ABSTRACTS

תקצירים

הכנס השנתי ה-58 של האיגוד הישראלי לנפרולוגיה ויתר לחץ דם

איגוד ISNH

Impact Of BCM Use On Hydration Status In A Dialysis Network

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Introduction: Body Composition Monitor (BCM) is a whole-body bioimpedance spectroscopy medical device designed for improving the assessment of hydration status (HS) of dialysis patients. It provides objective measurements of HS, normohydration weight, volume of distribution, and anthropometric parameters. In 2023, we implemented the routine usage of BCM in 28 NephroCare clinics (NC) of Fresenius Medical Care Israel (~2400 HD patients). The process included education for use and interpretation of results for nurses and nephrologists (~550 personnel). From January 2024, it has become a mandatory monthly assessment for all patients unless contraindicated. The aim of this study was to assess the impact of implementing BCM in our NC clinics on nephrologists' routine and patient outcomes during the first three months of the program.

Methods: The cohort included all NC prevalent patients (defined as more than 3 months on chronic HD treatments) in Q1/2023 and Q1/2024. A retrospective analysis was performed to compare the nephrologist's attention to changing the prescribed target weight and the outcome of the HS of the patients between Q1/2024 (routine use of BCM) and Q1/2023 (no routine use of BCM). The HS outcome was assessed by measuring the changes in predialysis BP, intradialytic hypotensive episodes, and admissions due to pulmonary edema between the two quarters.

Results: Nephrologist's attention: among 1876 prevalent patients who were treated in both Q1/2023 and Q1/2024, a mean of 2.22 Vs. 2.97 adjustments in the prescription of target weight per patient were made by nephrologists respectively ($P<0.01$). Patient's outcome: Among 1649 patients without missing information of pre-dialysis BP in both Q1/2023 and Q1/2024, there was a mean drop in Sys BP/Dia BP by 1.46/1.36 mmHg ($P< 0.05$) post implementation of BCM. A trend towards a decrease in intradialytic hypotensive episodes was seen (1.13% Vs 0.94% of treatments in Q1/2023 and Q1/2024 respectively, NS). There were no changes in reported admissions for pulmonary edema between Q1/2023 and Q1/2024.
Conclusions: In a very short duration of using BCM in NC dialysis clinics, we could notice a change in the attention of the nephrologists to adjust target weight as well as a trend for improving the hydration status of the prevalent patients.

Acute Asymptomatic C-Reactive Protein Rise Predicts Adverse Events In Peritoneal Dialysis Patients

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Introduction: C-reactive protein (CRP) increases in association with acute and chronic inflammation, including infectious diseases and noninfectious inflammatory disorders and also in metabolic stresses. The purpose of this work was to determine whether acute asymptomatic CRP elevations in peritoneal dialysis (PD) patients predict adverse events.

Methods: Cases of acutely increased serum CRP during regular patient visits without a clinical picture of inflammation or infection were collected. Follow-up analysis of each such elevated serum CRP test was performed.

Results: CRP elevations that were associated with adverse events during the following month reached higher values compared to CRP elevations without adverse events, for any event - 58.97±58.29 mg/l versus 31.67±24.57 mg/l (p=0.004), for severe event - 70.28±62.26 mg/l versus 31.16±24.67 mg/l (p=0.001), for peritonitis - 54.95±28.28 mg/l versus 37.81±39.96 mg/l (p=0.024), and for hospitalization - 81.03±72.27 mg/l versus 35.79±32.91 mg/l (p=0.010). Acute asymptomatic CRP elevations to a value above 50 mg/l were associated with increased risk of adverse events: odd ratio was 3.119 (p=0.004) for any event, 4.727 (p=0.000) for severe event, 3.091 (p= 0.038) for PD-related peritonitis, 5.023 (p=0.017) for hospitalization. Multivariate analysis demonstrated that acutely elevated serum CRP above 50 mg/l was independently associated with any adverse event and severe adverse event during the next month after the elevation. Odd ratio was 2.769 (p=0.016) for any event and 4.065 (p=0.002) for severe adverse event.

Conclusions: Acute asymptomatic increase of serum CRP above 50 mg/l among PD patients could predict future adverse event. Therefore, routine follow-up of CRP may be considered in PD patients

Nutritional and Inflammatory Aspects of Low Parathyroid Hormone in Maintenance Hemodialysis Patients – A Longitudinal Study

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Introduction: Low parathyroid hormone (PTH) is an accepted marker for adynamic bone disease which is characterized by increased morbidity and mortality in maintenance hemodialysis (MHD) patients. In light of the known cross-sectional associations between PTH and malnutrition-inflammation syndrome, we aimed to examine the longitudinal associations between PTH with changes in nutritional and inflammatory parameters and clinical outcomes.

Methods: Historical prospective, longitudinal study analyzed a clinical database at a single hemodialysis center between the years 2007-2020. Bone turnover, nutritional and inflammatory markers levels were recorded at 0, 6, 12, 18, 24, 30, and 36 months followed by a median 24 additional months of clinical observations. According to previous use of vitamin D analogs and/or calcium-sensing receptor agonists, the study participants were divided into treatment-related and disease-related groups.

Results: Of 459 MHD patients, (mean age of 71.4±12.9 years old, 171 women), 81 (17.6%) had PTH lower than 150 pg/ml. Among them, 30 patients had treatment-related and 51 had disease-related low PTH. At baseline, MHD patients with treatment-related low PTH had a higher rate of diabetes. In a linear mixed effects model, increased PTH was associated with decreased alkaline phosphatase (ALP) and C-reactive protein (CRP) and increased hemoglobin and albumin, but not geriatric nutritional risk index at 3-years follow-up. The survival rate did not differ, but the risk of hospitalizations due to fractures was higher (HR 4.04 with 95% CI 1.51-10.8) in the disease-related group. Statistical significance of this association was abolished after adding CRP or ALP to the multivariate models.

Conclusions: Low PTH in MHD patients behaves differently depending on its cause, with a higher risk of fractures in the disease-related group. This association is dependent on inflammation.

Montreal Cognitive Assessment in Candidates and Prevalent Peritoneal Dialysis Patients

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Introduction. Peritoneal Dialysis (PD) is a home dialysis technique, while patient or patient's assistant are responsible for perform the dialysis. A successful treatment requires appropriate physical and cognitive skills. The profile of patients on chronic dialysis has shifted during the last decades: overall dialysis patients became older in terms of population including PD. Patients with Chronic Kidney Disease (CKD) are at higher risk for developing cognitive impairment, before and after onset of dialysis. Early recognition of cognitive impairment is critical because of the autonomous nature of PD technique. Sometimes it is difficult to recognize minor cognitive changes. In our PD unit we started to use Montreal Cognitive Assessment (MOCA) test for all elderly (>65 years old) candidates to PD and in doubtable and inconclusive cases already on PD. Tests were performed by occupational therapy specialists. Normal range is 26 and more out of 30. **Methods**. Retrospective analysis of clinical data and results of MOCA test performed during study period (1.06.2023-31.03.2024) in our service. **Results**. MOCA test was performed on 21 patients, 13 were predialysis, and 8 were already treated by PD. Mean age of all patients was 78.3 years. Mean age of predialysis patients was 77 years (71-88) whereas average age of dialysis patients was 80.4 (73-86). Dialysis mean vintage was 2.1 years (0.01-6.2). Mean MOCA result was 20 (15-26). In predialysis group mean MOCA was 21.5 (16-25) vs 20 (13-26) in dialysis group. In 2 cases results of cognitive assessment by MOCA helped to make the decision of exclusion of patients from PD. In 5 cases it helped to adjust PD training and treatment program. **Conclusions**. Some grade of impaired cognitive function seems to be common among old and very old CKD patients and patients treated by PD. Baseline MOCA was already below the normal values in predialysis elderly candidates to PD. Cognitive assessment by MOCA is a simple, effective and important tool useful for planning and adjustment of peritoneal dialysis treatment.

Depression and Anxiety Symptoms Among Chronic Hemodialysis Patients During "Sword of Iron" War

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INTRODUCTION. On October 7 Israel plunged into the "Swords of Iron" war**.** As the war continues, numerous difficulties and challenges arise, with potential impact on depression and anxiety symptoms development among chronic hemodialysis patients. These symptoms can negatively impact their mental health, potentially affecting the effectiveness of dialysis treatments, decreasing adherence and persistence with treatments, and shortening the duration of dialysis. The aim of this study was to assess the development and impact of depression and anxiety symptoms among chronic hemodialysis patients at Barzilai University Medical Center in Ashkelon.

METHODS. After obtaining consent, we collected PHQ9 and GAD7 questionnaires to evaluate the presence of depression and anxiety symptoms upon entry to study and after 4 months. In addition, demographic, socioeconomic, educational, family status, dialysis data and routine laboratory tests were collected.

RESULTS. Thirty chronic hemodialysis patients were included in the study. 41.3% and 24.1% of patients had depression and anxiety symptoms, respectively. Symptoms were significantly more frequent in women (57.1% vs 42.9% in men), in non-married (60% vs. 35.3% in married), in non-religious (53.9% vs. 38.5% in religious) and in patients with academic education (57.2% vs. 36.4% in non-academic education). Depression symptoms were related with more temporal transfes to other dialysis units (33.3% vs. 11.7%), higher percentage of patients with Kt/v<1.2 (50% vs. 37.5%) and shortening dialysis sessions. We did not find correlation with driving time to dialysis or existence of a protected area at home.

CONCLUSIONS. We found that depression and anxiety symptoms were common among chronic hemodialysis patients during "Sward of iron" war and had impact on delivered dialysis sessions.

Patient Participation In Hemodialysis Treatments In Community And Hospital-Based Units

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Introduction Patient self-management improves both subjective and objective outcomes in chronic diseases. Yet, patients in hospital and other ambulatory settings tend to be passive recipients of treatments. Hemodialysis units in particular tend to have an atmosphere of dependency and passivity. The aims of this study were **t**o gain insights into patient participation in treatment-related tasks within hospital- and community-based hemodialysis units and to assess what patient and unit related factors are associated with expression of interest and/or actual participation in treatment care tasks.

Methods A multi-centered, cross-sectional, questionnaire-based study. Patient interest and actual participation were assessed by a Likert-type, 1-4 scale with responses ranging from never to always. The association between patient characteristics and interest and actual participation was tested using logistic regression and accounting for the type of hemodialysis unit (community or hospital based).

Results Questionnaires were collected from 339 patients in four hemodialysis units. Most patients expressed interest in participating in care tasks, this was linked to education and marital status. About 40% of patients participated in at least two treatment tasks. Factors influencing actual participation included religion, economic status, venous access, years on dialysis, unit location, and interest in participation. No significant differences were found between community- and hospital-based units in interest, yet actual participation was greater in hospital versus community units.

Conclusion While the majority of patients expressed interest in participating, only a minority actually participated. There is need for greater engagement of interested patients. Organizational factors play an important role in determining actual

participation, above and beyond personal patient factors. Patients should be presented with the opportunity to participate according to their interest and capabilities.

Risk of Long-Term Chronic Kidney Disease and Hypertension in Childhood Cancer Survivors: A Matched Cohort Study

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Introduction: The improvement in childhood cancer survival over the last decades has resulted in adverse effects, including chronic kidney disease (CKD) and hypertension. However, the extent, timing and risk factors of CKD and hypertension in childhood cancer survivors (CCS) are unclear. We used administrative data from Ontario to study our hypothesis that CCS are at increased risk for long-term CKD and hypertension.

Methods: Design: population-based retrospective matched-cohort study of all CCS in 1993-2020 in Ontario, Canada. Cohorts: CCS (exposed)- children registered in Ontario's childhood cancer database; Two matched comparator cohorts: at-risk- children who were hospitalized; general pediatric population (GP)- healthy children. Follow-up started at cancer-treatment end and terminated in 2021, outcome acquisition, death, or new/ relapsed cancer. Exclusions: previous cancer, transplant, CKD, hypertension. Outcomes were defined using administrative healthcare codes. Primary outcome: a composite of CKD or hypertension; Secondary outcomes: CKD, hypertension (separately). We calculated cumulative incidences of the outcomes, and performed Cox proportional hazard modeling to determine the association between cancer treatment and outcomes.

Results: The CCS, at-risk, and GP cohorts (median[IQR] age 7[4-13] years, 54.5% males) included 10,182, 831,214, and 2,145,854 participants, respectively, and median(IQR) follow-up time was 7.8(2.4-14.8), 14.9(7.8-21.5), and 8.6(4.6-13.6) years, respectively. Overall, during observation of up to 27 years, 20.85% of the CCS

cohort acquired CKD or hypertension. The CCS cohort had an increased risk of CKD or hypertension compared the at-risk cohort (HR 2.0[CI 1.86-2.14], p<0.0001), and the GP cohort (HR 4.71[CI 4.27-5.19], p<0.0001).

Conclusion: CCS are at an increased risk of CKD and hypertension compared to children who were hospitalized and the GP. As CKD and hypertension are strongly associated with mortality and are treatable, early detection and treatment of these outcomes in CCS may decrease late mortality.

Mild to Moderate Kidney Injury in Adolescence and Advanced Kidney Disease in Early Adulthood – Historical Cohort Study

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Introduction: Renal injury in adolescence is associated with end stage renal disease in later life, but data regarding the association between mild kidney injury at this age and renal morbidity in early adulthood is scarce. We aimed to evaluate this association.

Methods: This is a longitudinal historical cohort utilizing Clalit Health Services' (CHS) database, the largest of four integrated health care organizations in Israel, which insures 4.7 million patients. The cohort included all patients born between 1986 and 1995 who were followed at CHS from childhood and had at least one recorded serum creatinine result at age 14-18 years, or a recoded diagnosis of a congenital anomaly of the kidney or urinary tract (CAKUT). They were followed since the establishment of CHS' database (2000) until 2022, move to another health network, or death. The cohort was divided into a study group - including adolescents with CAKUT and/or mild-moderately increased serum creatinine (1.2-1.7 mg/dl in males, 0.95-1.35 in females) and controls. Our outcomes were defined as CKD3, CKD 4-5 (based on serum creatinine level at last follow up) or ESRD (based on EMR diagnoses) at last follow up.

Results: The cohort included 304,574 patients, 299,752 (98.5%) in the control group, and 4,603 (1.5%) in the study group. At baseline, study group patients were more likely to be diagnosed with CKD (2% vs 0.1%, $p<0.01$), proteinuria (2.1% vs. 0.1% $p<0.01$), and hypertension (1.1% vs. 0.8%, $p=0.02$). At last follow up, 244 patients (0.08%) had CKD3, 115 (0.04%) had CKD4-5, and 240 (0.08%) had ESRD. On a multivariate analysis, study group patients were more likely to have CKD3 (OR 10.9, 95% CI 7.4-15.9), CKD3-5 (OR 7.7, 95% CI 4.2-14.1), and ESRD (OR 5.7, 95% CI 3.2-10.0) at last follow up, independent of diagnoses commonly associated with CKD (hypertension, proteinuria, acute kidney injury, glomerular disease, cystic kidney disease, etc.)

Conclusion: Mild to moderate kidney injury in adolescence is associated with more severe kidney disease, including ESRD, in early adulthood, and requires close monitoring and steps to prevent such progression.

Can We Predict Which Children with Idiopathic Nephrotic Syndrome will be Steroid Dependent?

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Introduction: Around half of children with idiopathic nephrotic syndrome will develop steroid dependent or frequent relapsing disease. Clinicians often wait to diagnose steroid dependence until the patient relapses more than once while on steroids. Finding an early, reliable predictor of steroid dependent nephrotic syndrome can help clinicians to confidently initiate immunosuppressive therapy earlier in these patients, thus avoiding additional steroid courses.

Methods: Children diagnosed with nephrotic syndrome in a single center were enrolled prospectively. We performed a post hoc analysis comparing the outcomes of patients with relapses on prednisone doses of 0.5 mg/kg/every other day or higher to those that relapsed while on lower doses or no steroids.

Results: Of the 122 enrolled patients with nephrotic syndrome, 51/122 (42%) relapsed on doses of at least 0.5 mg/kg/every other day with 29/51 (57%) of these patients relapsing for the first time during induction. Fourteen of these patients were switched to alternative therapy before they experienced another relapse. The other 36 patients that relapsed on doses beyond this threshold were not switched immediately to steroid alternatives. The vast majority, 33/36 (92%) went on to have at least one more relapse above this threshold and were then switched to alternate therapy.

Conclusions: Patients that relapsed once on steroid doses equal to or higher than 0.5 mg/kg/alternate days are very likely to continue to relapse on similar or higher doses of steroids. It might thus be reasonable to consider initiation of immunosuppression following the first relapse on steroid doses beyond this cut-off.

Chronic kidney disease following treatment with Extracorporeal membrane oxygenation (ECMO) in children- an underestimated complication

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Introduction:

Extracorporeal membrane oxygenation (ECMO) is a medical technology of in vitro oxygenation using artificial equipment, which has been operating for approximately 30 years. High rates of mortality have been seen in children receiving ECMO and among those who survive there have been reports of multiorgan complications. Acute kidney injury has been reported at high rates among these children but the rate of long-term chronic kidney disease (CKD) among the surviving children is less known specifically in the pediatric population.

Objectives of the research:

This study aimed to assess the rate of CKD following ECMO therapy at Schneider Children's Medical Center and identify the associated risk factors.

Research methods:

The study is a retrospective cohort study that included patients treated with ECMO at Schneider Children's Medical Center between 2010 and 2020. Demographic data, ECMO duration, need for dialysis, type and dosage of medications, and laboratory test results were collected from patients' electronic medical records. CKD was defined as a GFR (glomerular filtration rate) below 90 ml/min/1.73m2.(CKID formula).

Research Results:

The study population included 229 patients, 95 (41.5%) of whom constituted the study's base group. Twenty-five (26.3%) of surviving patients developed CKD. GFR at hospital discharge was found as a strong predictor for the development of CKD. ($P<0.01$)

Research Conclusions:

This study found that estimated GFR at hospital discharge is an important predictive factor for CKD. It is important to establish long-term nephrology follow-up for children following ECMO therapy who have abnormal estimated GFR at hospital discharge for appropriate monitoring of renal function proteinuria and hypertension.

Case Series: Overcoming Steroid and Tacrolimus Resistance in Pediatric Nephrotic Syndrome with Combination Therapy

Meidad Greenberg, Keren Cohen – Hagai

Background: Pediatric Nephrotic Syndrome (NS) is clinically categorized based on the patient's response to steroids. Approximately 15% of NS patients are classified as having Steroid Resistant Nephrotic Syndrome (SRNS). In the past, SRNS had a poor prognosis, with 50% of patients progressing to end-stage renal disease (ESRD) within five years. However, currently, up to 90% of SRNS patients may respond to treatment with calcineurin inhibitors (CNIs). For the small percentage of SRNS patients who do not respond to CNIs, treatment options include Rituximab (an anti-CD20 antibody) or participation in clinical trials. Patients who do not respond to Rituximab are categorized as having multidrug-resistant nephrotic syndrome, which is associated with a worse prognosis.

Methods and results: We report two cases of SRNS that did not respond to calcineurin inhibitors (CNI). One patient had congenital nephrotic syndrome, and the other had idiopathic nephrotic syndrome, with both displaying non-minimal change disease on kidney biopsy. Both patients achieved complete remission using a combination of CNI and additional immunosuppressive therapy, either high-dose steroids or Rituximab. During a 12-month follow-up, both patients maintained normal serum creatinine levels and blood pressure.

Conclusion: Pediatric patients with multidrug resistant nephrotic syndrome, may benefit from combination of CNI with a second immunosuppression medication.

Childhood CKD Epidemiology and Trajectories in Israel: A Population-Based Study

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Introduction: Epidemiological data regarding chronic kidney disease (CKD) in children is scarce, including its trajectories, during and beyond childhood. We performed a population-based assessment of chronic kidney disease (CKD) rates, characteristics and outcomes in Israeli children.

Methods: Based on Israel's largest health care maintenance organization electronic database for the years 2008-2020, we included all children aged 2-18 years with at least two serum creatinine levels taken 3-12 months apart. "Ever CKD" (e-CKD) was defined as two subsequent eGFR measurements <75 ml/min/1.7m^2. Long term outcomes including incident or reversal of ("aborted") CKD, need of kidney replacement therapy, and death were investigated.

Results: Out of 324,093 eligible children, 3,729 (1.1%) had e-CKD along the study period, 33.2% of them with stage 3 or higher, diagnosed at a mean age of 10.2 ± 5.5 years, 53.9% of them were male. More e-CKD children belonged to the higher socioeconomic status groups in comparison to non-CKD ($p<0.001$). Incident CKD was found in 1,282 children (34.4%) who had an originally normal eGFR. Contrary to that, 2,176 eCKD children (58.4%) improved their eGFR to >75 ml/min/1.73m^2, thus considered as aborted CKD. After a mean follow-up of 6±3.7 years, 0.38% of the e-CKD group died (Vs. 0.14% of the non-CKD, $p<0.001$), and 4.4% needed kidney replacement therapy. Median (IQR) annual incidence was 257 (204-269) new cases/million/year. Point prevalence (with 95% CI) of pediatric CKD in Israel on December 31, 2020 was 692 (647, 739) per million.

Conclusions: In this population-based study, CKD incidence and prevalence rates are much higher than previous reports of hospital based, overt CKD. The over-representation of children of higher socioeconomic status in the CKD group, and the absence of albuminuria-based CKD diagnosis in this study hint for much higher actual CKD rates. A significant proportion of children defined as CKD by eGFR measurements (most of them at stage 2) normalized their eGFR. Still, being defined as e-CKD is associated with increased morbidity and mortality.

Metformin Treatment and Chronic Kidney Disease Progression in Diabetic Patients Receiving SGLT2 Inhibitors

Tali Steinmetz, Eshcar Miesel, Avigail Shabtai, Benaya Rozen-Zvi and Dana Bielopolsky

Background: Metformin, widely prescribed for type 2 diabetes, has shown promise in attenuating kidney disease progression. However, its impact remains unassessed in patients treated with SGLT2 inhibitors. This study aims to evaluate whether metformin retains its renoprotective effects in conjunction with SGLT2 inhibitor treatment.

Methods: In this retrospective study, we employed propensity scores to match metformin users and nonusers within a cohort of diabetic patients undergoing SGLT2 inhibitor treatment. We conducted both univariate and multivariate Cox analyses stratified for albuminuria and CKD stage, as well as competing risk analyses to assess the risk of kidney disease progression. Progression was defined as a composite outcome, including a 40% reduction in eGFR, eGFR dropping below 15 ml/min/1.73m², or the need for renal replacement therapy.

Results: There were 13,548 patients in the cohort, with 192 experiencing the outcome event; 80 were in the metformin-treated group, and 112 were in the control group. In CKD stage and albuminuria stratified Cox analysis, metformin treatment was associated with a reduced rate of kidney disease progression (Hazard ratio (HR) 0.67, 95% Confidence Interval (CI) 0.51-0.90, p=0.007). Similarly, multivariate Cox analysis yielded consistent results (HR 0.65, 95% CI 0.48-0.87, p=0.004), as did competing risk analysis with mortality as the competing event (HR 0.70, 95% CI 0.52-0.93, p=0.014).

Conclusion: Our findings suggest that metformin treatment exhibits renal protective effects in the context of SGLT2 inhibition.

Rituximab for Treatment of Steroids Dependant or Frequent Relapsing Nephrotic Syndrome – A Single Center Experience

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Introduction: While Minimal Change Disease (MCD) is characterized by high response rate to steroid treatment, up to one-third of patients become steroid dependant (SD) or frequent relapsers (FR). The response rate is much lower in primary Focal Segmental Glomerulosclerosis (FSGS), estimated as 47-66%, with a relapse rate of up to 36%, resulting in prolonged steroid exposure. Due to the significant toxicity associated with steroid therapy, a safe and effective steroid sparing treatment is required, with Rituximab emerging as a promising agent. We aimed to evaluate the efficacy of Rituximab in adults with SD/FR nephrotic syndrome (NS).

Methods: A retrospective single center cohort study, evaluating patients with SD/FR NS treated with Rituximab between January 2014 – December 2023. Rituximab was given as induction, most commonly in 2 doses of 1,000mg each. Additional doses were subjected to the treating nephrologist decision, according to disease severity. Primary outcome was number of relapses.

Results: Twenty one adult patients were included in the cohort, 10 (47.6%) were males, median age was 54 years. MCD was diagnosed in 16, and FSGS in 5 cases. Median follow-up time was 1198 days after first Rituximab dose. Number of relapse before Rituximab was 1-3 in 60% and more than 4 in 40%. After the first Rituximab course, 19 patients (90.5%) achieved remission and 14 (66.7%) maintained prolonged remission and did not receive additional steroid treatment. Median Rituximab cumulative dose was 3,000mg (IQR 2,000-4,750). Treatment was well-tolerated. The only serious adverse event was hospitalization due to cholecystitis one week after treatment.

Discussion: Rituximab appears to offer an efficient safe alternative to steroids in patients with SD/FR NS.

Long Term Follow Up of Israeli SLE Patients with Lupus Nephritis

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Introduction: Kidney involvement is common among patients with Systemic lupus erythematosus (SLE) and its presence is associated with morbidity and mortality. Ethnic variations in clinical response to treatment and outcomes have been described, and data from real-life, long term cohorts of Middle East white population are needed.

Methods: This retrospective study, conducted at 2014–2023, included adult patients with SLE of at least 12 months since diagnosis. Kidney involvement was defined based on a diagnosis of lupus nephritis (LN) on kidney biopsy. Disease-related characteristics, kidney-related factors, comorbidities and all-cause mortality were assessed.

Results: A total of 182 adult patients with SLE were included: 54 had LN (29.6%) and 9 reached ESKD during the study (14.8% of patients with LN). Mean follow up since diagnosis was 16.2±13.8 year. Patients with LN were diagnosed in younger age and had comparable baseline eGFR before LN diagnosis (26.8±12.9 vs. 35.5±15.4, $p<0.01$ and 110±48 vs. 107±39 ml/min/m^2 , $p=0.66$, respectively). Patients with LN had higher prevalence of SLE exacerbations, (38.4% vs 24.5%, OR for SLE exacerbations in LN group 1.9, 95%CI 1-3.9, $p=0.06$). 14.8% of LN patients (8/54) developed ESKD in LN group as compared with 1/128, $p<0.001$. On univariate analysis, the development of ESKD was significantly associated with LN, hypertension heart failure and employee state of the patient; it was not significantly associated with gender, APLA, ethnicity, fibromyalgia. On multivariate regression analysis, LN and the existence of hypertension were the most important predictors for developing ESKD. Mortality was high among patients with ESKD (22%) vs. non-ESKD SLE patients (4.6%, $p=0.02$).

Conclusion: Despite advances in SLE treatments in the last decades, kidney involvement in SLE is associated with significant morbidity and mortality burden.

ESKD is not uncommon and associated with mortality. Different ethnic Israeli group had comparable rates of ESKD.

Non-Paraprotein Mediated Amyloidosis

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Amyloidosis is a complex group of disorders characterized by the deposition of misfolded proteins in the extracellular space of various tissues and organs, leading to progressive organ dysfunction. Amyloid deposits are identified on the basis of their apple green-orange birefringence under a polarized light microscope on Congo red stain and the presence of rigid, non-branching fibrils 7.5 to 10 nm in diameter on electron microscopy. Based on the amyloid precursor protein, various types of amyloidosis are recognized. To date, 36 protein types, and many more variants, have been officially recognized as associated with amyloid formation. The kidneys constitute a very common site affected, most notably by the two most common types of amyloidosis: paraprotein-mediated (AL , AH and AHL amyloidosis) and serum amyloid (AA) amyloidosis but other types have been incriminated as well, causing significant morbidity and mortality. They include leukocyte chemotactic factor 2 (ALECT2), apolipoprotein (AApo), Fibrinogen α-chain amyloidosis () along with mutant proteins in several hereditary forms of amyloidosis (transthyretin [ATTR], gelsolin [AGel] and lysozyme [ALys]).
The clinical features of renal amyloidosis, laboratory and renal pathology findings are helpful in the diagnosis and typing of non-AL amyloidosis.

This review aims to provide an overview of the current knowledge on non-paraprotein mediated amyloidosis with renal involvement, including its epidemiology, pathophysiology, clinical presentation, diagnosis, and management. The review will

also discuss the challenges in diagnosing and treating this rare group of diseases and highlight the importance of a multidisciplinary approach to patient care.

A Novel Risk Score for Predicting Acute Mortality in Patients with Acute Kidney Injury Based on Clinical Complications

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Background: Acute kidney injury (AKI) is associated with high morbidity and mortality. Traditional AKI severity scores like RIFLE and AKIN have limitations in predicting acute mortality. This study introduces the Complications Score (COSCO), a novel risk score based on clinical complications during AKI, to predict all-cause mortality within 3 months post-diagnosis.

Methods: This retrospective observational study analyzed 382 adult AKI patients from Soroka Medical Center admitted between 2016-2018. COSCO was developed based on complications like sepsis, pulmonary edema, resistant hyperkalemia and need for dialysis. Multivariable logistic regression and ROC analysis evaluated COSCO's predictive accuracy compared to RIFLE, AKIN, and CREDENCE scores.

Results: COSCO scores showed strong predictive value for mortality, with 0.5% mortality for COSCO-0, 47% for COSCO-1, and 80% for COSCO 2-4 ($p<0.001$). COSCO High (2-4) had superior predictive metrics vs AKIN and CREDENCE: AUC 0.80, sensitivity 85%, specificity 72%, PPV 80%, NPV 78%. Stratification by gender and age showed consistent patterns.

Conclusion: The COSCO score is a robust predictor of acute mortality in AKI patients, outperforming traditional severity scores. It can guide risk stratification and targeted interventions to improve AKI outcomes. Further validation in another patient cohort is underway.

Hyponatremia and Urinary Retention

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Introduction. Hyponatremia is the most common electrolyte disorder, with an incidence up to 10% of patients admitted to the emergency room (ER). Among elderly patients, it may be observed in up to 17%. There are few reports about urinary retention in context of hyponatremia. In our hospital the protocol of hyponatremia evaluation and treatment includes an urinary catheter insertion for follow up of urinary output. The working hypothesis of this study was that patients with hyponatremia and urinary retention reach sodium correction more rapidly than other patients. **Methods**. We performed a retrospective analysis of clinical and laboratory data of all adult patients with moderate to severe hyponatremia (<130 meql/L) admitted to our hospital ER during 2021. **Results**. A total of 190 cases were included into the final analysis. Average age was 83.8 years (24-99), most of them were females (72.6%), 30% with diabetes mellitus. Forty two percent of patients received chronic diuretic therapy, while 22% of them received more than one type of diuretic. Almost 56% of patients received different benzodiazepines, or antidepressants, anticonvulsants, anti-psychotics like haloperidol, as well as risperidone. In 37.4% of cases severe hyponatremia (<120 meq/L) was observed. An urinary catheter was inserted in 104 cases; in 54 of them urinary retention of more than 300 ml was recorded. Patients in the catheter group had a tendency to more severe hyponatremia (57% of them were with sodium <120 meq/L vs 9% in patients without urinary catheter insertion), and there was a trend to more prolonged hospital stay (median 5 days vs 2). In the urinary retention group there was a trend to shorter hospitalization (median 5 days vs 5.5 in non-retention group). Three months all-cause mortality was observed in almost 19%, while mortality was higher in patients without urinary retention (42% vs 17%, p<0.0001). **Conclusions**. Elderly women have higher incidence of moderate to severe hyponatremia than men. Since 3 months all-cause mortality is high in these patients, probably hyponatremia is a sign of more serious prognosis, especially in absence of urinary retention. More data are needed for better understanding of pathogenesis and implications of hyponatremia and urinary retention.

Urinary NGAL as a Marker of Disease Activity and Pregnancy-Related Adverse Outcomes in Pregnant Women with Inflammatory Bowel Disease

Elayan Nour, Shavit Linda, Shitrit Ariella

INTRODUCTION: Control of disease activity in pregnant women with inflammatory bowel disease (IBD) is crucial as an uncontrolled disease is associated with higher risks of adverse pregnancy outcomes for both the mother and newborn. Human neutrophil gelatinase-associated lipocalin (NGAL) is an acceptable biomarker in some pathological conditions such as acute and chronic kidney injuries and high levels of NGAL were observed in the colon, serum, and stool of patients with IBD. In pregnancy, first-trimester NGAL was found to be an early marker of late-onset preeclampsia. However, no data exists on urinary NGAL in pregnant women with IBD. This study aimed to compare the levels of urinary NGAL in pregnant IBD patients with active disease versus quiescent disease and to explore whether urinary NGAL levels may predict pregnancy-related adverse outcomes and IBD flares in these patients.

METHODS: The study recruited women with (IBD) who attended the IBDMOM clinic for antenatal and postnatal follow-up. The correlation of urinary NGAL levels with baseline clinical characteristics and its predictive capacity for pregnancy-related adverse outcomes such as preterm birth, preeclampsia, stillbirth, low birth weight, and IBD flares were assessed by univariate and multivariate stepwise regression analyses. The sensitivity and specificity of urine NGAL at different cutoff values were assessed using a conventional receiver operating characteristic curve.

RESULTS: The median age of patients was 28 years and the median duration of IBD at the time of conception was 6 years. A total of 252 urine samples (172 samples from patients with Crohn's disease, 77 with ulcerative colitis, and 3 with unclassified IBD) were examined. Urinary NGAL measurements were obtained from 192 pregnancies, throughout the different gestational periods (1st trimester n = 90; 2nd trimester n = 111; 3rd trimester n = 92). Urinary NGAL levels were not significantly higher in patients with active disease compared with inactive (median 47.714 ± 4.7, ng/mL vs. 52.827 ± 3.98 ng/mL, p = 0.242). Out of the participants, 27 patients had preterm deliveries, 8 had abortions, and 14 had adverse pregnancy outcomes including preeclampsia, IUGR, and stillbirth), there was no statistically significant

correlation between urinary NGAL levels and obstetric adverse outcomes. However, a strong correlation was found between disease activity and delivery type ($p = 0.011$), patients with active disease had a higher incidence of cesarean sections compared to patients with inactive disease. Treatment regimen changes and hospital admissions during pregnancy were found to be higher in patients with active disease ($p = 0.001$). The study's findings do not provide a sufficient correlation between disease activity and other adverse pregnancy outcomes. This is due to the small number of patients who experienced adverse outcomes, combined with the study's limited sample size.

CONCLUSIONS: our data suggest a limited predictive capacity of urinary NGAL levels for predicting disease flares or obstetric adverse outcomes in pregnant patients with IBD.

Real-World Effectiveness of SGLT2 Inhibitors on the Progression of Kidney Disease in CKD Subjects without Diabetes, with and without Albuminuria

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Background: Renal outcome trials show that sodium-glucose cotransporter 2 (SGLT2) inhibition slows progression of kidney injury in subjects with and without diabetes. It is important to examine the renal effects of SGLT2 inhibition amongst subjects without diabetes and with chronic kidney disease (CKD) in a real-world setting.

Methods: We collected de-identified data on adult subjects without diabetes and an estimated glomerular filtration rate (eGFR) of 25-60 ml/min/1.73 m^2, and initiated SGLT2 inhibitor dapagliflozin or empagliflozin between 9/2020 and 11/2022 at Maccabi Healthcare Services, an Israeli health maintenance organization. We assessed the effects of SGLT2 inhibitors on renal function (changes in eGFR slope/time). Index date was defined as date of first dispensing SGLT2 inhibitors. Annual baseline slope was calculated using all eGFR measurements during the 2 years prior to index date (median=7 measurements), while annual follow-up slope was calculated from all evaluations during 90-900 days post index date, along with baseline measurement on index date (median=6 measurements). Paired t-test compared differences between baseline and follow-up annual slopes.

Results: Of 354 subjects with CKD, without diabetes, who received SGLT2 inhibitor and were followed for a median of 527 days: mean age was 72.8±11.8 years, 26%

were female, and 91% used renin-angiotensin system blockade. Mean eGFR was 45.4±9.5 ml/min/1.73 m^2. Mean BMI was 29.1±5.4 kg/m^2.

During the year before the index date, 146 (41%) of participants had a urinary albumin-to-creatinine ratio (UACR) <30 mg/g, 81 (23%) a UACR of 30-300 mg/g, 74 (21%) a UACR >300 mg/g, and 53 (15%) no UACR evaluation. The mean slope of eGFR over time was -5.6±7.7 ml/min/1.73 m^2 per year at baseline, which improved to -1.7±6.8 ml/min/1.73 m^2 per year after SGLT2 inhibitor administration (p-value <0.001). This effect was independent of UACR.

Conclusion: In a real-world study of primarily older adults without diabetes, with CKD, SGLT2 inhibition was associated with a slower rate of kidney function decline, regardless of baseline UACR levels.

Incidence and Risk Factors for Gout in Non-Dialysis Chronic Kidney Disease Patients with Asymptomatic Hyperuricemia

Ilia Beberashvili, Abu Marsa Hamza, Elad Nizri, Shai Efrati

Introduction: The relationship between asymptomatic hyperuricemia and gout onset in non-dialysis CKD stage 3-5 patients remains unexplored. This study aims to assess the incidence of gout and identify its risk factors in this population. Identifying high-risk patients could justify early intervention with antihyperuricemic therapy.

Methods: We carried out a retrospective analysis using a clinical database of non-dialysis dependent CKD outpatients with asymptomatic hyperuricemia and no prior history of gout, from 2010 to present. Gout diagnoses during the follow-up were confirmed in our institution's rheumatology clinic based on the Rome criteria.

Results: We analyzed data from 771 non-dialysis CKD stage 3-5 patients, with an average age of 72 years, approximately 44% of whom were women. During a median follow-up of 47 months, 18% developed gout. Using the Cox proportional hazards model with backward conditional elimination, we identified four independent predictors of gout: age, diuretic use, and levels of uric acid and creatinine. We set cut-off points for continuous variables using ROC curve analysis, then combined these predictors into a scoring system based on coefficients from a multivariate logistic regression. This scoring system helped assess gout risk, yielding a hazard ratio (HR) of 2.25 (95% CI: 1.60-3.16) for CKD patients under 71 years old, using diuretics regularly, with uric acid levels above 8.3 mg/dl and creatinine levels below 1.5 mg/dl. The association persisted even after adjusting for multiple variables, including the Charlson comorbidity index and BMI.

Conclusions: Gout incidence is high in CKD patients with asymptomatic hyperuricemia. Early antihyperuricemic treatment could benefit high-risk groups. These findings require validation by intervention studies.

Early Detection of Chronic Kidney Disease in Patients with Dyslipidemia and Risk Factors for Chronic Kidney Disease

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Introduction

Patients with dyslipidemia have comorbidities known as risk factors for chronic kidney disease (CKD). CKD is a common disease that is underdiagnosed and undertreated. In 2023, the CKD One Pager ISN toolkit (CKDOPIT) was published to promote CKD early identification and intervention in primary care settings. This work focused on implementing the use of CKDOPIT by clinical pharmacists (CPs) for patients with dyslipidemia who have risk factors for CKD and providing recommendations for follow-up and treatment.

Methods

Patients included in dyslipidemia quality indicators were selected as part of this work. CPs reviewed patients' files, identified risk factors for CKD (hypertension, diabetes, cardiovascular disease, etc.), reviewed their medications and laboratory tests. CPs then wrote recommendations to primary care physicians for improving the treatment of dyslipidemia and for the diagnosis, identification or treatment of CKD according to CKDOPIT.

Results

During the time from August to December 2023, CP interventions were given for 96 patients. Most of them (65%) were non-diabetic. 30 patients (63%) out of 47 for whom the addition of statins was recommended started treatment. 22 patients (34%) among 64 performed a urine test for albuminuria. In 5 of them, albuminuria was identified. 6 patients out of 19 (32%) for whom an ACEI/ARB and/or SGLT2i was recommended started treatment. 6 patients (19%) out of 32 patients were given a diagnosis of CKD.

Conclusions

There is underdiagnoses and undertreatment of CKD in primary care. Integrating CPs into quality processes may aid in the treatment of dyslipidemia and in identifying risk factors and providing recommendations for diagnosis and treatment of CKD.

Patients with CKD Secondary to Glomerular Disorders have Lower Arterial Stiffness, as Compared to Hypertensive and Diabetic CKD.

Ori Lencovsky, Avital Angel-Korman, Erick Glasswine, Rotem Tal-Ben Ishay, Mor Amital, Olga Kukuy & Adi Leiba

Introduction

Chronic kidney disease (CKD) manifested as reduced GFR and/or albuminuria, has been known to accelerate arterial stiffness and early vascular aging (EVA) manifested as higher pulse wave velocity (PWV). No previous comparisons of PWV according to CKD etiology (hypertension, diabetes, glomerulonephritis) were done.

Methods

We set out to compare the difference in PWV between inflammatory and non-inflammatory-related CKD.

Clinical data and pulse wave velocity were collected on 56 patients followed at the Nephrology and Hypertension Institute in Samson Assuta Ashdod University Hospital. All patients had at least one visit at our Nephrology clinics before recruitment. All patients with a glomerular disorder had a clinical-pathological diagnosis based on a recent kidney biopsy.

Results

PWV was significantly higher in the hypertensive/diabetic CKD group, compared to the CKD-GN (CKD-glomerulonephritis) group, with an average of. 12.2 m/s vs 8.3 m/s, respectively ($p < 0.001$).

In a multivariate linear regression model, having CKD secondary to glomerulonephritis was associated with a significantly lower PWV ($B = -3.262$, $p < 0.001$)

Conclusion

CKD Patients secondary to glomerulonephritis, have lower PWV when compared to CKD patients with diabetes and/or hypertension, even after adjusting for age, renal function, and the presence of comorbidities.

Mild COVID-19 Infection has no Influence on Chronic Kidney Disease Indices- Lessons Learned from a Community Based Cohort

Avital Angel-Korman, Tal Brosh-Nissimov, Ori Meyer, Adi Leiba

Introduction: COVID-19 infection in hospitalized patients has been implicated in the deterioration of several indices associated with chronic kidney disease (CKD), including new onset hypertension and worsening of proteinuria and kidney function. Nevertheless, the influence of COVID-19 on these parameters in patients with CKD in a community setting has not been fully elucidated.

Aims: we aimed to study the effect of COVID-19 infection on blood pressure (BP), proteinuria, and eGFR in a community-based cohort of patients with CKD.

Methods: A cohort study including all adults with CKD stages I-V from the Maccabi Healthcare Services database who had a first documented mild-moderate laboratory-confirmed COVID-19, not requiring hospitalization. All reported BP clinic measurements within one year prior to and following COVID-19 infection, were averaged, and so were urine albumin and serum creatinine (sCr) measurements.

Results: 213,604 patients were registered at Maccabi HMS during 2023 in the CKD registry and 43,875 of them had a documented 1st COVID-19 infection between the years 2020-2022. Mean age was 69.3 (±12.9) years and 21,775 (49.6%) were males. Following COVID-19, systolic BP was 1 mmHg lower and diastolic BP was 0.6 lower compared with pre-COVID-19 infection (P-value 0.03 and 0.004, respectively). 8919 patients had at least two documented urine albumin to creatinine ratio (UACR) measurements. The mean UACR was 65mg (±251) before COVID-19 and 93mg (±326) following COVID-19 infection, accounting for an absolute difference of 28mg (±298), p<0.001. eGFR in 37,923 patients who were tested for sCr was 73.2ml/min (±19.8) and 72.2ml/min (±20) before and after COVID-19, respectively, with an absolute difference of 1ml/min (±8.9), p<0.001.

Adjustment for change in medications including ACE INH, ARBs, diuretics MRAs and SGLT2 inhibitors did not significantly affect the results.

Conclusions: Although some differences in CKD indices were statistically significant given the large cohort size, none were clinically significant. Mild-moderate COVID-19

did not affect indices of CKD and is therefore unlikely to be associated with CKD progression.

Differentiating Infectious from Nom-Infectious Inflammation in Non-Dialysis Chronic Kidney Disease Patients: The CKD-INF Score

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Introduction: Distinguishing chronic, low-grade inflammation from infection in chronic kidney disease (CKD), often indicated by high C-reactive protein (CRP), is challenging. Our goal was to create a tool for early infection detection in CKD patients, surpassing CRP's effectiveness.

Methods: Our retrospective analysis examined 831 non-dialysis CKD patients admitted for various reasons between January 2007 and January 2023, ensuring the availability of all necessary study data. We created and validated the CKD-Infectious Inflammation (CKD-INF) score using 665 and 166 patients, respectively. This score, based on adjusted odds ratios and 95% confidence intervals from logistic regression, differentiates inflammation types. Infection was classified following the International Sepsis Definition Conference criteria.

Results: The study's participants had an average age of 76.2 ±11.2 years, with 37% female and over half diagnosed with diabetes. The resulting score was as follows:

CKD-INF=1.8*CRP(mg/L) + 3.3*NLR + 7.9*WBC(K/μL) + 172.1* Fever≥38ºC(no=0, yes=1)

where NLR refers to the neutrophil-to-lymphocyte ratio, and WBC indicates white blood cell count. CKD-INF exhibited a higher AUC of 0.85 (with a 95% CI of 0.82–0.87), higher sensitivity (75.3%) and specificity (82%) compared to its components including CRP. The CKD-INF score showed higher weighted κ values (0.57) for infection prediction at hospital admission than its individual components. In both training and validation groups, the CKD-INF score outperformed CRP as a predictor of infection in univariate and multivariate analyses.

Conclusion: The CKD-INF score, derived from routine laboratory tests, can be an effective tool for predicting infections in CKD patients, potentially aiding in their early management.

True Refractory Hypertension in 2023: Lessons Learned from a National Registry of 1.82 Million Adults

Ori Lencovsky, Carmil Azran , Orpaz Hadad, Avital Angel-Korman , Naomi Nakash Niddam , Vladimir Rappoport , Adi Leiba

Introduction:

Refractory hypertension is defined as blood pressure that remains uncontrolled on maximal therapy, which is defined as the use of 5 or more antihypertensive agents of different classes. We aimed to define the prevalence of true refractory hypertension in a real-life national registry of a Health Maintenance Organization (HMO).

Design and Methods:

In this real-life, retrospective, observational database study, we utilized the Maccabi Healthcare Services (MHS) database during 2023. Apparent refractory hypertension was defined as patients included in the Maccabi “Hypertension Registry” during 2023 and taking 5 different antihypertensive medications of different classes, four of which were of pre-specified groups (diuretics, CCB, RAAS inhibitors, and MRAs). True refractory hypertension (unlike apparent refractory hypertension) was defined as being fully adherent to the antihypertensive medication regimen with at least 6 prescriptions and purchases (refills) during 2023, as well as blood pressure which is not optimally controlled during the year (less than 80% of blood pressure measurements equal or below the well-defined target of 130/80mmHg).

Results:

Out of 1,821,685 adult members of Maccabi HMO during 2023, 361,721 patients were defined as hypertensive patients (20%) and included in the registry. 0.5% (1750) of the hypertensive population were at some stage during 2023 on at least 5 anti-hypertensive medications (i.e., apparent refractory hypertension). Of them, only 264 patients (15%) adhered to their medications during the year. Patients were in their seventh decade (average age 71.3 years, median age 72). 205 patients (77% of the well-adherent group) were not optimally controlled and thus regarded as true refractory hypertension. True refractory hypertension was thus evident in 0.056% of the hypertensive population.

Conclusion:

In an “optimal world” in which a rational four-medication regimen is augmented, if needed, with alpha-blockers, beta-blockers, central alpha-2 agonists, or direct vasodilators, and in which all medications are fully adherent, true refractory hypertension is extremely rare (0.056% of hypertensive patients). Realizing that almost every hypertensive patient can be well controlled with the current anti-hypertensive armamentarium is important for clinicians and health policymakers.

Elderly Men are Underscreened for Primary Aldosteronism Even in Hypertension Excellence Center

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Introduction: the Endocrine Society (ES) guidelines recommend screening for primary aldosteronism (PA) in high-risk hypertensive patients presenting with at least one of seven criteria (resistant HTN, hypokalemia, adrenal adenoma, and several others). Although guidelines are clear and screening is simple, compliance rates among clinicians are extremely low. This results in underdiagnosis of early disease, leading to cardiovascular complications and extra-burden of advanced chronic kidney disease (CKD).

Aims: we aimed to evaluate the screening rates in our Nephrology and Hypertension clinics, as an example of a dedicated Hypertension Excellence Center.

Methods: data on adult hypertensive patients was retrieved during January 2018 to December 2020. Included in the study were hypertensive patients who had at least one of the ES criteria for PA screening. Of all suitable patients, we compared those who were screened for PA to patients who were not screened. Univariate and multivariate cox regression analysis were used for comparison between groups.

Results: of 661 patients with HTN, 218 patients (33%) met the ES guidelines for PA screening. Forty-six of them (21.1%), were referred for screening. Advanced age and male gender were associated with lower screening referral rates. Odds ratio for age was 0.945 for every year (95% CI 0.915-0.975). There was a trend towards decreased referral rate in advanced kidney disease.

Conclusions: a 21% screening rate, suggests that many cases of PA are likely missed, more often in older patients. We therefore advocate for PA screening of all hypertensive patients, especially elderly patients with CKD, in whom clinicians' awareness is low but the absolute risk is high.

Diagnosing White Coat Hypertension Among Soldiers at Stressful Duties –is There an Alternative to 24 Hout ABPM?

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Objective:

White Coat Hypertension (WCH) is defined as elevated office blood pressure (BP) readings with a normal blood pressure during ambulatory blood pressure monitoring (ABPM). We recently established a dedicated "fast track" clinic for diagnosis of hypertension among soldiers.

We assumed that WCH might be highly prevalent among these examinees, whose blood pressure is measured in a stressful, non-standardized, military setting.

Since home BP for diagnosing of WCH is not feasible among most military personnel, we aimed at comparing possible alternatives: standardized hospital clinic BP, aortic (central) BP measurement or 24-hour ABPM.

Design and method:

We estabished a dedicated hypertension clinic, in which soldiers who are off duty for a long weekend (Thursday-Sunday) undergo full hypertension workup during 2 consecutive work days. The workup consists of standardized clinic BP, measured by an experienced medical technician, central BP measurement and 24-hour ABPM as well as echocardiography, renal ultrasound, renal artery doppler, fundoscopic exam, blood and urine tests.

Results:

During 2023, 56 examinees were seen in our clinic.

Thirty-five of those (68.6% men, median age 20) were referred due to repeated elevated BP in a military setting (BP>=140/90mmHg), but no clear diagnosis of hypertension.

Sixteen of these patients (45.7%) were diagnosed as WCH by 24-hour ABPM. Standardized office BP measurements done by a medical technician unmasked the white coat effect (WCE) in 5 patients (31.2% of WCH). Central (aortic) BP measurements followed the standardized BP measurements and were within normal limits in patients with normal standardized brachial BP measurements. Similarly, central BP was elevated in those with elevated standardized brachial BP measurements.

Conclusion

WCH is more common among women, elderly and obese and occurs in up to 30% of subjects with elevated blood pressure. We found a prevalence of 45.7% among young examinees, most of whom were men.

Standardized clinic BP measurements unmasked 31.2% of WCH cases, possibly, as they were performed by a technician and not a physician. However, 24 hour ABPM is mandatory in order to diagnose WCH. Central BP measurement adds no value as compared to brachial BP.

Bilateral Renal Artery Occlusion in Fabry Disease

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Introduction: Progressive accumulation of glycosphingolipids in patients with Fabry disease (FD) causes a diversity of clinical manifestations including vascular and kidney injury. Podocythopathy and proteinuria are the main signs of nephropathy, while vascular manifestations are rare, and their pathogenesis poorly understood. We present a patient whose kidney disease evolution was abrupt and inconsistent with classic Fabry nephropathy (FN).

Case: 50-year-old man was diagnosed with FD in 2020 after being hospitalized due to complete AV block, treated since then by enzyme replacement therapy (ERT). GFR at diagnosis was 55 mL/min/1.73 m2. The first albuminuria was detected in 2021. An abdominal US was performed at the end of 2022 showing normal size kidneys. Three months later,US Doppler was performed for evaluation of poorly controlled hypertension, demonstrating 11.7 cm long right kidney and atrophic left kidney. For further investigation CT angiography was performed showing atrophic left kidney, thrombotic occlusion of the left renal artery and critical stenosis of the right renal artery due to focal thrombus. The patient underwent urgent catheterization and stent placement in the right renal artery, improving blood pressure and GFR stabilization. Evaluation for autoimmune disease, inflammatory condition or hypercoagulable state was negative.

Conclusion: We describe a patient with FN evolving bilateral renal artery occlusion while being on ERT and antiproteinuric therapy. Despite ERT that relatively quickly eliminate detectable GL3 accumulation in endothelial cells, severe macrovascular damage was detected. Renovascular disease should be considered in patients with FD and uncontrolled hypertension even with a clinical presentation consistent with classical FN.

Exploring the Impact of Hemodialysis Modalities on Netosis in Diabetic and Non-Diabetic Patients

Etty Kruzel-Davila, Olga Vdovich, Faten Y. Andrawes Barbara, George Jiries, Lital Remez

Background: Patients suffering from chronic kidney disease (CKD) and diabetes mellitus (DM) face an increased risk of developing cardiovascular complications and infections. Neutrophils, the predominant innate immune cells, are recruited to sites of infection and tissue injury. Neutrophil extracellular traps (NETs), a conserved evolutionary mechanism known as NETosis, function to ensnare and eradicate pathogens by releasing decondensed chromatin decorated with proteins from neutrophil intracytoplasmic granules. However, when NETosis becomes dysregulated, it can potentially exacerbate the detrimental inflammatory pathways linked to complications of CKD and diabetes. Considering the higher survival rates observed among patients treated with hemodiafiltration (HDF) as opposed to hemodialysis (HD), along with the dysregulated NETosis observed in individuals with HD and DM, our objective is to investigate the impact of hemodialysis modality on NETosis in patients undergoing hemodialysis, with and without diabetes.
Methods: Twenty hemodialysis patients participated in the study, comprising 10 diabetic patients, 10 non-diabetic patients, and 10 healthy controls. Blood samples were obtained from patients undergoing hemodiafiltration (HDF) and subsequently transitioning to high flux hemodialysis (HFHD). Neutrophils were isolated from these samples and stimulated with 100 nM PMA for one hour. Subsequently, they were stained for markers of NETosis such as PAD4, PE, MPO, Histone H3, and 7AAD Viability Dye. Data acquisition was performed using a flow cytometer.
Results: Our findings reveal significantly reduced levels of NETosis markers following HDF treatment compared to HD, irrespective of diabetes status ($p<0.05$).
Conclusions: The study suggests that the reduction in dysregulated NETosis may contribute to the favorable outcomes of HDF, ultimately leading to decreased mortality among hemodialysis patients.

Human Amniotic Fluid Organoids as Personalized Real-Time Models of the Developing Fetus

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Introduction: Despite biomedical advances, major knowledge gaps regarding human development remain, and many developmental disorders lack treatment. This results from fetuses being largely inaccessible for analysis. Here, we aimed to use fetal progenitors found in amniotic fluid (AF) to generate personalized models of the fetal kidney and lung, which could serve to study development and model developmental problems in real-time. Methods: AF samples were seeded in 'kidney' or 'lung' media, resulting in formation of organoids recapitulating the native organ, which were analyzed by immunostainings, RNA-sequencing and functional assays. Results: We established protocols for generating kidney and lung organoids (AFKO and AFLO, respectively) from AF, which recapitulate fetal organs at the single-cell level. AFKO harbor key fetal kidney cell types, including nephrogenic, urothelial and stromal, and take-up albumin. Upon injection into the nephrogenic cortex of human fetal kidney explants, AFKO cells integrate in the host progenitor niche and contribute to developing tubules. AFLO comprise both alveolar airway cells, upregulate surfactant expression upon steroid treatment, and show functional CFTR channels. Conclusion: This platform represents a new tool for personalized modeling of developing organs from clinical AF samples in real-time. Hence, it provides a readily-accessible way to study development and mechanisms of developmental pathologies, such as congenital anomalies and prematurity-related complications, using bona fide human fetal cells, which until now has been challenging.

CD24 Upregulation Aggravates Renal Damage in CRF Mice, a Possible Role for Klotho Inhibition and FGF23 Activation.

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Background: CD24 is a protein, which is induced during tissue damage and is not expressed in matured renal tissue. We have shown that, during AKI, upregulation of CD24 promotes renal inflammation and worsen renal function. In the current studies, we aim to explore a possible role for CD24 in chronic renal failure (CRF) as well.

Methods: CRF was achieved by a 0.2% adenine diet administered to WT and CD24-/- mice. Renal function tests, histology, immunohistochemistry, western blot analysis, and ELISA were performed to assess the severity of renal damage and explore the mechanism

Results: CRF induced CD24 in the distal tubular epithelial cells. Compared to WT mice, CRF CD24-/- mice exhibited an attenuated decrease in renal function, less albuminuria, and decreased histological injury. The augmentation of TGFβ and αSMA expression (a pro-fibrotic proteins) induced by CRF was significantly reduced in CRF CD24-/- compared to CRF WT animals. In CRF CD24-/- animals the increase in serum FGF23, renal FGF23R and the decrease in renal Klotho was significantly attenuated compared to WT CRF mice.

Conclusion: Renal CD24 induction in CRF aggravates the severity of the disease. These findings are associated with attenuation of CRF induced decrease in renal klotho and increase in serum FGF23 and renal FGF23 receptor.

Predictors and Adverse Outcomes of Acute Kidney Injury in Hospitalized Renal Transplant Recipients

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Introduction Data about in-hospital acute kidney injury (AKI) in renal transplant recipients (RTRs) is lacking.

Methods We conducted a retrospective study of 292 RTRs, with a total of 807 hospital admissions between the years 2007-2020, to reveal predictors and outcomes of AKI during admission. AKI was defined as a difference of ≥50% between peak creatinine during admission and baseline creatinine.

Results AKI during admission developed in 149 patients (51%). AKI in a previous admission was associated with a more than twofold increased risk of AKI in subsequent admissions (OR 2.13, *P*<0.001). Other major significant predictors for in-hospital AKI included an infection as the major admission diagnosis (OR 2.93, *P*=0.015), a medical history of hypertension (OR 1.91, *P*=0.027), minimum systolic blood pressure (OR 0.98, *P*=0.002), maximum tacrolimus trough level (OR 1.08, *P*=0.005), hemoglobin level (OR 0.9, *P*=0.016) and albumin level (OR 0.51, *P*=0.025) during admission. Compared to admissions with no AKI, admissions with AKI were associated with longer length of stay (median time of 3.83 vs. 7.01 days, *P*<0.001). In-hospital AKI was associated with higher rates of mortality during admission, almost doubled odds for rehospitalization within 90 days from discharge (OR 1.95, *P*<0.001), and increased the risk of overall mortality in multivariable mixed effect models.

Conclusions In-hospital AKI is common in RTRs and is associated with poor short- and long-term outcomes. Strategies to prevent AKI during admission in this population should be implemented to reduce re-admission rates and improve patient survival.

Mismatched Blood Types between Donor and Recipient Increase the Risk of BK Viremia One Year Post-Kidney Transplantation

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Background and Aims: Kidney transplanted recipients are at increased risk of infections, including BK virus, for which there is no specific treatment. Current prevention strategies include surveillance and risk stratification. We sought to estimate the contribution of non-identical but compatible (mismatched) ABO blood types to the risk of BKV viremia.

Method: A retrospective single-Center study was conducted in kidney transplant recipients between 1/1/2011 and 1/12/2021. The primary outcome was viremia (>10,000 copies per ml in two consecutive measurements at least one week apart) during the first year following transplantation. The secondary outcome was the time to BK viremia. We created a multivariate model using stepwise forward regression to assess the risk of viremia.

Results: During the study period, there were 1244 transplantations, with 1084 performed between donors and recipients with identical blood types (BT). Grafts were received from a living donor in 787 (63.3%) cases, 158 (98.8%) of which were in the mismatched BT group, and 629 (58%) were in the control group. There were 78 episodes of significant BK viremia within the first year post-transplantation, with 60 (5.5%) occurring in the matched BT recipients and 18 (11.3%) in the mismatched BT group (OR 2.16, p=0.006). Among grafts from living donors during the first year following transplantation, there were 47 (6%) cases of viremia, with 29 (4.6%) in the matched BT group and 18 (11.4%) in the mismatched BT group (OR 2.22, p=0.001). Multivariate analysis showed that the risk of BKV viremia in the living donor group increased in the presence of mismatched BT (OR=2.75, p=0.002).

Conclusion: The association between donor and recipient BT mismatch and BKV viremia was demonstrated for the first time. Mismatched BT recipients experienced higher rates of BKV viremia compared to identical BT recipients. This might be a preventable risk factor that should guide clinicians in organ procurement.

GI Pathogen Detection Using Multiplexed PCR Assay in Kidney Transplant Recipient with Diarrhea - before after study

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Background: Diarrhea is a frequent complication after kidney transplantation, but the etiology is often not identified. Multiplexed PCR assays may increase the detection of diarrheal pathogens among kidney transplant recipients (KTRs) with diarrhea and lead to better management of this population.

Methods: Single center, retrospective before-after study, conducted in a high-volume transplant center. In September 2017, Multiplexed PCR assay (biofire GI panel) was introduced in our center as an additional diagnostic tool for diarrhea. We reviewed all adult KTRs from January 2015 to august 2017 (pre-GI PCR, n=111) and from September 2017 to December 2021 (post-GI PCR, n=159) and followed them for 3 years after transplantation.

Results: Among 270 hospitalized KTRs with diarrhea, only 64 (24%) had an identified infectious diarrheal pathogen. The proportion of KTRs with an identified infectious diarrheal pathogen increased from 20% (13/64) in the pre-GI PCR to 80% (51/64) post GI PCR ($p<0.01$). GI PCR was used more likely in younger KTRs (52 years vs 61) who had more recent transplantation 3 years (4 months-8 years) and had a higher creatinine level at admission (2.7+1.8) as compared to baseline (2.1+1.5). Implementing GI PCR in the work up of KTRs who present with diarrhea, had significant increase in pathogen detection (OR=21, CI95% 10-44; $P<0.001$).
Conclusions: Infectious etiologies of diarrhea were identified in a higher proportion of KTRs after the implementation of GI PCR. This emphasizing the importance of integrating this diagnostic tool into diarrhea workup in KTRs.

The Long-Term Outcome of Kidney Transplant Recipients in the 8th Decade Compared with Recipients in the 7th Decade of Life.

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Introduction: With the aging of the population, more elderly patients are being considered for kidney transplantation. Therefore, it is crucial to evaluate the risks and benefits of transplantation in this population. This study aimed to assess long term outcomes of kidney transplantation, in a cohort of patients who underwent kidney transplantation at the age >70, compare to patients who were 60-69 years old at transplantation.

Methods: Included in the study 261 consecutive kidney transplant recipients: 52 were >70 years old and 209 were 60-69 years old at transplantation. Data was collected retrospectively and analyzed using multivariate logistic regression to identify potential risk factors for outcomes.

Results: The number of transplants in both groups increased during the study period. Mortality after transplantation was strongly correlated to age (HR=1.11, 95% CI 1.05-1.18, p<0.001), deceased donor (HR=2.0, 1.1-3.8, p=0.034) and pre-transplant diabetes (HR=2.9, 1.7-4.9, P=0.001).

Recipients >70 had an increased risk of death censored graft failure (HR=2.98, 1.56-5.74, P=0.001). In living donor transplant, 3-year survival was 80% in recipients >70, compared to 98% in group of 60-69 years. 5-year survival was 71 and 92%, respectively. In deceased donor transplant, 3-year survival was 63 and 78%-, and 5-years survival was 58 and 72%, respectively.

The risk of malignancy (excluding non-melanotic skin cancer) was nearly triple in the >70 group (HR=2.96, 1.3-6.8, P=0.01).

Conclusions:

Patient and graft survival in kidney recipients in the 8th decade is worse compared to recipients in their 7th decade of life. However, it is improved with living kidney donation.

Assessing Health-Related Quality of Life in Nondirected versus Directed Kidney Donors: Implications for the Promotion of Nondirected Donation

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Introduction: Living kidney donation has increased significantly, but little is known about post-donation health-related quality of life (HRQoL) of altruistic donors (ADs) vs. directed donors (DDs).

Methods: In this study, we analyzed outcomes in a cohort of 112 living kidney donors, comprising 82 ADs and 30 DDs. We compared the HRQol between these donor types, while also investigating disparities between the two groups in hospital length of stay (LOS), time to return to normal activity, and time to physical activity post donation.

Results: For the primary outcomes – namely, the mean physical component summary (PCS) and mental component summary (MCS) scores of the 12-item Short Form Survey (SF-12) questionnaire – scores were significantly higher for the ADs vs. the DDs (PCS: +2.69, MCS: +4.43). For secondary outcomes, ADs had shorter hospital stays (3.4 vs. 4.4 days), returned to physical activity earlier (45 vs. 60 days), exercised more before and after donation, and continued physical activity post-donation. Regression analyses revealed that donor type and white blood cell count were predictive of the PCS-12 score, and donor type was predictive of the MCS-12 score. Altruistic donation was predictive of a shorter hospital stay (by 0.78 days, $p < 0.001$) and the odds of having PCS-12 and MCS-12 scores above 50 were almost 10 and 16 times higher in ADs, respectively ($p < 0.05$).

Conclusion: These findings indicate the safety and potential benefits of promoting altruistic donation. However, careful selection processes must be maintained to prevent harm and exploitation.