 at baseline did not significantly alter the main results (mean difference 4.0%, 95% CI –5.4% to 14.3%).

Thirty-two subjects randomised to Mg treatment experienced gastrointestinal side effects compared to 11 subjects randomised to placebo. There were five deaths and six CV events in the Mg group, compared to two deaths and no CV events in the placebo group.

Conclusion: Mg supplementation did not slow the progression of VC in CKD, despite a significant increase in plasma Mg. There were more deaths and CV events in the Mg group compared to placebo, although the trial was not powered to investigate these endpoints.

Conclusions: Celiac disease was associated with an increased risk of renal co-morbidities, especially glomerulonephritides. The risk depends on the phenotype of celiac disease. The possible association between renal disorders and celiac disease should be investigated more in the future and kept in mind also in clinical practice.

O3

Prevalence of Sarcopenia in Chronic Hemodialysis Patients, A Single Center, Cross-Sectional Study

Zdenek Lys, Tomas Balner, Stanislava Kollarova, Monika Kupcova, Ivo Valkovsky, Jan Vaclavik
University Hospital Ostrava, Ostrava, Czech Republic

Background: Sarcopenia is a progressive muscle disease associated with age and various factors including chronic kidney disease that increases the risk of falls, fractures, and mortality.

Methods: In our dialysis center, we have started a prospective observational study to monitor the development of sarcopenia in 2020. We perform repeated SARC-F (simple five-item questionnaire), grip strength, bioimpedance analysis of body composition, short physical performance battery, muscle sonography and MNA (Mini Nutritional Assessment) in chronic hemodialysis patients. Here we report the first results of the prevalence of probable sarcopenia (according to the recommendations, enough to trigger assessment of causes and start intervention) defined by EWGSOP2 (the European Working Group on Sarcopenia in Older People).

Results: The median age in our cohort was 64 years (IQR 16.5). We examined 44 patients (30 men and 14 women) who signed informed consent. The prevalence of probable sarcopenia was 25.0%. A higher prevalence was observed in women than in men (35.7% vs 20.0%, P=0.22), in patients ≥65 years than <65 years (38.1% vs 13.0%, P=0.06) and in the group of patients more than one year on dialysis compared to the group up to one year (26.7% vs 21.4%, P=0.51). We observed reduced physical performance in 18 subjects (40.9%) and risk of malnutrition according to MNA in 24 subjects (54.5%).

Conclusions: Sarcopenia is a serious and potentially impactful problem. The prevalence of probable sarcopenia in our cohort was 25.0% and tended to be higher, although not statistically significantly, in women and in patients ≥65 years of age.

O4

Urokinase-plasminogen promotes amiloride-sensitive C3a and C5a generation in vitro – a potential therapeutic target in proteinuria

Gustaf L. Isaksson [1], Gitte Rye Hinrichs [2], Henrik Andersen [3], Jan Erik Henriksen [4], Kirsten Madsen [2], Claus Bistrup [2], Boye L. Jensen [3], Yaseelan Palarasah [3]
[1] Odense University Hospital/University of Southern Denmark, Odense C, Denmark, [2] Odense University Hospital, Odense C, Denmark, [3] University of Southern Denmark, Odense C, Denmark, [4] KI, Steno Diabetes Center, Odense, Denmark

Background: Proteinuria leads to progressive kidney injury with only few exceptions, but the mechanism is not well known. Aberrantly filtered plasminogen is activated by urokinase-type plasminogen activator (uPA) in tubular fluid. We hypothesized that that uPA-plasminogen activate co-filtered complement in tubular fluid, and that activation can be inhibited by amiloride, an off-target uPA inhibitor.

Methods: Purified C3 and C5, plasminogen, urokinase, normal human serum (NHS) and urine from healthy humans were used for in vitro/ex vivo reactions. After incubation, in vitro activation was assessed by SDS-PAGE, immunoblotting or ELISA. Urine and plasma samples from patients with type-1 diabetes with or without nephropathy, before and after treatment with high-dose amiloride were analyzed.

Results: uPA-plasminogen activated C3 and C5 and generated C3a and C5a which could be inhibited by amiloride and aprotinine. uPA or plasminogen alone did not activate complement. Urine from healthy controls activated C3 and generated C3a when exogenous plasminogen was added. Urine also activated NHS and generated C3a and C9 neoantigen in a cation dependent manner that was not affected by aprotinine. In patients with diabetic nephropathy, amiloride reduced urinary excretion of C3dg and C9 neoantigen, but also lowered blood pressure, eGFR and albuminuria.

Conclusion: uPA-plasminogen generated C3a and C5a in vitro and healthy urine activated C3 in the presence of plasminogen in an amiloride-sensitive way. These reactions might contribute to kidney injury in patients with proteinuria. In perspective, the mechanism links proteinuria to intratubular proinflammatory signaling and implies that amiloride or direct complement inhibitors might have therapeutic effect.

O5

Using the Borg scale for exercise prescription and for monitoring self-administered aerobic endurance exercise is safe and effective for patients with CKD

Philippa Svensson [1], Matthias Hellberg [1], Yunan Zhou [1], Anita Wisén [2], Naomi Clyne [1]
[1] Clinical Sciences Lund, Lund University and Skåne University Hospital, Lund, Sweden, [2] Division of Physiotherapy, Lund University, Lund, Sweden

Background: The Borg Rating of Perceived Exertion (RPE) scale can be used to prescribe and monitor exercise intensity during unsupervised exercise, but has not been studied in patients with chronic kidney disease (CKD). The aims of this study were to examine adherence, performance, and safety of self-administered aerobic endurance exercise using the Borg RPE scale in patients with CKD, and the relationship between performed exercise and change in walking distance.

Methods: In this sub-study of the RENEXC trial, 147 patients (mean age 66 ±14 years, mean measured GFR 22 ±8 ml/min/1.73m^2) were prescribed 60 minutes aerobic endurance exercise/week at an intensity corresponding to a RPE of 13-15 (somewhat strenuous to strenuous). Exercise was self-monitored and reported in a training diary. The 6-minute walk test was measured at baseline and after 4, 8 and 12 months of exercise.

Results: 100 patients completed the study. Our training program had an excellent level of adherence, at 12 months 80% of the patients reported performed exercise and 74% performed exercise within the prescribed intensity. The mean exercise intensity was 13±1 on the Borg RPE scale and the median duration 56 (33-109) minutes/week. No exercise-related incidents were reported. Walking distance improved significantly by 30± 56meters ($p<0.001$).

Conclusions: The Borg RPE scale is a useful, acceptable, simple and safe method for prescribing and monitoring intensity of self-administered aerobic endurance exercise in patients with CKD. A RPE of 13-15 improved walking capacity in deconditioned patients with CKD, within a wide range of weekly duration of exercise.

O6

Glomerular macrophage index (GMI) in kidney transplant biopsies is associated with graft outcome

Johan Mölne [1], Björn Peters [2], Salmir Nasic [3], Bernd Stegmayr [4]
[1] Institute of Biomedicine, Göteborg, Sweden, [2] Skaraborg Hospital, Skövde, Sweden, [3] Institute of Medicine, Göteborg, Sweden, [4] Public Health and Clinical Medicine, Umeå, Sweden

Macrophages in renal transplants have been shown to mediate antibody-mediated rejection and to be associated with impaired renal function. We calculated the glomerular macrophage index (GMI) in a large transplant biopsy cohort, studied its quantity in different diagnostic groups and its impact on graft survival.

GMI, defined as the mean number of macrophages in ten glomeruli, was prospectively quantified in 1462 renal transplant biopsies over a 10-year period. The main pathology diagnoses were grouped into eight disease entities and GMI was compared to normal transplant biopsies as the reference group. Impact of GMI on graft survival was analyzed.

GMI was highest in chronic (mean 9.4) and active (9.7) ABMR, mixed rejections (7.6) and recurrent or de novo glomerulonephritis (7.5) and differed significantly from normal transplants (1.3) in almost all diagnostic groups. Hazard ratios for graft loss were significantly increased for all biopsies with GMI ≥1.9 compared to GMI <0.5 (reference group) in an adjusted cox regression-model and increased with higher GMI-levels. Biopsies with GMI ≥ 4.6 had <60% 10-year graft-survival, compared to >80% with GMI ≤ 1.8.

In conclusion, increasing GMI levels are predictive for graft loss in a large transplant biopsy cohort.

O7

A comorbidity index and pretransplant physical status predict survival in older kidney transplant recipients

Vasiliki Tsarpali [1], Karsten Midtvedt [2], Kjersti Lønning [2], Tomm Bernklev [3], Anders Åsberg [2], Nanna Von der Lippe [2], Anna Varberg Reisæter [2], Kristian Heldal [2]
[1] Telemark Hospital Trust, Skien, Norway, [2] Oslo University Hospital, Oslo, Norway, [3] Vestfold Hospital Trust, Tønsberg, Norway

Background: Kidney transplantation (KT) is considered the optimal treatment for end-stage kidney disease (ESKD). In the increasing elderly ESKD population, KT should be reserved for carefully selected candidates who are expected to experience favorable outcomes. We aimed to prospectively evaluate pre-transplant recipient factors that may predict post-transplant patient survival.

Methods: KT candidates aged ≥ 65 years, enlisted between January 2013 and November 2016 at the Norwegian national transplant center were included. Pre-transplant comorbidity was assessed at waitlisting, according to the Liu Comorbidity Index (LCI). Health-related quality of life was assessed using the Kidney Disease Quality of Life Short Form version 1.3 (KDQOL-SF). The Cox proportional hazard regression was used to evaluate predictors of patient survival.

Results: Among 289 included candidates, 192 received a deceased brain-dead donor kidney. Mean age at KT was 72 (4.1) years, 133 (69%) were males, and 47 (24%) were transplanted preemptively. During a median observation time of 4.6 (3.2, 6.3) years post-KT, 66 recipients died. Elevated LCI ≥ 4 (N=156) predicted poor patient survival, and was associated with a 2.2-times increase in mortality risk. In recipients with LCI ≥ 4, dialysis ≥ 2 years increased mortality by 2.5-times, compared with recipients on dialysis ≤ 2 years. Pre-transplant physical function significantly predicted survival, with scores ≤ 60 being associated with a 2-fold increase in mortality risk.

Conclusion: The implementation of LCI and a physical function score during the evaluation of older KT candidates may improve the selection and thereby optimize post-transplant outcomes.

O8

Is lithium treatment associated with increased risk of acute kidney injury?

Gisli Gislason [1], Olafur Skuli Indridason [2], Engilbert Sigurdsson [2], Runolfur Palsson [3]
[1] University of Iceland, Reykjavik, Iceland, [2] Landspitali–The National University Hospital of Iceland, Reykjavik, Iceland, [3] University of Iceland, Reykjavík, Iceland

Background: Lithium has been associated with acute kidney injury (AKI) at toxic blood levels, but the risk of AKI has otherwise not been well studied. The aim of the study was to examine the risk of AKI in individuals on lithium treatment.

Methods: This was a retrospective cohort study of all individuals treated with lithium in Iceland in 2003–2018. A control group comprised patients with affective disorders attending the outpatient clinic of the Mental Health Services at the University Hospital in 2014–2016. Clinical and laboratory data were obtained from nationwide electronic medical records. Individuals with <2 serum creatinine (SCr) values were excluded. AKI was defined using the SCr component of the KDIGO criteria. Multivariable logistic regression was used for risk assessment.

Results: The lithium-treated group consisted of 2682 individuals, of whom 2310 (86.1%) were included in the study and 297 (12.9%) developed AKI. Of 1426 individuals in the control group, 1218 (85.5%) were included and 97 (8.0%) developed AKI. Lithium use was not significantly associated with AKI (OR 0.93, 95% CI 0.72–1.20) in multivariable analysis. When lithium users were analyzed separately, lithium intoxication (OR 2.34, 95% CI 1.33–4.09), duration of lithium therapy (OR 1.01, 95% CI 1.00–1.01) and mean lithium concentration (OR 1.22, CI 1.14–1.30) were all significant risk factors for AKI.

Conclusion: While lithium use does not increase the risk of AKI, lithium intoxication, time on lithium therapy and blood lithium concentration may contribute to AKI in lithium users. Lithium levels should be followed carefully in these patients.