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Basel (Switzerland), December 5–6, 2024

56TH ANNUAL MEETING OF THE SWISS SOCIETY OF NEPHROLOGY (SGN-SSN)

BASEL, DECEMBER 5–6, 2024

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LONG ORAL PRESENTATIONS

OC 1

Advance Care Planning with a Conversation Game: Quantitative Results of a Feasibility and Acceptability Study among dialysis patients in Geneva's nephrology unit

Dr. Anne Dufey Teso[1], Prof. Gora Da Rocha[2], Mrs. Pascale Lefuel[3], Mrs. Catherine Bollondi[3], Mr. Adrien Anex[2], Mrs. Jelena Stanic[2], Prof. Monica Escher[4], Prof. Christine Clavien[5]

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Background: Patients on dialysis suffer from high morbidity and mortality. Advanced care planning (ACP) is rarely carried out, due to multiples barriers. Our research team has developed a card game (Anticip'action) to help patients clarify their values and priorities in life and engage in an ACP process. We present the results of a 3-step ACP intervention with the use of this game, implemented in the dialysis unit of the HUG. Our goals were to 1) evaluate the acceptability, feasibility and impact of this intervention, from patients and health professionals' points of view, and 2) observe the effect of the intervention on ACP documentation.

Method: Two ACP discussion sessions with the use of the game *Anticip'action* were offered by trained nurses to their patients, followed by an ACP consultation, involving the patient, the nurse, and a nephrologist. We collected pre-post responses of patients and nurses to questionnaires, and pre-post ACP documentation in medical records. Qualitative feed-backs are reported in another talk.

Results: 33 patients were included from Jan 2022 to July 2023. 75% stated the ACP intervention and 55% fulfilled the whole procedure. 33% of failed retention was due to premature death. 12 nurses were recruited, trained and conducted the ACP procedure. 3 withdraw during the study. Overall, participants provided good evaluations (±4 on 1-5 scales) of the quality, relevance, and impact of the game and intervention. Organisational difficulties however were reported by nurses (2.9 on 1-5 scale). We observe significant pre-post increases in patients' reported engagement in ACP (+1.04 on a 1-5 scale, n = 18, $p = <.001$) and quality of ACP documentation (+2.68 on a 1-5 scale, n = 25, $p = <.001$).

Conclusions: Overall, this study shows that an ACP intervention using a card game is relevant to many patients, and has a good feasibility, acceptability, and impact. Domains for improvement are highlighted.

OC 2

Aging uncovers the critical role of WDR72 for kidney function in mice

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WDR72 is a scaffolding protein, member of the WD-40-repeat protein family. In the kidney, although barely studied, it is enriched in proximal tubules, distal tubules and intercalated cells. WDR72 is hypothesized to play a role in urine acidification in the distal nephron, through vesicular trafficking and assembly of H^+ATPase subunits. However, its role in the proximal tubule remains unknown. In GWAS, *WDR72* has been associated with several renal phenotypes, namely urinary pH, CKD, GFR, creatinine, nephrolithiasis and increased uromodulin. Young *Wdr72*$^{-/-}$ mice develop alkaline urine under baseline conditions. Additionally, *Wdr72*$^{-/-}$ females are unable to adapt to an acid challenge, and develop an incomplete distal renal tubular acidosis and decreased urea clearance. Males seem partially protected of this phenotype. Overall, *Wdr72* defects appear to alter the kidney's ability to manage an acid-load metabolic challenge. We used 18-months-old *Wdr72*$^{-/-}$ mice and their wild-type littermates, to characterize the role of *Wdr72* in age-related kidney function decline. *Wdr72*$^{-/-}$ females developed compensated metabolic acidosis, increased diuresis and decreased urine osmolality, compared to their wild-type littermates. Additionally, animals with *Wdr72* deficiency display elevated BUN and increased lactate. This phenotype appeared with age and was not present in young *Wdr72*$^{-/-}$ mice. Altogether, aging uncovers a critical role of *Wdr72* in kidney function. The absence of *Wdr72* could alter the kidney's ability to handle renal stress and enhance kidney function decline. Increased lactate might reflect proximal tubule metabolic dysregulations, such as mitochondrial impairment or a shift from gluconeogenesis to glycolysis, two hallmarks of CKD. A detailed evaluation of tubular metabolic pathways will give a comprehensive overview of the involved pathways to deepen our understanding of the role of *Wdr72* in kidney health and disease.

OC 3

Brain functional connectivity including the autonomous system is altered in hypertensive patients

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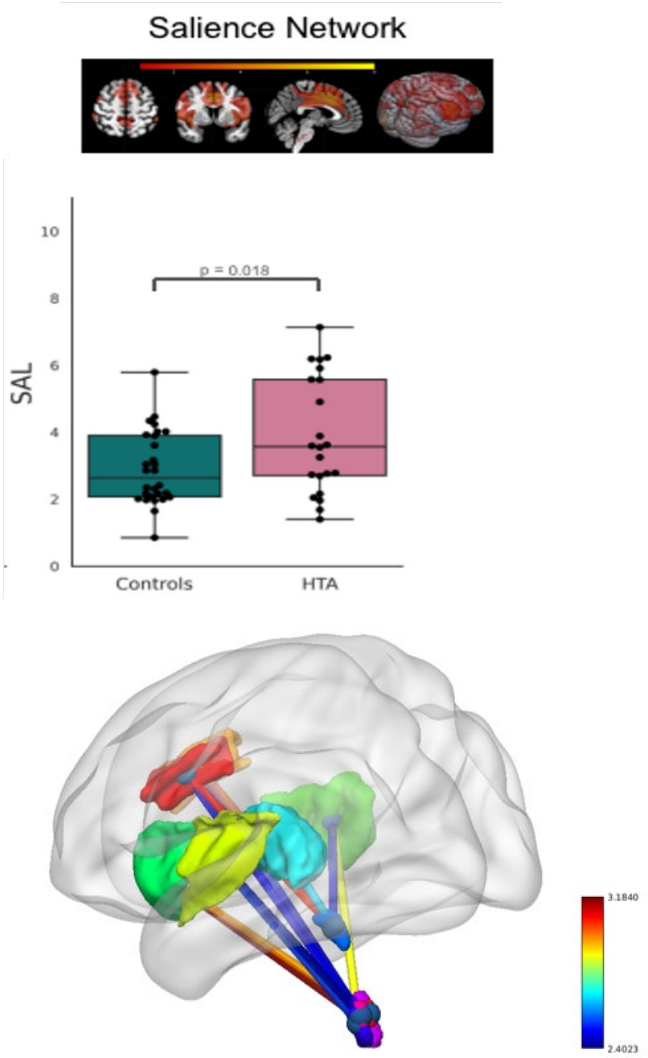
Background: Functional connectivity refers to the temporal correlation of neural activity between different regions of the brain, that can be studied using function magnetic resonance imaging (fMRI). So far most of the studies in hypertensive participants have been conducted in the resting state. The mechanisms underlying these differences are poorly understood. Our objective was to compare brain connectivity in hypertensive (HT) and normotensive (NT) participants under stress conditions using the cold pressor test (CPT).

Methods: MRI data were collected on a 7 Tesla MRI scanner in the resting state and during CPT. Group-level independent component analysis (G-ICA) was conducted to identify 20 spatially independent components using CONN's default settings. We first assessed between-group differences in spatial representation of the preselected independent components using voxel-wise approach. We were further interested in the functional connectivity within the autonomic control network (ACN)

Results: Data from 22 HT and 31 NT participants were used in our analysis. Analyses of mean spatial connectivity within the three brain networks showed that HT (M = 3.9 ± 1.8) displayed stronger connectivity within the salience network during rest as compared to the NT (M = 2.9 ± 1.1, t(48) = -2.4, p 0.018) (Fig 1). When comparing the HT and NT functional connectivity of the autonomic control network (ACN) during rest, no difference was found. However, when comparing ACN functional connectivity during the CPT, the NT had stronger connectivity than the

HT (t = 2.4, p = 0.035). NT showed stronger connectivity between the brainstem regions and the cortical-subcortical regions within the ACN (Fig 2).

Conclusion: Functional connectivity during stress condition reveals altered connectivity that is not seen during resting state suggesting that studying the central effect of physiological stress may be important to understand the pathophysiology of the autonomic nervous system in hypertensive patients.



OC 4

CENSUS-EU: An observational study to investigate prevalence and burden of chronic kidney disease-associated pruritus in Europe

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Background: Chronic kidney disease-associated pruritus (CKD-aP) is a common, burdensome symptom of patients undergoing haemodialysis (HD) which negatively affects their health-related quality of life (HRQoL). More specifically, sleep and mood disorders are directly associated with severity of pruritus. Data from the Dialysis Outcomes and Practice Patterns Study (DOPPS) demonstrated that the prevalence of at least moderate pruritus ranged from 26% (in Germany) to 48% (in the United Kingdom). Despite the significance of this burden, there is a lack of evidence about its epidemiology which impacts the current standard of care. Herein, we present the interim analysis of CENSUS-EU, a study seeking real-world evidence to assess the prevalence of CKD-aP and its impact on patients' HRQoL in Europe, including Switzerland.

Methods: CENSUS-EU is a prospective, cross-sectional, multicentre European study. Eligible patients (≥18 years under HD for ≥3 months), were asked to complete 5 questionnaires, such as the Worst Itching Intensity Numerical Rating Scale (WI-NRS), and 4 questionnaires evaluating HRQoL. Additionally, all subjects completed a survey on the communication and management of their itching as well as current anti-pruritic medication. Finally, the medical records of the participants were analysed regarding dialysis characteristics, treatment, and healthcare patterns.

Results: In total, 1,482 patients (42 from Switzerland) across severity subgroups were included. The overall CKD-aP prevalence was 52.6% (59.5% in Switzerland), of which 17.5% revealed moderate and 13.5% severe pruritus. Patients reported greater impact on HRQoL, sleeping disorders and feeling depressed as pruritus severity increased. Nevertheless, 40.6% of the HD patients with severe pruritus were not receiving antipruritus treatment.

Conclusions: The interim results of CENSUS-EU suggest that 31% of HD patients experience moderate and/or severe CKD-aP and similar conclusions can be drawn from the Swiss data too. The study clearly shows that pruritus affects HRQoL, however CKD-aP is still underreported and underestimated.

OC 5

Change of eplet verification status by using a novel adsorption/elution technique

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Background: Eplet are functional parts of HLA epitopes assumingly targeted by complementarity-determining regions within the paratope of B cell receptors or antibodies. If HLA high resolution typing of both donor and recipient is available, all eplets on mismatched donor HLA molecules can be assigned and are considered as potential triggers of an alloimmune response in the context of transplantation. A significant proportion of the eplets listed in the eplet registry (epregistry.com.br) is not well verified. Eplets are currently categorized into five different levels of evidence (namely A1, A2, B, C, D) based on a study by Besztarosti et al.

Methods: We investigated five postnatal serum samples that were previously examined by Duquesnoy et al. for eplet specificities of child-specific antibodies, using high resolution HLA typing data of mother and child. Magnetic microspheres coated with single HLA types (MagSort™) to specifically adsorb and thereby isolate only the antibodies of interest were used. Following an elution and washing steps, the separated antibodies were re-analyzed by single antigen bead assay.

Results: Based on the clearly determinable eplet specificities of the antibodies investigated, three eplets of the low verification status B, namely 79GT, 131S, 138MI, and one eplet without verification status (66NV) could be identified. We therefore propose changing the evidence of these four eplets to level A2,

which requires confirmation by adsorption/elution studies as done here.

Conclusion: Analysis of antibody binding profiles after adsorption/elution allows for a facilitated eplet assignment compared with binding patterns observed in heterogeneous antibody mixtures. MagSort™ beads are easy to handle and currently available for fifty-nine HLA specificities. The applied adsorption/elution protocol is straight forward and can be used to change the verification status of previously defined eplets or even to define new eplets, which are important steps towards a more accurate 'epitope-based HLA matching'.

OC 6

Combined molecular mismatch approaches to predict immunological events within the first year after renal transplantation

Ms. Cäcilia Jäger[1], Dr. Matthias Niemann[2], Dr. Gideon Hönger[1], Dr. Caroline Wehmeier[3], Dr. Helmut Hopfer[4], Dr. Thomas Menter[4], Dr. Patrizia Amico[3], Prof. Michael Dickenmann[3], Prof. Stefan Schaub[3]

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Background: Several molecular mismatch assessment approaches exist, but data on their combined use is limited. In this study, we aimed to define distinct risk groups for rejection based on the combination of three molecular mismatch assessment approaches (i.e., eplet mismatch count, the number of highly immunogenic eplets, and PIRCHE-II score) in 439 consecutive immunological standard risk transplantations.

Methods: For each molecular mismatch assessment approach, ROC analyses were used to define cutoffs for prediction of (sub)clinical rejection according to Banff 2019 classification within the first year posttransplant as a reference. If all three scores were below the cutoff, the patient was assigned to the low-risk group (19% of patients); if all three scores were above the cutoff, the patient was assigned to the high-risk group (21% of patients).

Results: The one-year incidence of (sub)clinical rejection was 12% in the low-risk group and 33% in the high-risk group (p = 0.003). Internal validation of the assigned risk groups for prediction of other outcomes revealed a high consistency: clinical rejection (6% vs 24%; p = 0.004), ATG-treated rejection (1% vs 16%; p<0.001) and development of de novo HLA-DSA at five years post-transplant (6% vs 25%; p = 0.003). The molecular mismatch risk group was an independent predictor for (sub)clinical rejection (high-risk vs low-risk: hazard ratio 3.11 [95%-CI 1.50-6.45]; p = 0.002)

Conclusion: Combining molecular mismatch approaches allows to distinguish lowand high-risk groups among standard renal allograft recipients. Independent validation in other patient populations and different ethnicities is required.

OC 7

Early complications in kidney donors and course of health-related quality of life 12 months after donation: An analysis of the Swiss Organ Living-Donor Health Registry

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Background: Since 1998, the Swiss Organ Living-Donor Health Registry (SOL-DHR) has recorded peri- and postoperative complications of living kidney (LK) donors, as reported by all Swiss transplant centers, and has collected follow-up data prospectively.

Methods: We analyzed the incidence and risk factors of early complications of 2379 consecutive individuals who donated a kidney between January 1998 and June 2022 and assessed their kidney function, metabolic parameters, and health-related quality of life (HRQoL) one year after donation.

Results: In total, 447 early complications in 404/2379 LK donors (17.0%) were reported to the SOL-DHR. The frequency of donors with major complications (i.e., Dindo-Clavien classification 3/4) was 2.4%. In total, 31 donors needed reoperation, and in 13/31 (42%), donors reoperation was necessary due to bleeding complications. Independent risk factors for major early complications were older donor age (p = 0.005) (Figure 1A) and type of surgical approach (i.e., the laparoscopic retroperitoneal compared to laparoscopic transabdominal surgery; p = 0.01), but not sex. We observed a U-shaped association of body mass index (BMI), where very low/high BMIs had higher odds of major early complications, without reaching statistical significance (Figure 1B). Although HRQoL was affected by kidney donation, 96.5% of donors indicated that they would donate their kidney again. The only independent risk factor for low HRQoL based on mental health scores was worsening EB after LKD (p<0.0001).

Conclusions: Overall, LKD is a safe procedure, however, donor age and type of surgical approach affect the risk of early complications. A decline in emotional bonding with the recipient after donation may worsen the quality of life of the donor.

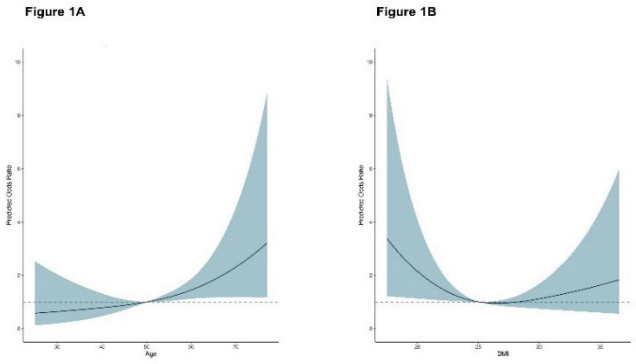

Figure 1. Restricted cubic spline plot of the association between donor age and BMI with major early complications. The dark line indicates the predicted OR for age (A)/ BMI (B) with major complications . The blue area represents the 95% CI.

OC 8

Empagliflozin for urinary supersaturation reduction in non-diabetic patients with calcium and uric acid kidney stones: a randomized crossover, phase 2 trial (SWEETSTONE)

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Background: Efficacy of sodium-glucose cotransporter 2 (SGLT2) inhibitors for kidney stone prevention in non-diabetic patients is unknown.

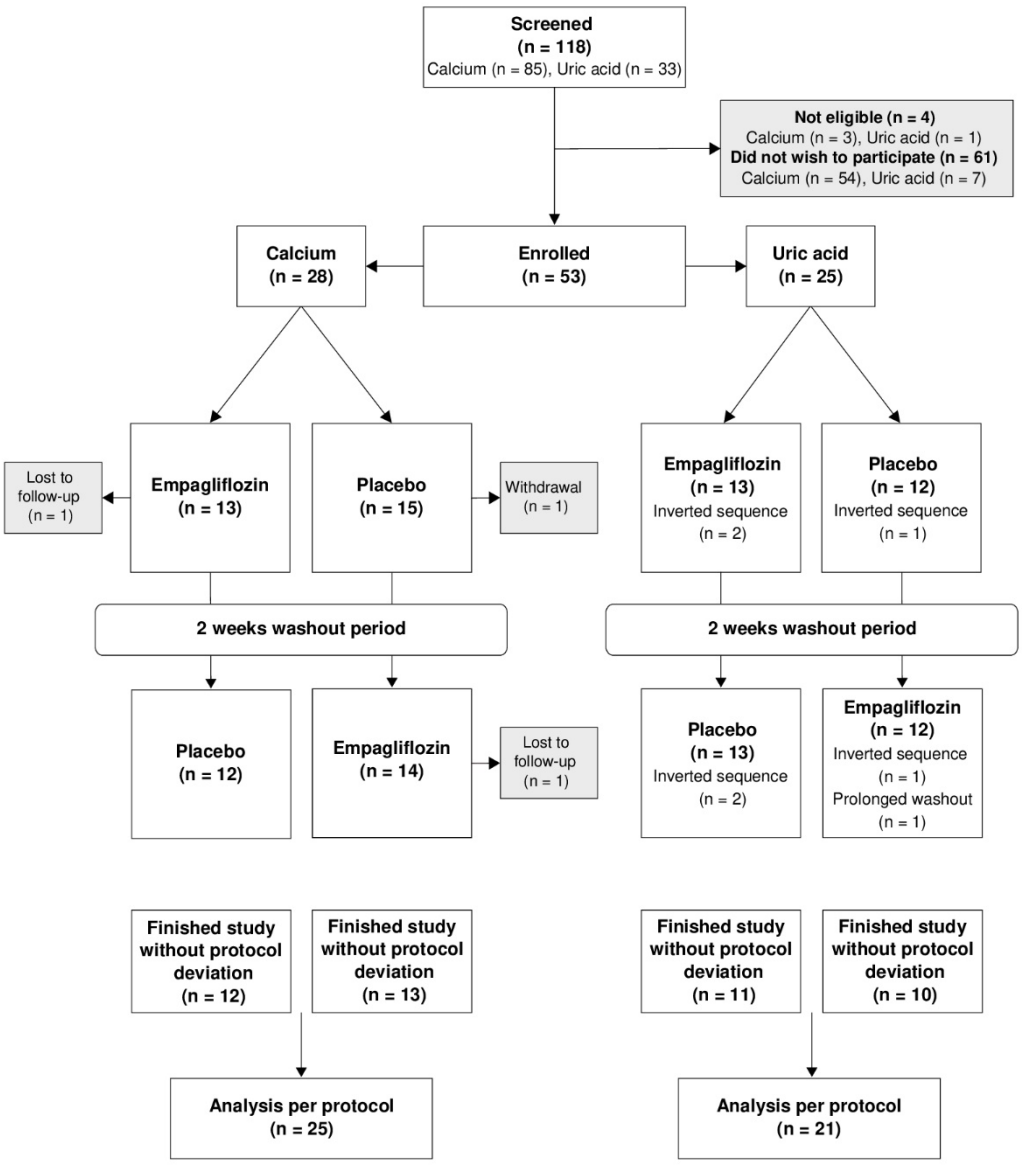
Methods: In a double-blind, placebo-controlled, single-center, crossover phase 2 trial, 53 adults (≥18 and <75 years) with calcium (n = 28) or uric acid (UA; n = 25) kidney stones (≥1 past kidney stone event(s)) without diabetes (HbA1c <6.5%, no diabetes treatment) were randomized to once daily empagliflozin 25 mg followed by placebo or reverse (2 weeks/treatment). Randomization and analysis were performed separately for both stone types. Primary analyses were conducted in the per-protocol set. Primary outcomes were urine relative supersaturation ratios (RSRs) for calcium oxalate (CaOx), calcium phosphate (CaP), and UA, validated surrogates for stone recurrence.

Results: Pre-specified RSR reductions (≥15%) were met in both groups of stone formers. In patients with calcium stones, empagliflozin reduced RSR CaP (relative difference to placebo, -36%; 95% confidence interval [CI], -48% to -21%; *P*<.001), but not RSRs CaOx and UA. In patients with UA stones, empagliflozin reduced RSR UA (-30%; 95% CI, -44% to -12%; P = .002) but not RSRs CaOx and CaP. Empagliflozin substantially increased urine citrate in both strata (relative difference to placebo, 60%; 95% CI, 39% to 85% in patients with calcium kidney stones and 40%; 95% CI, 22% to 62% in patients with UA kidney stones). With empagliflozin compared to placebo, urine pH was lower in patients with calcium stones (5.6 [IQR 5.5-6.1] versus 5.8 [IQR 5.6-6.4], relative difference -4%; 95% CI, -7% to 0%]), and higher in patients with UA stones (5.6 [IQR 5.2-5.6] versus 5.3 [IQR 5.2-5.5], relative difference 3%; 95% CI, 1% to 5%]). No serious or pre-specified adverse events occurred.

Conclusions: Empagliflozin substantially improved the urinary lithogenic risk profile in non-diabetic adults with calcium and UA kidney stones.

Funding: Inselspital, Boehringer Ingelheim. ClinicalTrials.gov registration: NCT04911660.

Fig. 1. screening randomization and follow-up in the sweetstone trial consort flow diagram



OC 9

Evolution of outcomes and recipient age: what can we learn for future endpoint definitions in renal transplantation trials?

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Background: Advancements in immunosuppressive therapy, immunological understanding, and changes in donor-recipient demographics have shaped transplantation medicine in recent decades. This study aims to evaluate how these developments have impacted patient and graft survival in individuals undergoing kidney transplantation at the University Hospital Basel, and to explore potential areas for improvement.

Methods: We conducted a retrospective cohort study of 1,743 kidney transplantations between January 1995 and August 2022. Primary outcomes were patient and death-censored graft survival, with secondary outcomes focusing on causes of death and graft failure. Data were analyzed across three time periods (1995–2004, 2005–2014, and 2015–2022) and stratified by age groups at transplantation (<40, 40–60, and >60 years).

Results: Overall patient survival remained stable over 27 years. However, among patients aged >60 years at the time of transplantation, a trend toward declining survival rates was observed in the most recent period. Death-censored graft survival significantly improved in the last two time periods, with reductions in early graft failure playing a key role. Graft loss causes varied by age: 80.3% of graft losses in patients <40 years were due to graft failure, with rejection being associated with 75.5% of these cases. In patients >60 years, graft loss was primarily due to death with a functioning graft (76.1%). Causes of death, including cardiovascular events, infections, and cancer, remained consistent over time, each responsible for 22.5% of deaths (n = 103).

Conclusions: Age significantly influences graft loss patterns. In older patients, death-censored graft survival is less meaningful as most die with a functioning graft, suggesting the need for different endpoints in future studies. In younger patients, the high rate of graft rejection highlights the need for more tailored immunosuppressive regimens and potentially better donor-recipient matching. Declining survival in older patients may indicate limitations in expanding donor and recipient criteria.

OC 10

FceRIneg dendritic cell 2 (DC2) subset accumulates in the urine of patients with nephrotic syndrome (NS) in complete remission: a potential role in the resolution of NS?

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Nephrotic syndrome (NS) is a glomerular disease characterized by increased permeability of the filtration barrier. Although structural damage has been identified, the underlying immune mechanism is largely unknown, particularly the role of dendritic cells (DCs), as pivotal cells that orchestrate the balance between immunity and tolerance. The aim of this study is to characterize different subsets of DCs in the urine of patients with nephrotic syndrome (NS). Urine and blood samples were collected from children with NS (n = 7) and compared with controls (n = 10). Cells were analyzed by FACS with markers identifying different bona-fide DC subsets, including the DC2 population categorized by CD14 and FceRI expression, as well as T cells, NK, neutrophils and macrophages. Flow cytometry data, analysed by principal component analysis, allowed the discrimination of NS patients from controls in both urine and blood samples, suggesting that the FACS panel used was relevant in identifying a cellular signature of NS in this study. Preliminary data show that, although the frequencies of CD3T-cell populations in urine are very low (<0.05% total cells), the frequency of the HLA-DR population may reach up to 5% of total cells. Among the different DC subtypes, the DC2-CD14$^+$ population was significantly increased in the urine of NS patients compared to controls. Screening the composition of DC2-CD14$^+$ population, a higher frequency of DC2 not expressing the FcεRI-receptor accumulates in the urine of patients with complete remission compared to patients in remission but still on treatment or patients in relapse. These results suggest that the FcεRI^{neg}DC2-CD14$^+$ population may develop during patients' recovery and open the question of whether it is involved in the resolution of NS. These findings demonstrate for the first time that a DC subset can be found in urine in pediatric patients with NS and may be related to the remission status of NS.

OC 11

Hypnosis can enhance ultrafiltration efficiency in hemodialysis: a preliminary experience and a systematic review of the literature

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Background: Hemodialysis (HD) have improved survival rates, but patients face several adverse outcomes, including hospitalizations, infections, and complications related to vascular access. Additionally they experience subjective issues like pain, cramps, and psychological concerns such as anxiety and depression. To address these issues, alongside pharmacological therapy, research has explored complementary therapies, including hypnosis. This study evaluates the effectiveness of hypnosis in enhancing ultrafiltration (UF) among patients suffering from pain and severe cramps. Furthermore, we conduct a systematic review regarding the application of hypnosis in HD population.

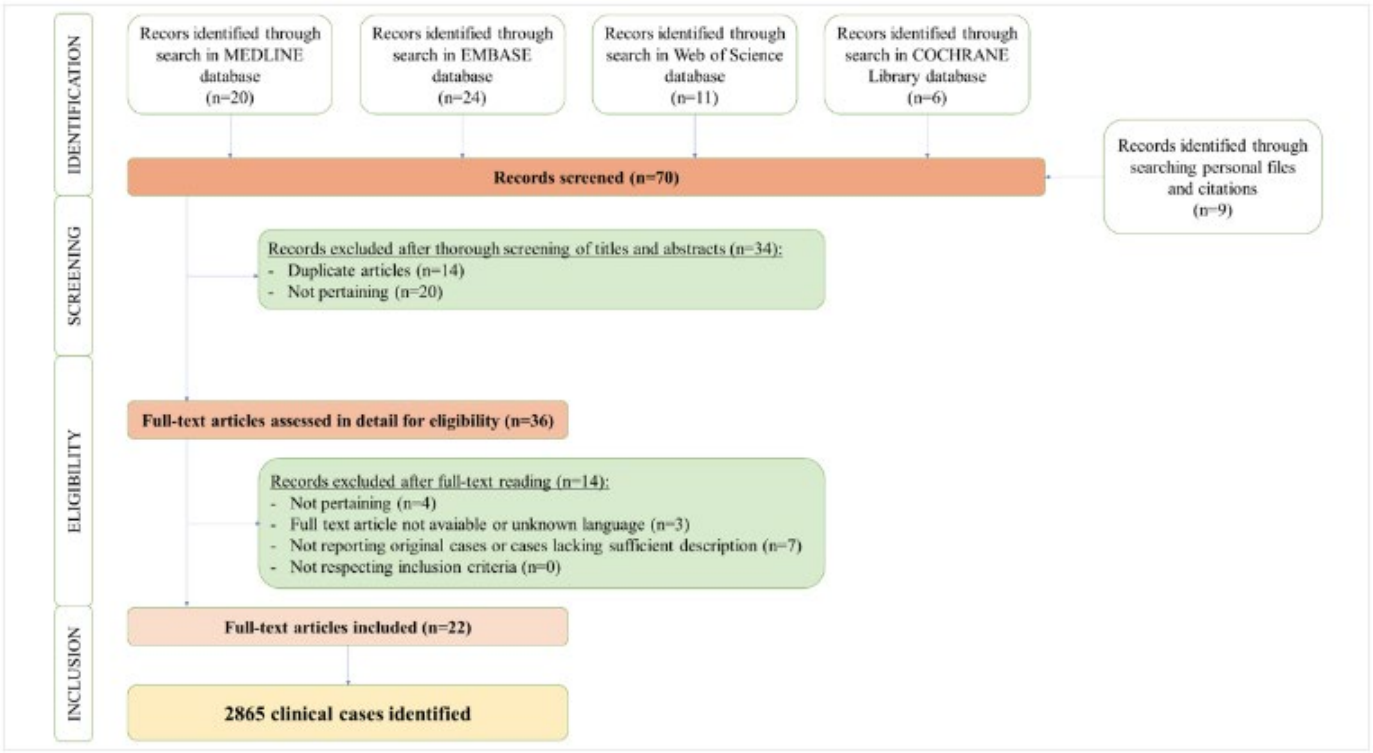
Methods: We present a preliminary report on two patients who benefit from hypnosis sessions during HD, assisted by a specialized nurse. Data collected over approximately 10 months included HD session details and efficiency, UF performance, patient fluid status. We systematically reviewed MEDLINE, EMBASE, Web of Science, and COCHRANE databases, to assess cases reports or series involving hypnosis in HD patients (Figure 1). We adhered to PRISMA guidelines (PROSPERO_CRD42024583647).

Results: Over a year, hypnosis allowed for a substantial post-HD weight reduction in our two patients (6.6 kg and 5.4 kg) (Figure 2). Severe cramps and musculoskeletal pain improved,

as measured by the Visual Analog and Numeric Rating scales. No changes were observed in dialysis efficacy (Kt/V).

The review of the medical literature revealed twenty-two articles encompassing 2865 subjects. No adverse effects from hypnosis were reported. Most patients reported anxiety reduction, improvement in emotional well-being, depressive symptoms, and pain management. In particular, twelve studies involving 325 patients suggest a marked improvement in anxiety, while seven studies reported improved depressive symptoms (2416 subjects), emotional health, pain control. Finally, data also suggested improved therapeutic adherence (Table1).

Conclusions: Hypnosis appears to be a promising complementary treatment for HD patients, helping manage symptoms and improve their subjective experiences. Our preliminary report suggests that hypnosis may improve UF efficiency, particularly when pain complicates treatment.



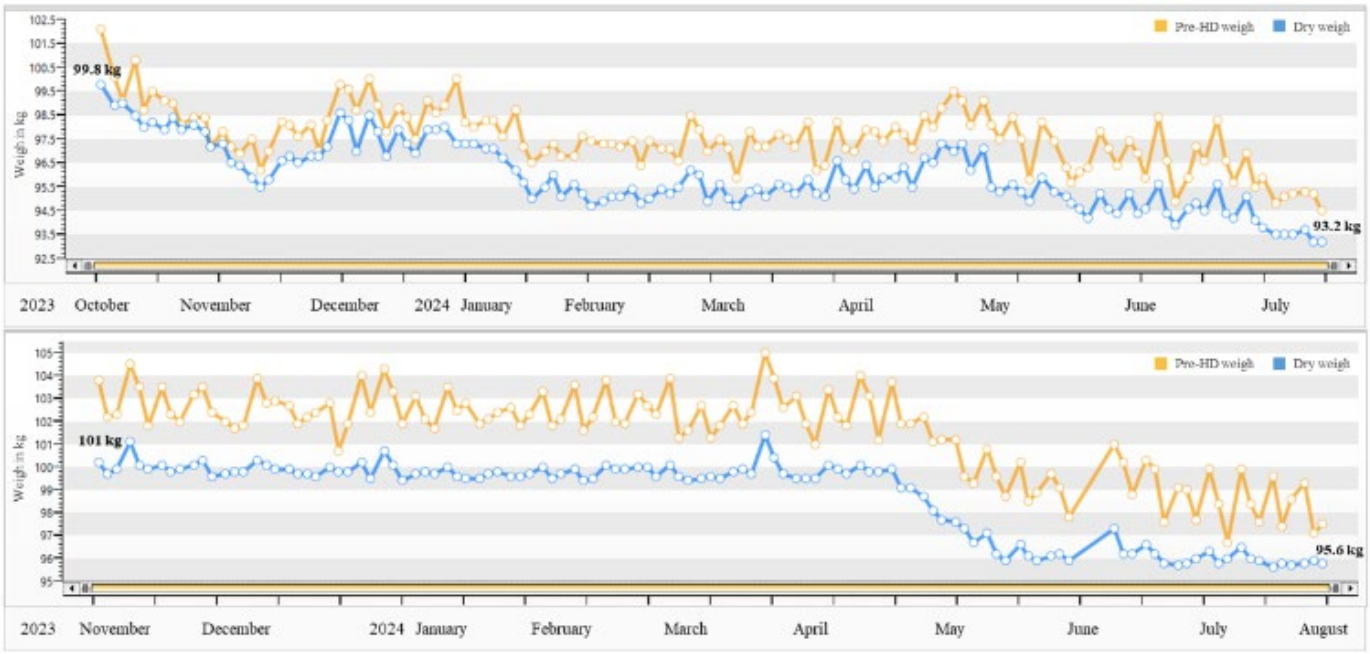


Figure 2. The graphs represent the trend of weight in the two patients studied. Pre-dialysis weight is shown in yellow, and dry weight is shown in blue. In both cases, it was possible to reduce the dry weight of the initially hypervolemic patients through the use of hypnosis. The patients were studied for approximately 10 months.

Analysed Outcome	Reference	Dy et al.	Untas et al.	Surman et al.	Beižaee et al.	Kaplan Serin et al.	Scott et al.	Dimond et al.	Krumlovsky et al.	Seregina et al.	Martin et al.	Idier et al.	Krespi et al.	Ebrahimzadeh et al.	Zins et al.	Bargiel-Matusiewicz et al.	Natale P. et al.	Lu et al.	Samuels et al.	Shabandokht-Zarmi et al.	Cavallaro et al.	Wati et al.	Sohn et al.	Synthesis
Emotions and mental health								+		+	+	+	-/+	+									+	7
Depression and psychological sufferance			+	+	+										+	+	+					+			7
Anxiety		+	+	+	+		+	+		+	+			+		+		+					+		12
Quality of life						+						+	-												3
Fatigue						+									+										2
Pain					+	+					+			+	+			+			+				7
Vital signs and Biochemical markers					-																			+	2
Adherence and compliance to treatments		+						+			+	-											+		5
Sleep disorders			+				+																		2
Needle phobia				+							+							+	+						4
Others physical symptoms (cramps, pruritus, headache …)				+				+			+								+						4
Number of patients enrolled		1	29	5	80	96	1	1	3	1	8	2	153	5	15	139	2056	16	2	114	92	39	7	2856

Table 3. Systematization of the literature review: report of studied symptoms with hypnotic intervention. (+): the study reveals a positive impact of hypnosis on the symptoms; (-): the study does not reveal a significant impact of hypnosis on the symptoms; (-/+): the study does not show a statistically significant impact of hypnosis on the symptoms, but the patients reported subjective satisfaction with the intervention procedures.

OC 12

Identification of a naturally derived senolytic compound to prevent kidney aging

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Introduction: Cellular senescence is involved in kidney biology, aging and disease. This study is part of an interdisciplinary project aiming at the characterization of cellular senescence across organs and at the identification of pharmacological targets for age-related diseases. Here, we present data on the discovery of a new kidney-relevant senolytic compound.

Methods: Senescent cells were characterized by single-cell RNA sequencing and immunohistochemistry. High-throughput screening of a library of >2,600 purified molecules from plants and bacteria was conducted in cell lines transduced with a miR146a-EGFP senescence reporter. Promising compounds

were validated in mice *in vivo*. Transmission electron microscopy and MitoTracker probes were used to study the putative mechanisms of action.

Results: An extract from Gleditsia fruit emerged as a promising senolytic agent. Gleditsia treatment extended lifespan and reduced aging-associated issues such as kyphosis, osteoarthritis, and fur loss. In aging kidneys, senescent cells, particularly endothelial, interstitial, and immune cells, accumulated. Gleditsia treatment in old mice reduced markers of senescence, inflammation, and fibrosis in the kidneys. Transcription scores related to senescence and aging were restored to youthful levels across various kidney cell types. Mechanistically, we found that, the saponin NP12 from Gleditsia primarily drove these effects by inducing mitochondrial stress, which eliminated senescent cells and enhanced health of remaining cells via mitohormesis.

Conclusions: This study introduces a novel approach to modulate renal aging by triggering senolytic and mitohormetic responses and identified a compound with broad potential pharmacological applications in age-related diseases.

OC 13

Impact of the legalization of medical aid in dying (MAID) in the management of stage 5 CKD: investigation in 3 French-speaking countries

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Introduction: Belgium, Switzerland and Canada have adopted laws authorizing MAID under conditions. To find out if the management of stage 5 chronic kidney disease (CKD) is affected, a questionnaire was sent to Belgian, Swiss and Quebec nephrologists.

Methods: The questionnaire was sent electronically by professional organizations and was accessible from 01/11/23 to 31/12/2023.

Results: 127 nephrologists responded (53 Belgians, 40 Swiss and 33 Quebecers; 69 men and 58 women). 100/127 had >10 years of professional experience. 102/127 say they interrupt extrarenal replacement therapy (ERT) >once/year. 109/127 declare that they never or exceptionally resort to MAID in the event of stopping ERT. 95/127 say they never (40) or exceptionally (55) have received a request for MAID from patients in ERT. Of the 87 nephrologists who received such a request, 38 never or exceptionally responded favorably and 37 accepted systematically (however, 22/37 had only exceptional requests). 58/127 had exceptional requests for MAID by patients in CKD stage 5 without ERT. 27 have never or exceptionally responded favorably and 25 accepted systematically (but 21/25 had only received exceptional requests).

Conclusion: There is not widespread use of MAID among CKD patients in countries where it is legalized. This is explained by both, a low number of requests, and by a reserve of nephrologists to respond favorably. Nephrologists who say they systematically respond favorably to their patients' requests for MAID are only exceptionally confronted with such requests.

OC 14

Kidney and skin involvement in levamisole-induced vasculopathy: a systematic review

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Background: Levamisole, an antihelmintic and immunomodulatory drug, has been historically used in the treatment of nephrotic syndrome, autoimmune diseases and some cancers. In recent years, levamisole-adulterated cocaine has been increasingly implicated in vasculopathy, predominantly affecting skin and kidney. This study aims to delineate the features of levamisole-induced vasculopathy.

Methods: We conducted a systematic literature review following the PRISMA guidelines, analyzing 172 articles published between 1977 and 2024. Data on demographics, organ involvement, immunological findings, treatment and outcome were extracted and analyzed.

Results: We analyzed 300 cases (female to male ratio 1.48) of levamisole-induced vasculopathy: 280 cases following illegal use of cocaine adulterated with levamisole and 20 cases following medical use of levamisole. Skin lesions were identified in 272 cases, with the following distribution: purpura (N = 227), necrosis (N = 140), ulceration (N = 70), bullae (N = 68), eschar (N = 14), and livedo (N = 10). Kidney involvement was noted in 64 cases with the following findings: increased serum creatinine levels (N = 60), hematuria and proteinuria (N = 51), isolated proteinuria (N = 4), isolated hematuria (N = 2). Ear-nose-throat (N = 44) and the respiratory system (N = 30) were less frequently involved. Leukopenia (≤4.5 x 10^9/L) was detected in 123 cases. Anticytoplasmic autoantibodies, tested by immunofluorescence in 288 cases, were detected in 270 of them, mainly showing a perinuclear pattern (N = 197). The predominant pattern by solid-phase immunoassays was anti-myeloperoxydase (N = 138), followed by anti-proteinase 3 (N = 101). A skin biopsy detected a small vessel leukocytoclastic vasculitis (N = 52), a thrombothic angiopathy (N = 65) or both (N = 70). A kidney biopsy was performed in 45 cases and the predominant pattern was a pauci-immune glomerulonephritis (N = 18).

Conclusion: Levamisole-induced vasculopathy primarily affects cocaine users and mainly presents with cutaneous and renal features. Like in many other drug-induced vasculopathies, anticytoplasmic autoantibodies are often detected.

Table 1: Characteristics of 300 patients 6 to 70 years of age with a vasculitis associated with the use of levamisole. Results are given as frequency (and sometimes also percentage) or as median (with interquartile range).

	All	Adulterated Cocaine	Therapeutic use	P-value
Demographics	300	280	20	
Female : male ratio	1.48	1.51	1.11	0.6305
Age	11			
years	43 [35-49]	43 [36-49]	14 [10-49]	0.0029
≤18 years, N	11	0	11	
Organ involvement				
Skin, N	272 (91)	255 (91)	17 (85)	0.4145
Kidney, N	64 (21)	62 (22)	2 (10)	0.2657
Ear-nose-throat, N	44 (15)	44 (16)	1 (5)	0.3291
Lung, N	30 (10)	30 (11)	2 (10)	0.7055
Gastrointestinal tract, N	3	3	0	0.3883
Muscle, N	2	1	1	0.1291
Heart, N	1	1	0	>0.999

Table 2: Characteristic of cutaneous and renal involvement in 300 patients with a vasculopathy associated with the use of levamisole.

Skin N = 272	
Clinical presentation	
Skin lesions	
Purpura, N (%)	227 (84)
Necrosis, N (%)	140 (52)
Livedo, N (%)	10 (3)
Bullae/Blisters, N (%)	68 (25)
Ulcer, N (%)	70 (26)
Eschar, N (%)	14 (5)
Localization/Distribution	
Head and neck, N (%)	176 (65)
Ears, N (%)	147 (54)
Cheeks, N (%)	38 (14)
Nose, N (%)	36 (13)
Torso, N (%)	73 (27)
Upper extremities, N (%)	133 (49)
Lower extremities, N (%)	170 (63)
Biopsy, N (%)	218 (80)
Leucocytoclastic vasculitis, N (%)	52 (19)
Thrombotic vasculopathy, N (%)	65 (24)
Vasculitis and thrombotic vasculopathy, N (%)	70 (26)
Kidney N = 64	
Findings	
Increased serum creatinine, N (%)	60 (94)
Proteinuria, N (%)	4 (6)
Hematuria, N (%)	2 (3)
Proteinuria and hematuria, N (%)	51 (80)
Biopsy, N (%)	45 (70)
Pauci-immune necrotizing crescentic	18 (40)
Membranous nephropathy	6 (13)
Other glomerulonephritides	14 (31)
Not specified	7 (16)

Table 3: Laboratory characteristics, treatment and outcome in 300 patients with Levamisole induced vasculitis. Data are presented as frequency (with percentage)

Laboratory characteristics	
Hematological parameters	
Leukopenia, N (%)	123 (41)
Agranulocytosis, N (%)	13 (4)
Anemia, N (%)	87 (29)
Thrombocytopenia, N (%)	21 (7)
Autoantibodies	
ANA, N (%)	106 (35)
ANCA*, N (%)	246 (82)
Immunofluorescence	
Atypical, N (%)	21 (7)
c-ANCA, N (%)	52 (18)
p-ANCA, N (%)	197 (66)
Solid-phase immunoassays (ELISA)	
Anti-PR3, N (%)	101 (34)
Anti-MPO, N (%)	138 (46)
Anti-HNE, N (%)	20 (7)
Anti-phospholipids, N (%)	144 (48)
Other parameters	
Low C3, N (%)	56 (19)
Low C4, N (%)	48 (16)
Treatment and outcome	
Treatment	
Steroids, N (%)	143 (48)
Immunosuppression other than steroids, N (%)	56 (19)
Surgery, N (%)	43 (18)
Amputation, N (%)	8 (3)
Plasmapheresis, N (%)	12 (4)
Hemodialysis, N (%)	20 (7)
Outcome	
Good, N (%)	112 (37)
Bad+, N (%)	71 (24)

+scarring, amputation, residual organ damage, ongoing drug consumption and disease, death
* The predominant ANCA patterns, listed in descending order, were: isolated p-ANCA (61 patients), p-ANCA and anti-MPO (48 patients), p-ANCA anti-MPO and anti-PR3 (35 patients), p-ANCA c-ANCA anti-MPO and anti-PR3 (27 patients)

OC 15

Pattern Identification of Adverse Events to Predict Patient Trajectory during the First Two Years of Peritoneal Dialysis

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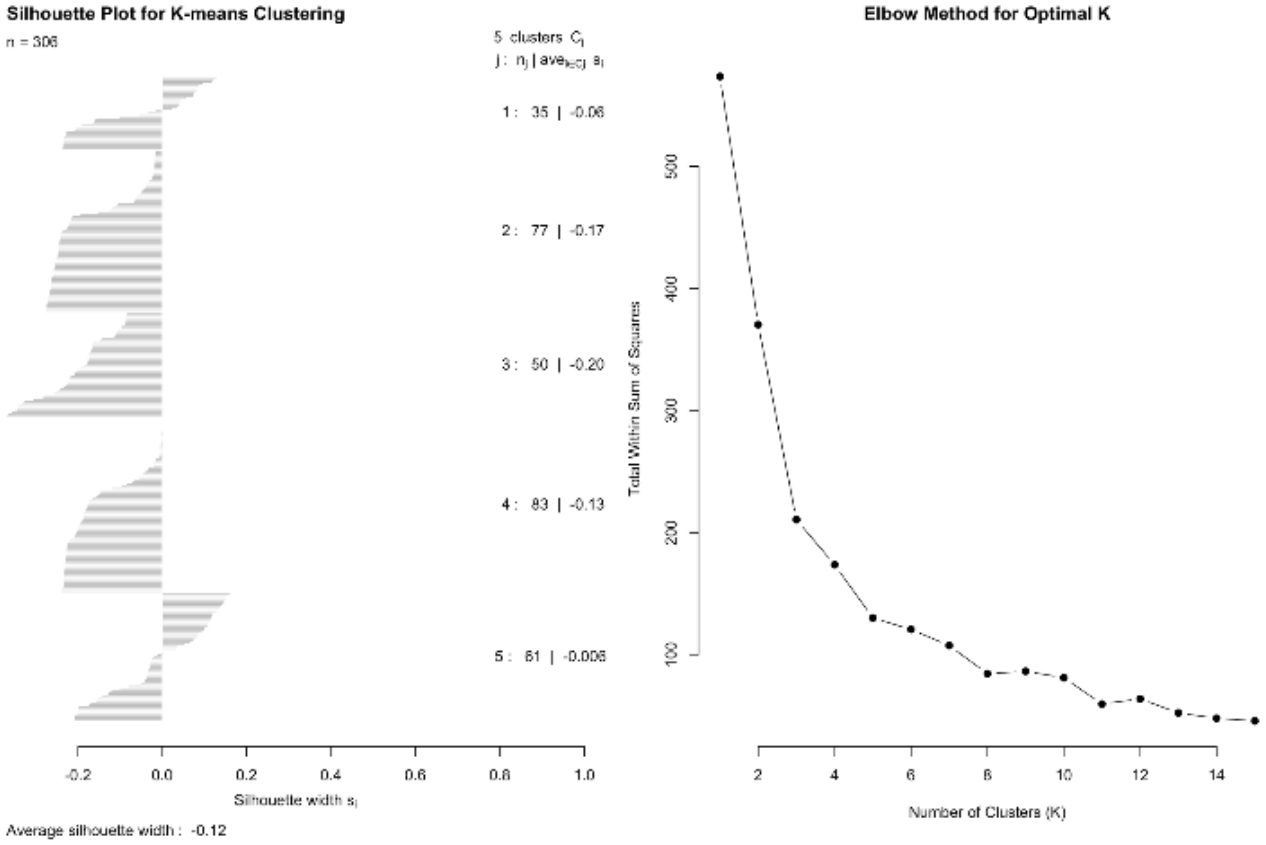
Importance: Adverse events (AE) during peritoneal dialysis are common and, along with technique failure, can lead to discontinuation of peritoneal dialysis (PD) treatment when severe. However, the relationship between different AE is not entirely understood.

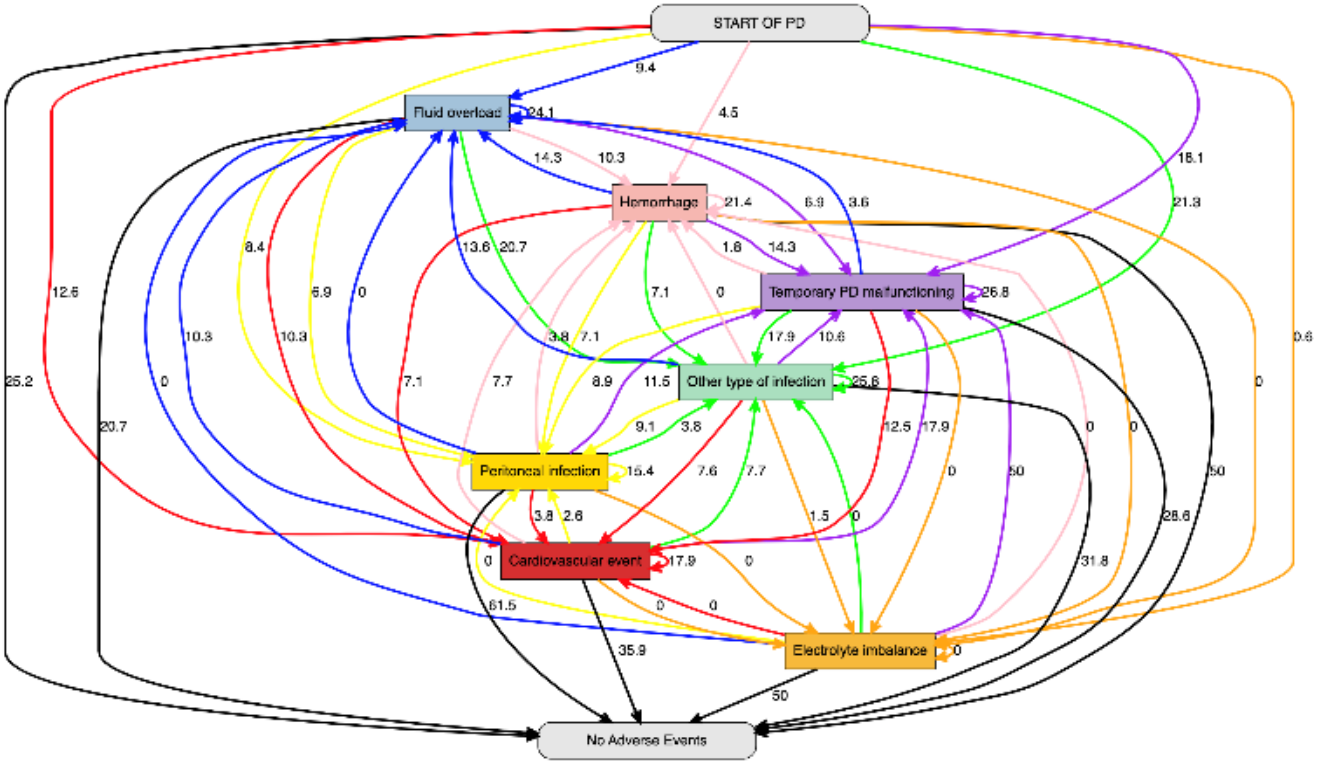
Objectives: We aim to investigate the association between AE during the first two years of PD treatment and create a Bayesian probability tree diagram to illustrate these relationships.

Design: In this retrospective cohort study, we analyzed 342 patients on PD from nephrology centers in Lugano and Brescia between 2000 – 2020. Clinical, laboratory, and outcome data were systematically collected every three months, starting 12 months before and ending two years after PD initiation. Our methods included descriptive statistics, Bayesian probability assessment and clustering based on patient characteristics and number of AE. The AE were analyzed in sequence, independent of their timing, to construct a Bayesian probability three that elucidates their relationship.

Results: The mean age of patients was 67 ± 15 years, with 63% males. Hypertension, dyslipidemia and diabetes were the most prevalent comorbidities. At the start of PD, the mean daily urine output was 1598 ± 593 mL, and the estimated mean glomerular filtration rate was 9.8 ml/min/m^2. PD discontinuation occurred on average after 773 days from inception. Only 25.2% had no AE during the first two years of treatment. Cardiovascular (CV) was the leading cause of death (20.0%). Overall, the AE included infections (21.3%), PD catheter malfunction (18.1%), CV events (12.6%), fluid overload (9.4%) and infections (8.4%). The Bayesian tree suggests that the AE sequence depends on the first AE type (Figure 1). Cluster analysis supports this finding, revealing five distinct pathways between the initial and subsequent AE (Figure 2).

Conclusions and Relevance: If confirmed, these preliminary findings allow for predicting the trajectory of patients during the first two years of PD treatment.





OC 16

Prediction of Peritoneal Dialysis Discontinuation at Two Years from Inception

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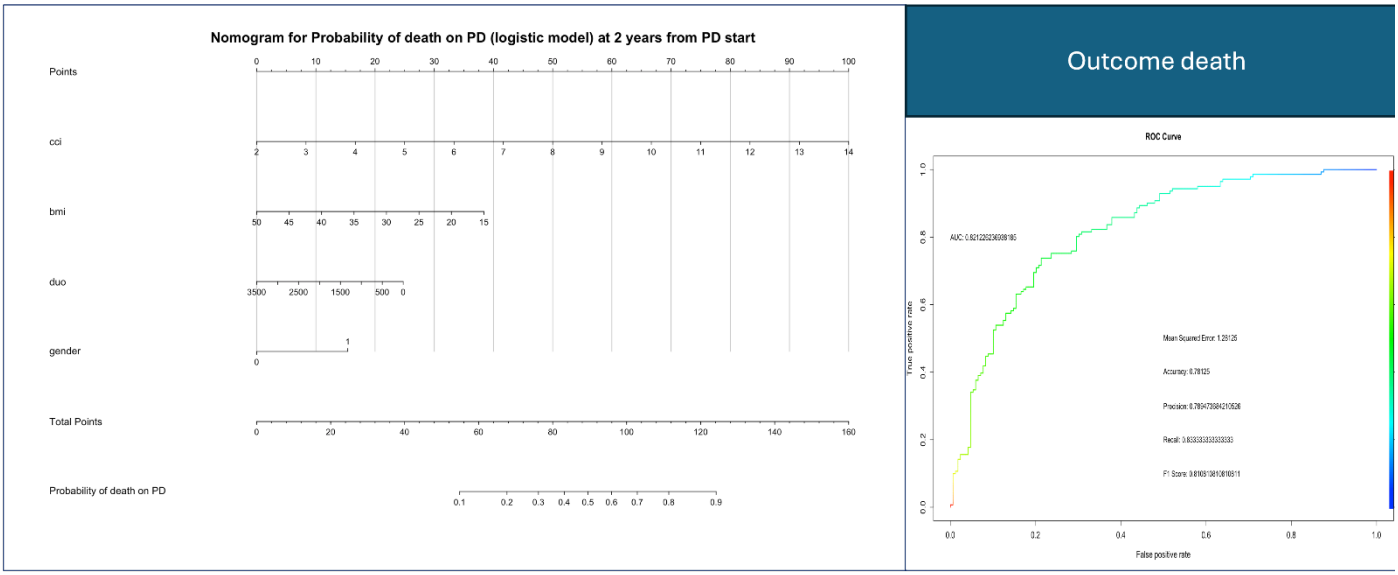
Importance: Peritoneal dialysis (PD) discontinuation is frequent in the first two years of treatment due to adverse events (AE), PD failure and deaths. Although several risk factors have already been identified, we need validated models to predict PD discontinuation.

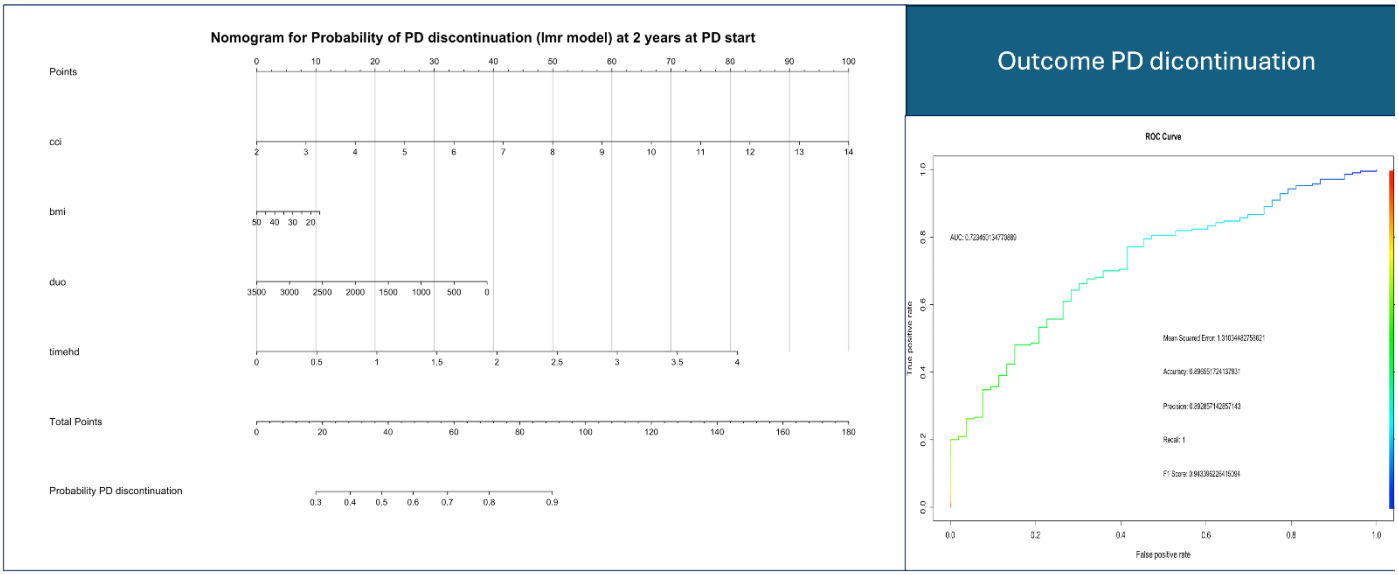
Objectives: We aim to identify risk factors and develop a nomogram to predict PD discontinuation and death within the first two years of treatment.

Design: In this retrospective cohort study, we analyzed 342 patients on PD from nephrology centers in Lugano and Brescia between 2000 – 2020. Clinical, laboratory, and outcome data were systematically collected every three months, starting 12 months before and ending two years after PD initiation. Statistical analysis included descriptive and survival statistics. Stepwise selection, cross-validation and receiver-operator characteristics curve (ROC) analysis identified the most parsimonious model for predicting PD failure and death.

Results: The mean age of patients was 67 ± 15 years, with 63% males. Hypertension, dyslipidemia and diabetes were the most prevalent comorbidities. At the start of PD, mean daily urine output (DUO) was 1598 ± 593 mL and estimated mean glomerular filtration rate was 9.8 ml/min/m^2. PD discontinuation occurred on average after 773 days from inception. Only 25.2% of patients had no AE during the first two years of treatment. Cardiovascular was the leading cause of death (20.0%). The best predicting models retained the following variables: Charlston comorbidity index (CCI) score, body mass index (BMI), DUO, gender and time on hemodialysis before PD (timeHD). The ROC for predicting deaths and treatment discontinuation at two years have an area under the curve of 0.82 and 0.72, respectively. The nomograms predicting these outcomes are shown in Figures 1 and 2.

Conclusions and Relevance: These preliminary findings may provide physicians with a useful tool for patient selection and prediction of PD discontinuation if confirmed and externally validated.





OC 17

Projecting the Clinical and Environmental Burden of CKD in Switzerland until 2032 – the IMPACT-CKD model in action

Dr. Stefan Buff[1], Dr. Thomas Campbell-James[1], Prof. Andrew Hall[2], Prof. Thomas Rosemann[3], Ms. Caterina Vecchio Rodriguez[4], Mr. Anthony Zara[5], Ms. Stacey Priest[5], Dr. Naveen Rao[6], Prof. George Wharton[7], Prof. Menno Pruijm[8]

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Background: Chronic kidney disease (CKD) is a leading cause of morbidity and mortality, impacting over 840 million worldwide. An estimated 10.9% of the Swiss population are affected, but projections for the future are lacking. This study aimed to support strategic planning by quantifying and projecting the burden of CKD on clinical, public health and environmental outcomes until 2032.

Methods: IMPACT-CKD, an internationally validated patient-level simulation model, was adapted to quantify and project CKD-progression and outcomes in the Swiss population over 10 years. Based on Swiss Real-World Evidence (RWE), one million simulated individuals were assigned an estimated glomerular filtration rate (eGFR), urine albumin-creatinine ratio (UACR), comorbidities and clinical events. The model categorised individuals into non-CKD or one of six CKD-stages (including KDIGO 1-5 and dialysis/transplant). Disease progression was predicted by annual eGFR-decline. CKD stage-associated environmental impact was calculated via Life Cycle Assessment (LCA). Input parameters and outcomes underwent validation against literature, RWE and expert consultation.

Results: Between 2022 and 2032, the model projected Switzerland's cases of CKD to rise by 6.7% to 1.03 million patients; of these, 65.5% could remain undiagnosed. Majority stage prevalence is projected to shift from stages 1 and 2 in 2022 (54.6%) to stages 3 to 5 in 2032 (50.3%), leading to a significant increase in CKD-related emergency room visits (+22.8%), hospitalisations (+25.2%) and deaths (+49.7%). The number of transplant and dialysis patients are also projected to increase by 62.3% and 51.4%, respectively. The associated total freshwater consumption and carbon production among CKD-patients are predicted to rise by 17.3% and 12.9% respectively. Results are summarized in Table 1.

Conclusion: By 2032, Switzerland's CKD-population is expected to undergo a shift to later KDIGO-stages, resulting in higher healthcare resource usage and heavy environmental impact. Significant preventive healthcare strategies and planning are required to mitigate this projected shift.

	Outcome	2022	2032	% Change from 2022 to 2032
Clinical Impact	CKD (All)	961 K	1.03 M	6.7%
	CKD (1-2)	525 K	510 K	-2.8%
	CKD (3-5)	437 K	516 K	18.1%
	Dialysis	3,896	5,898	51.4%
	Transplant	4,469	7,255	62.3%
	RRT	8,366	13,153	57.2%
	Deaths in CKD patients	26.4 K	39.6 K	49.7%
Healthcare Resource Use	ER Visits	126 K	155 K	22.8%
	Hospitalizations	238 K	298 K	25.2%
	Outpatient Visits	1.1 M	1.3 M	25.0%
Environmental Impact	Freshwater Consumption (m^3)	3,939,131	4,621,461	17.3%
	Overall Carbon Footprint (kg CO_2 eq.)	229,650,643	259,369,573	12.9%

OC 18

Purinergic calcium signaling drives tubulo-interstitial crosstalk in kidney disease

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Background: Chronic kidney disease (CKD) presents a major global health problem that affects patients, their families, and healthcare systems. CKD is triggered by injury to tubules, which induces the release of signaling factors that stimulate surrounding fibroblasts, resulting in excessive extracellular matrix deposition, interstitial fibrosis and progressive kidney damage. Identifying molecular mechanisms of tubulo-interstitial crosstalk could reveal new therapeutic targets to prevent tubular insults translating into CKD. Calcium is a critical second messenger that regulates multiple processes within cells, but its involvement in renal fibroblast activation was previously unclear.

Methods: To visualize intracellular calcium changes in kidneys, we generated transgenic mice expressing a highly sensitive fluorescent calcium reporter, and imaged these using intravital multiphoton microscopy. In parallel, we performed mechanistic studies in a rat renal fibroblast cell line.

Results: We discovered that renal fibroblasts display spontaneous calcium activity in vivo, which increased markedly in response to tubular injury (cisplatin toxicity) and upon induction

of fibrosis by unilateral ureteric obstruction (UUO). Moreover, damaged cells can release pyrimidine nucleotides, and we found that uridine diphosphate (UDP) or synthetic agonists of its target purinergic receptor (P2Y6R) produced acute rises in intracellular calcium in renal fibroblasts. P2Y6R activation also stimulated proliferation, migration, and expression of pro-fibrotic markers in renal fibroblasts in vitro. Conversely, knockout or pharmacological inhibition of the P2Y6R in mice exposed to UUO or folic acid nephropathy (another well-established CKD model) decreased fibroblast proliferation, myofibroblast activation, macrophage infiltration, collagen 1 expression, and fibrosis.

Conclusions: We provide evidence that purinergic calcium signaling mediates tubulo-interstitial crosstalk in CKD and represents a potential therapeutic target to reduce fibrosis.

OC 19

Single-nucleus analysis reveals excessive and adverse FGF23 effects in the distal nephron during early diabetic nephropathy

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Background: Circulating fibroblast Growth Factor 23 (FGF23) increases dramatically during progression of chronic kidney disease, in part attributable to end-organ resistance with diminished renal abundance of FGF23 co-receptor Klotho. Here, we investigated cell-specific renal actions of FGF23 in mice with early diabetic kidney disease (DKD).

Methods: DBA/2J mice received sex-adapted doses of streptozotocin or vehicle to induce DKD. After measurement of glomerular filtration rate (GFR), mice received FGF23 300ng or vehicle. After 1h, spot urines, blood samples and organs were collected. 10X Chromium Single Cell 3' Gene Expression kit v4 was used for renal single-nuclei profiling, followed by alignment in Cell Ranger, Seurat workflow, pseudo-bulk and gene ontology analyses.

Results: Streptozotocin-treated mice showed elevated blood glucose from the 15th day on. After 56 days, male mice developed early DKD with 6-fold increased urinary albumin/creatinine, a 50% increase in blood urea nitrogen, and 30% reduction in body weight but a preserved GFR. Females only tended to increase urinary albumin/creatinine 1.4-fold. From 16 males' kidneys, 300'000 nuclei were sequenced. Thirty cell clusters were annotated, containing the major renal cell types. Klotho expression was preserved in early DKD. FGF23 induced strongest *Egr1* expression in proximal tubule (PT)-segment 1. FGF23 predominantly induced *Cyp24a1* expression in distal convoluted tubule-connecting tubule (DCT-CNT) and PT segment 1, and stronger so in healthy mice than in DKD. ERK signaling and *Hbegf*, a secondary mediator of FGF23, were mostly induced in PT-segment 2. Pseudo-bulk analyses revealed a substantial hyperresponsiveness to FGF23 in DCT-CNT during DKD, dominated by gene ontologies of pro-inflammatory responses.

Conclusion: FGF23 induces heterogenous and renal tubular segment-specific signaling, with qualitative alterations favoring adverse effects in the distal nephron of murine early DKD. The present dataset will enhance the understanding of aberrant and cell-specific actions of FGF23 in kidney disease.

OC 20

Survival of hemodialysis versus peritoneal dialysis patients: A Swiss perspective

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Background: Research on survival between hemodialysis (HD) and peritoneal dialysis (PD) patients presents mixed outcomes. Some studies suggest an advantage with HD, while others find no significant differences or suggest PD might be superior for certain patient groups. This study aims to determine whether there are differences in survival between these dialysis modalities in Switzerland.

Methods: Data on 8'045 incident dialysis patients in Switzerland from 2014 to 2023 were obtained from the Swiss Dialysis Registry (srrqap). The cohort included 6'945 patients receiving HD and 1'100 patients receiving PD. An intention-to-treat analysis using cause-specific Cox regression was used to compare mortality rates between PD and HD patients.

Results: Baseline characteristics of the dialysis population, stratified by modality, are detailed in Table 1. The crude mortality rate was higher in HD patients, with 1'350 deaths per 10'000 person-years, compared to 1'153 deaths per 10'000 person-years in PD patients. Analysis of cumulative incidence of death, considering transplantation and renal recovery as competing risks, revealed significantly higher mortality in HD patients compared to PD patients (p = 0.013). However, after adjusting for age, sex, BMI, and Charlson score, the cause-specific Cox regression analysis showed that hemodialysis is associated with better chances of survival (HR = 0.857, 95% CI 0.756, 0.961, p = 0.008) when compared to peritoneal dialysis.

Conclusion: This study reveals that while crude survival is lower in HD patients compared to PD patients, the difference diminishes after adjusting for factors like age, sex, BMI, and Charlson score. The cause-specific Cox regression analysis indicates a slightly higher chance of survival for HD patients when these variables are controlled. Further research is needed to refine treatment strategies and understand the nuances of dialysis outcomes.

Table 1: Baseline characteristics according to dialysis modality

Characteristics	Total (n=8'045)	HD (n=6'945)	PD (n=1'110)	P value
Age, yrs	66.3 ± 15.8	67.4 ± 14.9	59.4 ± 19.3	**0.000**
Gender male, %	66.8	66.7	67.4	0.669
Caucasian, %	92.5	92.6	91.8	0.346
Dialysis vintage, yrs	2.84 ± 2.17	2.84 ± 2.18	2.79 ± 2.09	0.462
Public center/hospital, %	71.8	69.9	83.6	**0.000**
BMI, kg/m²	26.4 ± 5.6	26.5 ± 5.8	25.6 ± 5.2	**0.000**
Residual kidney function, ml/min	6.5 ± 5.2	6.3 ± 5.2	7.2 ± 4.7	**0.000**
Catheter, %	-	54.5	-	-
Diabetes mellitus, %	38.0	39.3	29.9	**0.000**
Myocardial infarction, %	10.7	11.2	7.6	**0.000**
Congestive heart failure, %	19.9	20.8	14.7	**0.000**
Peripheral vascular disease, %	19.6	20.8	12.4	**0.000**
Cerebrovascular disease, %	11.3	11.8	8.1	**0.000**
Chronic pulmonary disease, %	14.0	14.4	11.3	**0.006**
Liver disease, %	6.2	6.6	3.7	**0.000**
Cancer, %	17.4	18.3	11.7	**0.000**
Charlson comorbidity index, n	4.2 ± 2.2	4.3 ± 2.2	3.6 ± 2.0	**0.000**

OC 21

Swiss Salt Study 2, second survey on salt consumption in Switzerland

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The WHO calls for dietary sodium intake reduction in populations and recommends a salt intake below 5 grams per person per day. Low sodium consumption is also recommended for patients with hypertension and chronic kidney disease. Switzerland targets an intermediate goal of less than 8 g per person per day. The first national Swiss Salt Study (2010-2011) found an average salt intake of 9.1 g/day (women 7.8 g/day, men 10.6 g/day). The second Swiss Salt Study (2022-2023) aimed to monitor salt intake in the Swiss population. Dietary salt (NaCl) intake was estimated through 24-hour urine collections from a random sample of 863 adult residents in Switzerland (413 women, 450 men; mean age ± SD: 49.2 ± 16.4 years). Anthropometry and blood pressure (BP) were measured using standardized, validated methods during study visits. The urinary NaCl excretion (mean ± SD) was 8.7 ± 3.6 g/day (women 7.4 ± 2.8 g/day, men 9.9 ± 3.9 g/day). Only 20.9% of women and 7.8% of men had a NaCl excretion below 5 g/day. Hypertension prevalence was 24.0%, with 15.3% in women and 32.1% in men. A slight decrease of 0.42 g/24h (4.6%) in mean salt intake was observed between the surveys, while hypertension prevalence remained stable. In this cross-sectional study, BP was positively associated with urinary NaCl excretion. This relationship was stronger in men than in women and stronger in older than in younger people. Higher body mass index was also associated with higher urinary salt excretion and higher BP. Despite the encouraging decrease observed in the mean dietary salt intake between the first and second national surveys, salt intake of Swiss adults remains above the national and international targets. Efforts must continue to promote salt reduction and healthy weight in the population in the prevention of hypertension and associated complications.

OC 22

Targeting CD38 in antibody-mediated rejection – the potential of noninvasive biomarkers to detect rejection reversal and recurrence

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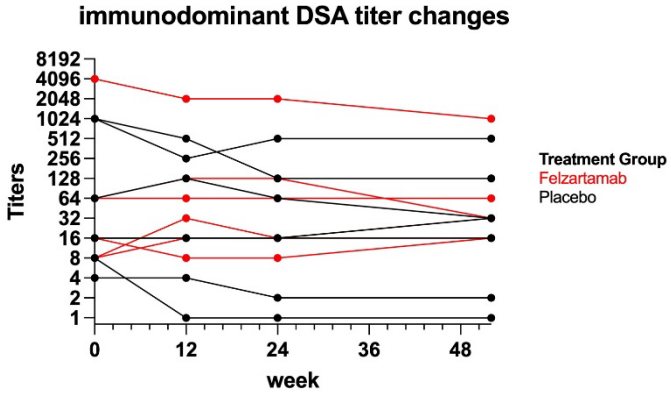
Background: In a recent phase 2 trial, the CD38 antibody felzartamab showed to reverse antibody-mediated rejection activity after kidney transplantation, presumably through the depletion of natural killer (NK) cells (Mayer et al., NEJM 2024; 391:122). In this sub-study of the felzartamab trial, we aimed to evaluate, whether noninvasive biomarkers – reflecting plasma cell activity (donor-specific antibodies [DSA]), graft injury (donor-derived cell-free DNA [dd-cfDNA]), inflammation (C-X-C motif chemokine ligand [CXCL]9 and 10), and NK cell integrity – could accurately indicate rejection resolution and/or recurrence after treatment discontinuation.

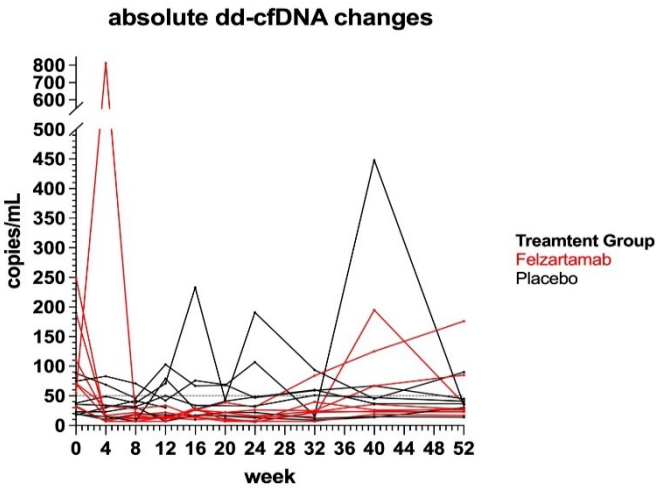
Methods: Twenty-two recipients were randomized to receive either felzartamab (n = 11) or placebo (n = 11) for 6 months, followed by a 6-month observational period. Follow-up biopsies were performed at weeks 24 and 52. DSA mean fluorescence intensities (MFI) and titers, along with (serum and urinary) CXCL9/10 levels were assessed using microbead assays. NK cell counts and dd-cfDNA levels were quantified via flow cytometry and digital droplet PCR, respectively.

Results: By week 24, treatment with felzartamab resulted in a profound reduction in $CD16^{bright}$ NK cell counts (-84.7% vs. 18.1% in placebo patients), with counts returning toward baseline by week 52. Similarly, after felzartamab treatment absolute dd-cfDNA levels profoundly decreased (-80.7% vs. 9.4%), followed by an increase towards baseline by week 52. A re-analysis of 16 patients (8 felzartamab patients) demonstrated a marked reduction in dd-cfDNA levels as early as 4 weeks after treatment initiation. However, dd-cfDNA began to rise within 12 weeks (at week 32) after the last felzartamab infusion (at week 20). DSA MFI levels/titers and chemokine levels in serum and urine showed no meaningful changes.

Conclusions: These results suggest that dd-cfDNA measurement may be a useful tool for monitoring responsiveness to fel-



zartamab already within the first weeks after treatment initiation. Additionally, dd-cfDNA could serve as an early indicator of rejection recurrence requiring further investigation.



OC 23

Taurine Deficiency Is a Hallmark of Injured Kidney Allografts

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Background: Taurine is a non-proteinogenic amino acid widely distributed in human tissues. In mammals, taurine is synthesized from cysteine via cysteine sulfinic acid decarboxylase (CSAD) or absorbed from the diet through the sodium chloride-dependent transporter SLC6A6 (TauT). Low taurine levels are associated with cellular senescence, mitochondrial dysfunction, DNA damage, and inflammation, all of which can be reversed by supplementation. It is unknown whether taurine metabolism is associated with kidney allograft function and survival.

Methods: We performed urine metabolomic profiling of kidney transplant recipients in the early and in the late phase after transplantation combined with transcriptomic analysis of human kidney allografts and single-nucleus RNA sequencing of mouse kidneys after ischemia–reperfusion injury. We analyzed the association of urinary taurine levels and taurine metabolism genes with kidney function, histology, and graft survival.

Results: Urine taurine concentrations were significantly lower in kidney transplant recipients who experienced delayed graft function. In a mouse model of ischemia–reperfusion injury, the taurine biosynthesis gene, *CSAD*, but not the taurine transporter *SLC6A6*, remained repressed in chronically injured cells. In kidney transplant recipients, low urinary taurine levels were associated with reduced kidney function and histological evidence of chronic kidney injury. Urine taurine levels in the lowest tertile were predictive of graft loss. The expression level of the taurine transporter *SLC6A6*, but not *CSAD*, was associated with chronic kidney injury and was predictive of graft loss.

Conclusions: Low urine taurine is a marker of injury in kidney allografts, is associated with poor kidney function and is predictive of reduced graft survival. Our findings suggest that different mechanisms might affect the taurine metabolism in the early and late phase after transplantation.

OC 24

Very long-term outcome of ABO incompatible kidney transplantation at the University Hospital Basel

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Background: This study aims to investigate and compare clinical outcomes between ABO-compatible (ABOc) and ABO-incompatible (ABOi) living donor kidney transplantations (LDKT) at the University Hospital Basel over a period of almost 20-years.

Methods: A retrospective single-center analysis was conducted on a cohort of 441 patients who underwent LDKT between January 2005 and July 2022. 348 patients received ABOc transplants, while 93 patients received ABOi transplants. Patient baseline characteristics and relevant follow-up parameters were systematically assessed. For ABOi-LDKT a desensitization protocol was used.

Results: Patient survival was not significantly different (p = 0.84) between ABOc and ABOi transplants in our cohort. Similarly, death-censored graft survival rates were similar at all time points (p = 0.57, Figure 1). Complication rates, including delayed graft function, primary non-function, and infections, did not differ significantly between the groups. Renal function (eGFR) was equal between the groups over the entire observation period (57 ml/min/1.73m^2 in both groups at one-year, p = 0.96, Figure 2). Sub- and clinical biopsy-proven antibody-mediated rejection episodes occurred more frequently in ABOi recipients (46.2% vs. 10.6%, p<0.001) as well as clinical rejections (41.9% vs. 25.6%, p<0.002). Multivariable analysis identified clinical biopsy-proven rejections (ABMR + TCMR) as a significant risk factor for graft loss (Odds ratio [OR] 4.13, 95% CI 1.66–10.25, p = 0.002).

Conclusion: ABOi-LDKTs in our cohort has an excellent outcome regarding patient and graft survival as well as graft function during long-term follow-up compared to ABOc-LDKTs. Incompatible kidney transplantation increases the number of LDKT by 20%, reduces the organ shortage and gives more patients the opportunity of preemptive transplantation. Although more antibody mediated and clinical rejections were observed in the ABOi group, there was no increased risk of graft loss. This study shows that when using an appropriate desensitization protocol, ABOi-LDKT is a safe procedure with comparable outcomes compared to ABOc-LDKT for patients with no compatible transplant available.

Figure 1

A Cumulative incidence of patient survival of all ABO-compatible and ABO-incompatible transpl
study period (Kaplan-Meier estimates). P-value according to the log-rank test.

B Cumulative incidence of death-censored graft survival of all ABO-compatible and ABO-incom
transplants during the study period (Kaplan-Meier estimates). P-value according to the log-rank te

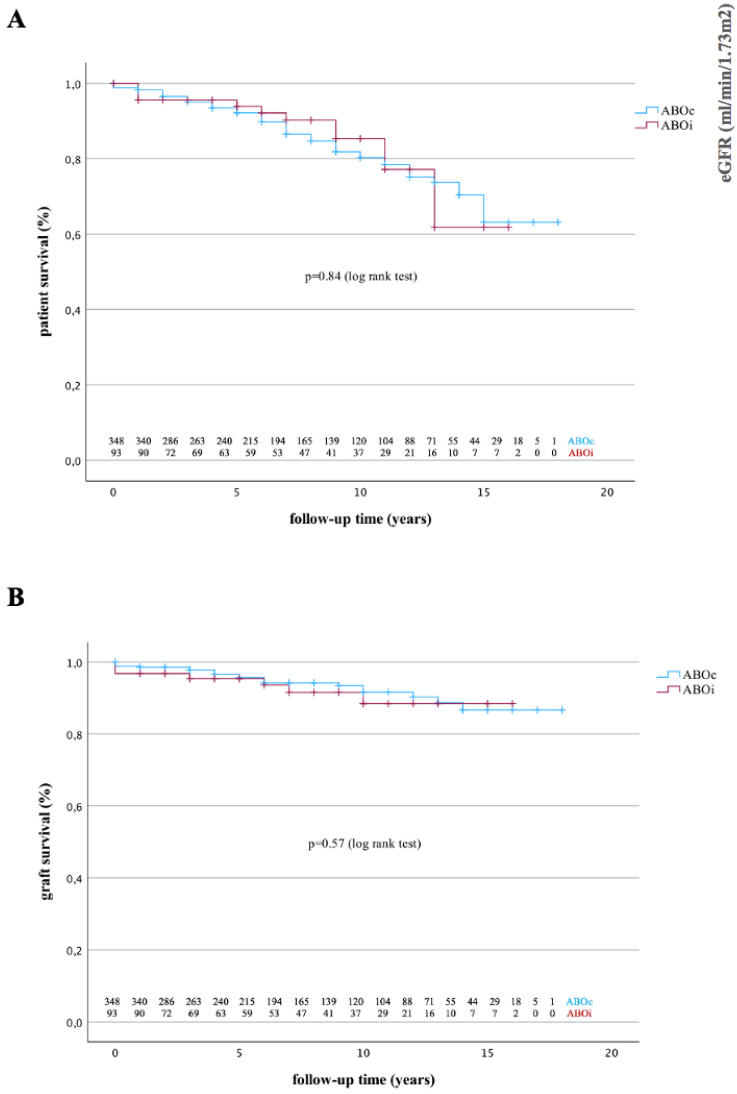
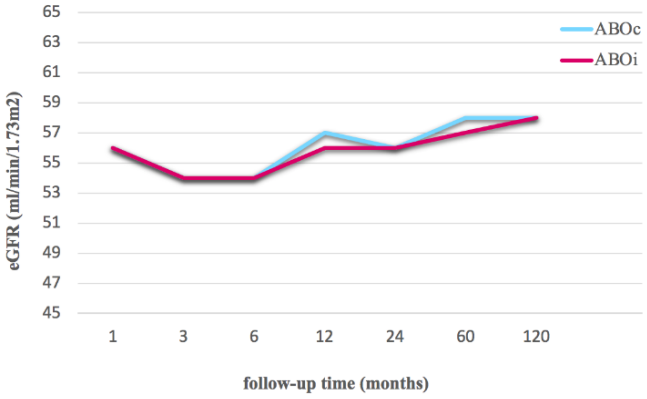


Figure 2. Graft function over 10-year follow-up time of ABO-compatible transplants and ABO-incompatible transplants. Shown is median.



SHORT ORAL PRESENTATIONS

OC 25

Biopsy-based transcript diagnostics show an early molecular AMR signature in cases with probable AMR independent from the individual active histological lesions

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Background: The category "suspicious for antibody mediated rejection (AMR)" in Banff 2013 was abandoned in Banff 2017 and replaced by "DSA-negative microvascular inflammation" and "probable AMR" in Banff 2022. Probable AMR represents a heterogenous group of DSA-positive cases with active AMR features (v/g/ptc/TMA) and/or chronic AMR features (cg/ptcml). Biopsy-based transcript diagnostics may add value in these cases.

Methods: We identified 64 cases with probable AMR by histology, that were categorized into active (n = 23), chronic-active (n = 20) and chronic (n = 21) cases. The Molecular Microscope Diagnostic System (MMDx) was performed in all cases including analyzed classifier scores and rejection phenotype scores.

Results: Among 64 cases with probable AMR, 10 showed molecular AMR (17%) and 6 (10%) possible molecular AMR (all AMR phenotype score >0.3). 7 of 16 cases (44%) with molecular/possible molecular AMR underwent kidney allograft biopsy for subclinical DSA. 10 of 23 cases (43%) with active, 4 of 20 cases (20%) with chronic-active, and 2 of 21 cases (10%) with chronic AMR features showed molecular/possible molecular AMR. 6 of 14 cases (43%) with v1-lesions, 10 of 31 (32%) with g1-lesions, and 2 of 5 (40%) with ptc1-lesions showed molecular/possible molecular AMR. Among 16 cases with molecular/possible molecular AMR, median rejection phenotype scores R4, R5, and R6 were 0.29 (IQR 0.06, 0.44), 0.03 (IQR 0.00, 0.11), and 0.07 (IQR 0.01, 0.17), respectively (p = 0.028). Interestingly, 2 chronic cases with molecular/possible molecular AMR showed elevated R5 and R6 scores only.

Discussion: Biopsy-based transcript diagnostics identified evidence of molecular AMR in more than a third of cases with active AMR features on histology, independent from the individual active AMR features (v/g/ptc). Predominant R4 scores suggest an early molecular AMR signature. Activity and chronicity appear to be gradually reflected by rejection phenotype scores. Whether donor-derived cell-free DNA could identify those cases needs to be addressed.

OC 26

Cell fate determination of directly reprogrammed mouse and human kidney cells

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Background: Despite an increasing demand to understand and treat kidney diseases, options for modeling these conditions *in vitro* remain limited. Our interest lies in deciphering the molecular programs guiding kidney development and disease, and we have pioneered the direct reprogramming of renal tubular cells [1]. Yet, the process of direct reprogramming isn't fully understood. Ongoing investigations are needed to characterize outcomes in terms of assay stability and cellular heterogeneity.

Methods: Cell type conversion from mouse fibroblasts to induced renal epithelial cells (iRECs) is achieved by the transduction of only four transcription factors. iRECs are morphologically and functionally highly similar to primary kidney cells but can be stably cultivated and bioprinted into tubular structures at near physiological scales [2]. Our current focus lies in a comprehensive exploration of the molecular nature of iRECs through a detailed analysis employing bulk and single-cell RNA sequencing.

Results: We tested the impact of culturing conditions, timing and stability-enhancing compounds on the direct reprogramming and thereby managed to optimize the efficiency from 1% to 10%. This allowed us to further investigate the nature of our iRECs in very detail by checking the transcriptome of individual cells. In that course we identify different kidney cell type identities. Furthermore, we were able to generate human iRECs which allowed us to test additional transcription factors and explore their impact during kidney development.

Conclusion: These efforts aim to refine direct reprogramming methods, enhancing their effectiveness and reliability for potential applications in drug testing and disease modeling in the future.

– Kaminski MM. et al. Direct reprogramming of fibroblasts into renal tubular epithelial cells by defined transcription factors. *Nat.Cell Biol.* (2016)
– Pichler R. & Rizzo L. et al. Tuning the 3D microenvironment of reprogrammed tubule cells enhances biomimetic modeling of polycystic kidney disease. Biomaterials (2022)

OC 27

cFGF23 alleviates kidney inflammatory pathways induced by sustained FGF23 signaling

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Background: Fibroblast growth factor 23 (FGF23) regulates renal mineral metabolism via FGF receptors (FGFR) and the coreceptor Klotho. FGF23 levels are highly elevated in patients with chronic kidney disease (CKD), but whether it serves merely as a biomarker or actively contributes to kidney inflammation remains unclear. It is unknown if the C-terminal FGF23 (cFGF23), a competitive inhibitor of FGF23-Klotho binding, can reduce kidney inflammation.

Methods: Immunoblotting, qRT-PCR, and comprehensive unbiased transcriptomics were performed in stably Klotho-expressing HEK293 cells following acute physiological or chronic pathological FGF23 treatments. RNA-seq was performed on the kidneys of Hyp-Duk mice (a model for lifelong elevated FGF23 levels) and Hyp-Duk mice harboring adeno-associated virus expressing cFGF23 (AAV-cFGF23).

Results: Acute physiological FGF23 levels *in vitro* elicit transient-ERK signaling with expression of canonical early-ERK targets (*EGR1, JUNB, FOSB*). In contrast, prolonged pathological FGF23 treatment revealed novel sustained-ERK signaling with upregulation of late-ERK targets (*ETV4/5, SPRED1/2, SPRY2/4*) and unique inflammatory and immune gene signatures. These effects were significantly mitigated by FGFR and ERK inhibitors,

as well as by recombinant cFGF23 treatment. Consistent with *in vitro* findings, Hyp-Duk mouse kidneys showed significantly upregulated late-ERK targets, but unchanged early-ERK targets, suggesting selective activation of sustained-ERK signaling. Furthermore, the key gene signatures of inflammation and immune pathways were also activated in the kidney of Hyp-Duk mice. Notably, both sustained-ERK and inflammatory and immune signaling pathways were significantly suppressed in the kidneys of AAV-cFGF23-treated Hyp-Duk mice.

Conclusion: Chronic high levels of FGF23 induce inflammatory and immune pathways in the kidneys through the FGFR-Klotho complex and sustained-ERK activation, which are successfully mitigated by cFGF23 gene therapy. FGF23 pathophysiology and therapeutics should extend beyond mineral metabolism and towards anti-inflammation.

OC 28

Early-stage antibody-mediated rejection: biopsy-based-transcript-diagnostics predict proteinuria in cases with subclinical donor-specific antibodies

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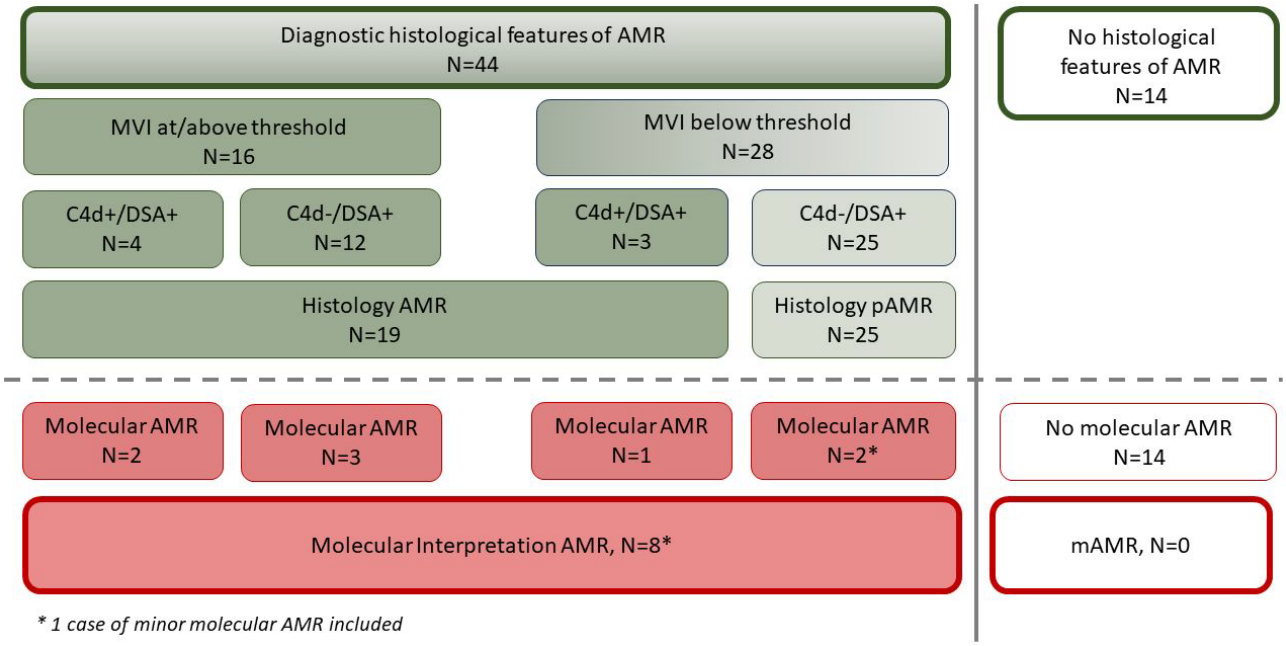
Background and hypothesis: While de novo or preformed donor-specific antibodies (DSA) accompanied by allograft dysfunction are accepted indications for kidney allograft biopsies, management of subclinical DSA lacks consensus. Biopsy-based transcript diagnostics using the Molecular Microscope Diagnostic System (MMDx) has the potential to add diagnostic clarification along the antibody-mediated rejection (AMR) continuum

Methods: In this single-center cohort of the University Hospital Zurich, we analyzed 58 indication biopsies performed for subclinical DSA that were assessed by histology, according to Banff 2022. The performance of MMDx concerning diagnostic specification and prognostication was investigated using the development of proteinuria ≥500mg/day during a median follow-up of 21 months.

Results: 6/19 (32%) cases with histological AMR (hAMR), 2/25 (8%) cases with probable hAMR, but 0/14 (0%) cases without hAMR showed molecular AMR (mAMR). mAMR was associated with higher median MFI levels (p = 0.007), more peritubular capillaritis (p = 0.04), and chronic-active hAMR (p = 0.048). Among 8 cases with mAMR, the early-stage AMR phenotype score R4 was significantly higher than the fully-developed and late-stage AMR phenotype scores R5 and R6 (p<0.05). 5/36 (14%) with hAMR features, but no mAMR showed possible mAMR with an all AMR phenotype score (R4+R5+R6) >0.3. 8 cases with mAMR were more likely to develop proteinuria >500mg/day than 36 cases with hAMR features but no mAMR (p = 0.03).

Conclusions: Biopsy-based transcript diagnostics identify early-stage AMR in subclinical DSA cases, with this detection remaining consistent even at molecular subthreshold levels. The development of proteinuria in cases with mAMR suggests the prognostic value of the MMDx in subclinical DSA cases.



OC 29

Elucidating the effects of sex, age and genetic variation on renal cell composition in two related genetically diverse mouse populations

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Background: Single-cell RNAseq data can be harnessed to infer cell type compositions of spatial or bulk transcriptomes, providing greater biological context for underlying systemic changes. Here, we used a transcriptome-based systems genetics approach to assess factors that influence renal composition, including sex, age and genetic variation in two genetically diverse mouse resource populations derived from the same 8 parental strains.

Methods: We used existing bulk RNAseq data from 188 Diversity Outbred (DO) mice and male/female pairs from 58 inbred strains of the Collaborative Cross (CC). DO mice were sacrificed at ages 6, 12 or 18 months. We used single-cell RNAseq data from healthy C57BL/6 mice as reference for cell-type decomposition of bulk transcriptomes. We then tested age and sex for associations with renal tubular segments and renal cell types. Furthermore, we assessed the genetic architecture of renal cell types through heritability estimation.

Results: Heritability of cell abundance traits substantially differed between inbred and outbred populations. We however observed a strong and consistent sex effect on renal proximal tubule (PT)-S3 and T cell abundance. Mice of sexes showed an age-related increase in B and T cells and overall renal immune cell content. The strongest quantitative trait loci (QTLs) in the CC mice were for proximal tubular or proliferating cell abundance, Monocytes/Granulocytes and T cells. For example, T cell abundance was strongly influenced by a wide QTL region overlapping the major histocompatibility complex on chromosome 17. QTLs in DO mice included one each for PT-S1, T cells, intercalated cells and distal-convoluted tubule.

Conclusion: This study emphasizes the value of these genetic resource populations for cross-validation of findings. Their outbred vs inbred genetic backgrounds allow for population-specific genetic effects and thus greater biological discoveries. Several of the renal tubular segments have narrow high confidence QTLs with promising candidate genes to follow up experimentally.

OC 30

Endo-lysosomal deacidification links disordered protein handling and lipid metabolism in kidney tubules

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Chronic kidney disease (CKD) is a global health problem and there is an urgent need to increase understanding of the underlying pathogenesis. CKD is characterized by increased urinary protein excretion (proteinuria) and dysregulated lipid metabolism in the proximal tubule (PT). The PT has a highly developed apical endo-lysosomal system (ELS) that normally retrieves and processes filtered plasma proteins, to prevent their loss in the urine. ELS defects are increasingly recognized as an important cause of CKD, but how exactly they produce CKD phenotypes is unclear. Acidification of endo-lysosomes is critical for their function; to visualize this process in the kidney we have designed fluorescent probes that target the PT in mice and provide ratiometric readouts of pH changes as they traverse through ELS compartments. By deploying intravital multiphoton microscopy and retrospective antibody staining, we have generated the first working maps of pH gradients within the PT ELS in vivo. Moreover, we have identified that acidified lysosomes are highly dynamic and interact with other organelles, including lipid droplets. Conversely, acute deacidification with the weak base hydroxychloroquine produces dramatic disturbances in ELS dynamics, including defective endocytic receptor recycling, extensive fusion of endo-lysosomes, and inhibition of lysosomal trafficking, culminating in impairment of protein uptake and proteinuria. Furthermore, increasing lysosomal pH also induces lipid accumulation in PT cells and enlargement of lipid droplets. In summary, we show that loss of endo-lysosomal acidification in the PT results in major defects in protein handling and lipid metabolism, which are two cardinal features of CKD in humans.

OC 31

FGF23 drives leukocyte migration to the kidney in glomerular disease

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Background: FGF23 excess is associated with morbidity and mortality, but the role of excessive circulating FGF23 concentrations as a mere biomarker or causative factor of pathology is controversial. Here, we investigated the renal consequences of FGF23 excess in murine and human kidney.

Methods: C57BL/6 mice were treated with Freud's adjuvant and nephrotoxic serum (NTS) to induce anti-glomerular basement membrane (anti-GBM) disease. Mice received intravenous injections of recombinant FGF23 1µg or vehicle for six consecutive days and were sacrificed 24h after the last injection. Glomerular filtration rate (GFR), serum biochemistry and 40 cytokines were measured. Kidneys were analyzed by histology, immunofluorescence and RNAseq. RNAseq data and published transcriptomes underwent bulk ligand-receptor interaction analysis and cell-type decomposition with reference to single-cell data. Renal transcriptomes of the KaroKidney cohort of 71 patients with IgA nephropathy underwent cell-type decomposition with reference to single-nucleus data, and patients' GFR and plasma FGF23 were measured.

Results: Anti-GBM mice showed a 45±27% GFR decline (mean±SD) compared to baseline; controls showed a GFR increase of 11±36% ($p<0.01$). Anti-GBM mice showed albuminuria and tubular casts. FGF23 increased circulating soluble TNF receptor-1. Renal transcriptomes revealed FGF23-driven proinflammatory transcriptional signatures in murine anti-GBM, but also adverse Vcam1, Pdgfrb and chemokine ligand-receptor signaling in anti-GBM but not in healthy mice. Finally, FGF23 excess was associated with transcriptome-inferred renal macrophage and overall leukocyte content in anti-GBM mice, *Fgf23* transgenic mice, Hyp mice and human patients with IgA nephropathy. Findings were confirmed by immunofluorescence in mice and histopathological grading reports of patients' biopsies.

Conclusion: FGF23-driven patterns of proinflammatory gene and protein expression or leukocyte migration to the kidney

were observed in different models or states of FGF23 excess. The present data may help to resolve controversies and provide additional evidence of FGF23 as a pathogenic agent, underlining the importance of phosphate restriction in kidney disease.

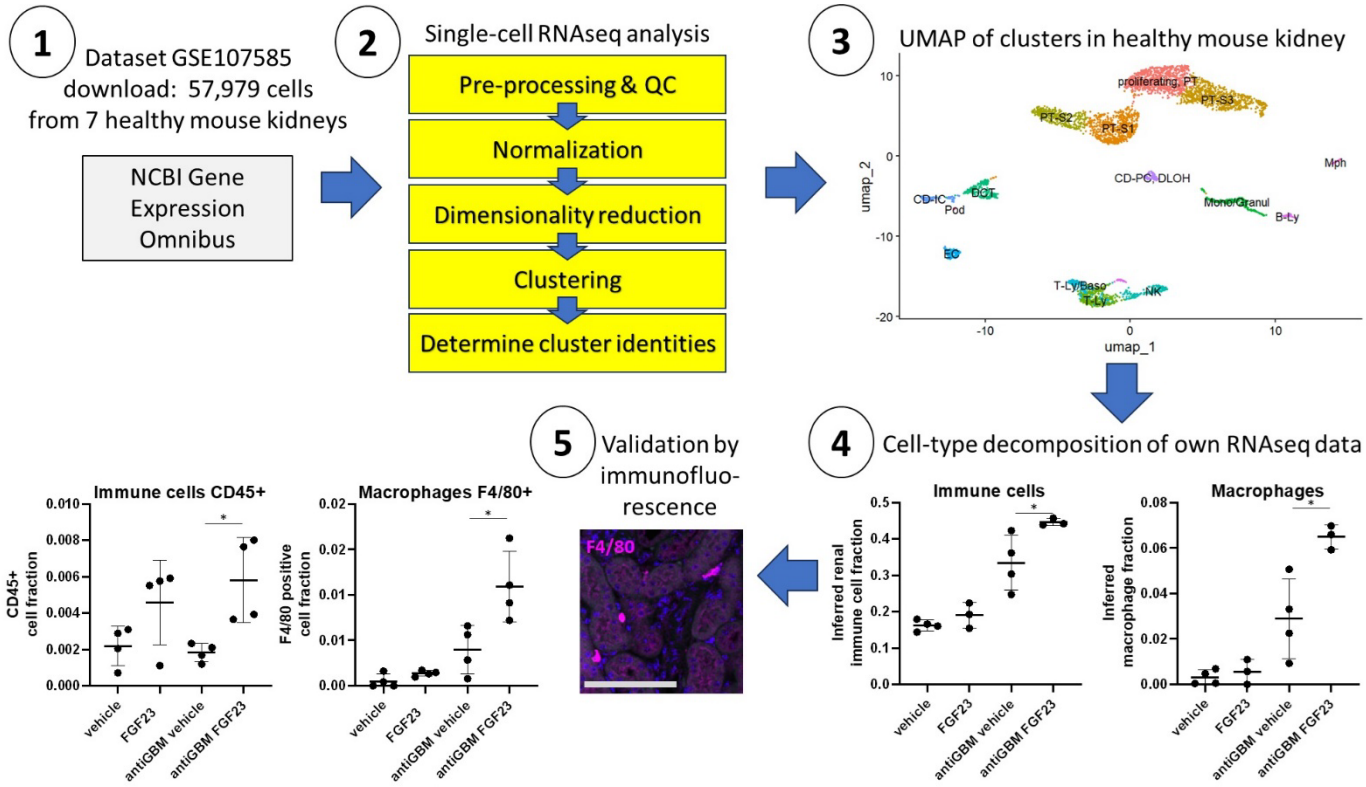

Figure 1. Analytical workflow to (1) import published single-cell RNAseq data (GSE107585), (2) reanalyze them using R/Seurat followed by (3) annotation and uniform manifold projection (UMAP) of cell clusters. Next, our own bulk RNAseq data were generated of kidney from mice with or without anti-glomerular basement disease (antiGBM), treated with FGF23 or vehicle for 6 days. Bulk RNAseq data then underwent cell-type decomposition using R/Bisque based on the single-cell reference. Transcriptome-inferred immune cells and macrophages were then (4) visualized across samples and (5) findings validated using renal immunofluorescence staining with antibodies against CD45 and F4/80 protein (shown). Scale bar = 100µm. Analysis by ANOVA and Holm-Sidak post-test.

OC 32

Gastric bypass-induced weight loss restores aldosterone reactivity to orthostatic stress in obese patients

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Introduction: Obesity is a major cause of hypertension. It is believed that the sympathetic nervous system (SNS), renin-angiotensin-aldosterone system (RAAS) and their effect on renal sodium handling play a predominant role in the pathogenesis of hypertension. Gastric bypass is associated with a decrease in blood pressure (BP), however the precise role of the SNS and RAAS after Roux-en-Y gastric bypass (RYGB) remains unclear. We investigated the effect of bypass-induced weight loss on the hemodynamic, hormonal, and renal responses to an orthostatic stress induced by lower body negative pressure (LBNP).

Methods: We conducted a monocentric observational study comparing response to LBNP (-30mbar) in two groups of patients. The first group underwent bypass surgery and diet counselling (RYGB group) and the second group received diet counselling only (control group). We studied sodium urinary excretion, hemodynamic and hormonal responses during a one-hour orthostatic stress induced by LBNP: 1 month before planned RYGB (intervention group), 3 and 12 months after the intervention.

Results: Thirty-seven adult obese patients were enrolled: 25 patients (72% women, age: 42.1yo ± 10.5) had RYGB and 12 were in control group (58.3% women, age: 44.8yo ± 13.6). At 12 months, the BMI decreased more in RYGB group (-15.02kg/m^2 ± 3.59) than in control group (-3.75kg/m^2 ± 5.97). During LBNP, the decrease in urinary sodium excretion was more marked in the RYGB (-0.03mmol/min; CI 95%, -0.062 to -0.005, p-value =

0.023) and during recovery (-0.04mmol/min, CI 95%; -0.079 to -0.004, p-value = 0.030). The increase in plasmatic aldosterone concentration was stronger in this group during LBNP (9.94pg/ml, CI 95%; 0.317 to 19.569, p-value = 0.043) and during recovery (11.68pg/ml, CI 95%; 2.376 to 20.985, p-value = 0.015).

Conclusions: Our study suggests that bypass-induced weight loss restores aldosterone response to orthostatic stress and enhances the sodium tubular response during orthostatic stress.

OC 33

Glomerulonephritis associated with acute human Parvovirus B19 infection: a report of 5 cases and a review of the literature

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Human parvovirus B19 (PVB19) infection has been associated with glomerular diseases, in particular collapsing focal and segmental glomerulosclerosis (cFSGS). We report five patients with newly diagnosed glomerulonephritis associated with acute PVB19 infection within a few months from three hospitals in the western part of Switzerland. Five patients (aged 23 to 53 years) were diagnosed with acute glomerulonephritis in three hospitals (Fribourg, Sion and Nyon) in spring 2024. Initial renal presentation varied from typical nephrotic syndrome (n = 2) to nephritic syndrome (n = 1). A mix of both syndromes was seen in 2 patients. Kidney biopsy specimens exhibited various histopathological and immunofluorescence patterns including cFSGS (n = 2), post-infectious glomerulonephritis (n = 1), "lupus-like" membranoproliferative glomerulonephritis (n = 1) and immune-complex proliferative glomerulonephritis (n = 1). We also noticed extrarenal manifestations at presentation in all five patients, preceded by mild flu-like symptoms (with fever in 3 patients) and diarrhea. Since these unusual phenotypes occurred during a possible PVB19 outbreak, we looked for a PVB19 infection in those patients. All five patients displayed positive PVB19 IgM serology and significant viremia. 4 patients were given intravenous immunoglobulins to reduce PVB19 viral load. They were treated with diverse immunosuppressive regimens, including glucocorticoids (n = 5), calcineurin inhibitors (n = 1), and eculizumab (n = 1). Clinical outcomes ranged from near complete remission (n = 1) or partial remission (n = 3) to therapy-resistant disease (n = 1). Although causality remains to be proven, human parvovirus infection may cause glomerulonephritis. Clinical presentation varies substantially. Such cases may be overlooked, especially in the context of a recent increase in the incidence of PVB19 infections in Switzerland. The treatment may depend on renal histology, but clinical management remains to be defined. We encourage screening for PVB19 infection in patients with glomerulonephritis, in particular in an epidemic context.

OC 34

Impact of covid-19 pandemic restrictions on hypertensive disorders of pregnancy according to country income levels: a systematic literature review

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Background: Hypertensive disorders of pregnancy (HDP) are a leading cause of maternal and neonatal morbidity and mortality, affecting 10% of pregnancies worldwide. During the 2020 COVID-19 pandemic, restrictions and lockdowns disrupted general healthcare services, including those for pregnant women globally. Isolation and reduced access to regular care may have increased the likelihood of missing high-risk pregnancies, particularly in developing countries. The aim of the present study was to analyze the frequency of HDP before and during the COVID-19 pandemic around the world, according to country income levels.

Methods: A systematic review was conducted on studies examining the pandemic's impact on HDP, including chronic and gestational hypertension, preeclampsia/eclampsia, and preeclampsia superimposed on chronic hypertension. We searched PubMed in accordance with PRISMA guidelines to identify relevant studies from the start of the pandemic. We excluded studies focusing on SARS-CoV-2 infected women and systematic reviews or studies lacking comparison groups.

Results: From 210 citations, 28 studies were selected, covering populations from 17 countries. Among these studies, 12 from High-Income countries (HICs), 1 from Upper-Middle-Income Countries (UMICs) and 1 from Low-Middle-Income Countries (LMICs) reported no significant change in HDP rates. By contrast, 12 studies documented an increase in HDP rates during the pandemic, including 7 from HICs, 4 from UMICs, and 1 from LMICs. 2 studies from HICs showed a decrease in HDP rates. Overall, there was no consistent effect on HDP rates across countries based on income levels.

Conclusions: HDP rates are largely determined by the population at risk of each country and were not significantly influenced by pandemic restrictions. While in HICs, maternal age and the rise in in vitro fertilizations contribute to higher HDP rates, poorer countries face challenges due to limited access to healthcare. Early identification of risks for HDP remains of primary importance in all countries.

OC 35

Impact of pre-implantation hernia screening in peritoneal dialysis patients on hernia surgery during dialysis

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Background: The development of a hernia during peritoneal dialysis (PD) treatment is a risk factor for technical failure. Therefore, it is crucial to detect any hernia before PD catheter implantation and to repair them simultaneously.

Methods: We evaluated 65 patient who started PD from June 2011 to June 2024. The mean duration of PD treatment was 23.2 months. During the first period, from June 2011 until December 2018, pre-implantation hernia screening consisted of only clinical examination alone. Thereafter, additional sonographic screening of all common hernia sites was performed. We analyzed the prevalence and location of the hernias before PD start and the incidence and location thereafter.

Results: During the first period, we detected 3 umbilical hernias in 28 patients which all were simultaneously repaired during PD catheter implantation. During follow-up, 5 patients developed 6 hernias (4 groin hernias and 2 umbilical hernias), which all were repaired without the need to switch to hemodialysis (HD). During the second period, with additional sonographic screening, we detected 8 hernias (5 umbilical hernias and 3 groin hernias) in 37 patients which were also simultaneously repaired during PD catheter implantation. During follow-up there was only 1/37 patient with a recurrence of an old groin hernia, which was repaired several years before PD start. The hernia was repaired without interruption of PD. The hernia repair technique always consisted of an extraperitoneal approach as in Lichtenstein hernia repair or preperitoneal net positioning in cases of umbilical hernias to avoid injury to the peritoneum.

Conclusion: Pre-implantation hernia screening with ultrasound enables simultaneous hernia repair and catheter implantation and reduces the risk of later symptomatically hernia development and the need of surgery during PD treatment with its risk of interruption of PD or switch to HD.

OC 36

Impact of Repeated Non-fatal Infectious Events on Patient and Graft Outcome in ABO Incompatible Living Donor Kidney Transplantation

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Background: Kidney transplantation (KT) is the preferred treatment for advanced and end-stage kidney disease. KT from living donors (LDKT) is associated with favorable renal and patient outcome and improved quality of life when compared to KT from deceased donors. Historically, ABO incompatibility (ABOi) was a limitation for LDKT. However, with the advent of desensitization protocols, ABOi LDKT has become feasible, yielding generally good outcomes and helping to expand the donor pool. The added risk of a ABOi procedure to the transplanted organ (graft dysfunction, rejection risk, graft loss) and patient (mortality, morbidity) is debated. We investigated repeated non-fatal infectious events and their consequences on graft loss or death in ABOc and ABOi LDTK recipients.

Methods: Retrospective, nationwide (Swiss Transplant Cohort Study) study, from May 2008 to December 2022. All patients with ABOi LDKT were included in the analysis. Viral, bacterial, fungal and parasitic infections were considered as non-fatal repeated adverse events.

Results: 227 ABOi LDKT and 1172 ABO compatible (ABOc) controls were included. 31% (4274/1399) of participants experienced at least two infectious events during follow-up. ABOi was independently associated to an increased risk of infectious events (HR 1.17, IQR 1.06-1.29, p <0.01). Results remained significant even after correction for co-factors. Patients with ≥ 2 infectious events within the first 6 months had a higher risk for graft loss or death, lower eGFR at 12 months and lower quality of life.

Conclusion: ABOi LDKT patients face a heightened risk of recurrent infections, especially within the first 6 months post-KT, which is linked to poorer patient and graft survival, diminished allograft function, and reduced quality of life. These recurrent infections are most common in frail and multi-morbid patients. For these patients, alternative strategies to ABOi KT should be considered.

OC 37

Injury- and rejection-associated transcripts are linked to short-term functional outcomes in belatacept late conversion: Providing insights beyond histological categorization

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Background: Injury- and rejection-associated transcripts (IRRAT) identified through biopsy-based transcriptomics have been associated with patient and graft outcomes in kidney transplantation. We hypothesized that biopsy-based transcript diagnostics could improve patient selection for belatacept late conversion, beyond histological characterization, in a population with relevant interstitial fibrosis and tubular atrophy (IFTA) undergoing late conversion.

Methods: 39 kidney transplant recipients (KTRs) undergoing belatacept late conversion were classified based on pre-conversion biopsies, incorporating molecular IRRAT-scores from the Molecular Microscope Diagnostic System (MMDx). IRRAT-scores were assessed both as semiquantitative subgroups (minimal/mild, moderate/extensive) and as continuous values. Estimated glomerular filtration rate (eGFR) was tracked 3-monthly during the first year post-conversion. Regression models identified MMDx and histology predictors associated with stable or improved eGFR at one year post-conversion.

Results: 35/39 (90%) of pre-conversion biopsies showed at least moderate IFTA (ci+ct≥2) by histology. Minimal/mild molecular IRRAT-scores were observed in 27 (69%) KTRs, while 12 (31%) had moderate/extensive scores. KTRs with minimal/mild molecular IRRAT-scores had significantly higher baseline eGFR than those with moderate/extensive scores (43 vs. 27ml/min/1.73m^2; p = 0.006) and a significantly better eGFR-slope (+8ml/min/year vs. -6ml/min/year). Continuous IRRAT-scores were inversely associated with stable or increasing eGFR at one year post-conversion (OR 0.317, CI 0.111-0.904; p = 0.032); independent of microvascular inflammation (MVI, g+ptc≥2; OR 0.331, CI 0.112-0.982; p = 0.046); transplant glomerulopathy (cg>0; OR 0.276, CI 0.089-0.859; p = 0.026); and vascular intimal thickening (cv>1; OR 0.274, CI 0.091-0.827; p = 0.022); but not baseline eGFR (OR 0.326, CI 0.1-1.059; p = 0.062) in different multivariable models.

Conclusions: Incorporating IRRAT-scores alongside histological categorization offers a more effective approach to patient selection for belatacept late conversion compared to relying on histology alone. This is especially valuable in high-risk cases with MVI at/above threshold or advanced chronic changes (IFTA). Given the cost and limited availability of belatacept, this strategy holds considerable potential for optimizing patient outcomes.

OC 38

Kidney transplantation in combination with RNAi therapy (lumasiran) instead of combined liver transplantation for primary hyperoxaluria type 1 – a case report

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Background: Primary hyperoxaluria type 1 (PH1) is a rare but severe autosomal recessive disorder. AGXT gene defects cause excessive hepatic oxalate production, which eventually leads to renal failure. Standard treatment consists of hyperhydration, citrate and pyridoxine (if B6-sensitive) to prevent renal failure and systemic oxalosis. Lumasiran, a novel RNAi therapy, reduces the production and excretion of oxalate in urine by inhibiting the hepatic enzyme glycolate oxidase (GO). In renal failure, combined liver-kidney transplantation is the treatment of choice to normalize oxalate production and prevent allograft damage. To date, 9 cases of PH1 patients who received a single kidney transplant plus lumasiran instead of a liver transplant have been reported. Here we describe the first case in Switzerland.

Case: A 38-year-old woman with a positive family history was diagnosed with PH1 after birth and was found to be compound heterozygous for pathogenic variants of AGXT (c.466G>A; c.508G>A). Apart from long-term conservative treatment with pyridoxine, she took lumasiran for 2 years before reaching renal failure without signs of systemic oxalosis. After two months of hemodialysis, she received a living kidney donation from her mother. Before, plasma oxalate levels had been consistently maintained below 30 µmol/L. PH1 treatment including lumasiran was continued and hemodialysis was not required after transplantation. Plasma oxalate levels normalized almost immediately. 5.5 months after transplantation, allograft function remained stable with an eGFR of about 35 ml/min/1.73m^2 while urinary oxalate excretion decreased but continue to be elevated. A protocol transplant biopsy 3 months after transplantation did not show any oxalate deposits.

Conclusion: In selectet patients, RNAi therapy for PH1 is an interesting option even after kidney transplantation instead of combined liver transplantation. However, the outcome data is very limited and treatment costs remain a concern.

OC 39

Longitudinal donor-derived cell-free DNA measurements of stable kidney transplant recipients for improving allograft health

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Background: Donor-derived cell-free DNA (dd-cfDNA) is emerging as a non-invasive biomarker in kidney transplant recipients (KTx) for monitoring allograft health. Conventional graft monitoring methods have either limited sensitivity or are invasive. Many studies have shown correlations between elevated dd-cfDNA fractions and graft rejections, potentially enabling earlier detection and treatment of graft dysfunctions. Our aim is to identify the interand intra-individual variability of dd-cfDNA in stable KTx within the first year after transplantation to determine baseline values and patterns.

Methods: Blood and urine samples from KTx were collected longitudinally at regular clinic visits. Mismatched HLA alleles between donor and recipient were used to perform droplet digital PCR, determining absolute (cp/mL) and relative (%dd-cfDNA) quantities of dd-cfDNA. Urinary dd-cfDNA was corrected for urine concentration with creatinine measurements in urine.

Results: For each stable KTx (n = 17) three timepoints were chosen (first_mean = 56 days, second_mean = 175 days, third_mean = 352 days). The mean %dd-cfDNA in plasma increased gradually from the first (0.19%, 0.218% for the second timepoint) to the third timepoint (0.311%). There was a decrease at the second timepoint and slight increase after one year for the mean absolute dd-cfDNA in plasma (first 9.16 cp/mL, second 5.12 cp/mL, third 7.45 cp/mL). In urine (n = 8) we similarly observed an increase in %dd-cfDNA with higher initial values (day_1 = 22.8%, day_2 = 20.2%, day_3 = 37%).

Conclusions: We did observe a dynamic of dd-cfDNA in the first year after transplantation with an increase of fractional values in both plasma and urine. The recipient's cfDNA has to be taken into account for the increase of fractional values. The different patterns in urinary vs. plasma dd-cfDNA will be investigated further, including the long-term outcomes and graft function one year post-transplantation.

OC 40

Membranous nephropathy secondary to graft-versus-host disease following hematological stem cells transplant

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Background: Membranous nephropathy (MN) induced by graft-versus-host disease (GVHD) after allogenic hematological stem cells transplant (HSCT) is a very rare complication.

Case description: We report the case of a 46 years old female suffering acute myeloid leukemia (AML) treated with HSCT and sorafenib. She developed time-limited GVHD with gastric and skin involvement, resolved after corticotherapy. Eighteen months after HSCT, she had no relapse of AML as per the control medullogram when she developed nephrotic syndrome (NS). The kidney biopsy showed a MN with glomerular intracapillary thrombi. There was no evidence of hemolysis, ruling out a systemic thrombotic microangiopathy. The immune work-up – including C3 and C4, anti-PLA2R or -THSD7A antibodies, ANF, anti-DS-DNA, extended lupus auto-antibodies panel, ANCA, HBV/HCV/HIV serologies – didn't show any primary or other common secondary causes. Since the membranous depositions was not staining for IgG4 and there was no obvious other cause of MN, it was considered secondary to GVHD or to Sorafenib. The patient was treated with prednisone 1mg/kg for 2 month, and the sorafenib was stopped. Nevertheless, the proteinuria and the NS massively worsened ruling out sorafenib as a causal agent. Because of massive proteinuria, anasarca and acute kidney injury, a second line therapy with rituximab 375 mg/m2 once weekly was introduced.

Learning point: GVHD is primarily T-cell–mediated and sensitive to steroids, calcineurin inhibitors or mycophenolate. In MN secondary to GVHD, the deposition of immunoglobulins implicates B-cells involvement with antibody – as well as antibody-independent – mechanisms, and rituximab has been shown to be efficient in some cases.

Conclusions: MN can complicate HSCT and can be steroid-resistant indicating second line therapy with B-cells targeting treatments.

OC 41

Molecular rejection phenotype scores predict kidney allograft loss and eGFR decline along the AMR continuum

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Background: The Banff update of 2022 suggests that biopsy-based transcripts related to antibody-mediated rejection (AMR) could substitute for microvascular inflammation (MVI). However, the new subgroups of AMR, DSA-negative MVI, and probable AMR need more outcome studies when molecular transcripts are used in the clinic.

Methods: We examined 297 kidney transplant biopsies by histology and the Molecular Microscope Diagnostic System (MMDx). Histologic findings were grouped into (1) probable AMR (n = 53), (2) DSA-negative C4d-negative MVI (n = 42), (3) AMR (n = 71), and no AMR (n = 131). Groups were subdivided into molecular AMR (n = 74) and no molecular AMR (n = 223). Outcomes were measured by kidney transplant loss and eGFR decline of >30% as a combined endpoint.

Results: Median follow-up was 18 months (IQR 10,29). Molecular AMR was found in 51% of AMR cases, 62% of DSA-negative MVI cases, 13% of probable AMR cases, and 7% of cases with no AMR. After 1, 3, and 5 years after biopsy, molecular AMR cases had higher rates of the combined endpoint than no molecular AMR cases (22% vs. 6%, 40% vs. 16%, 53% vs. 25%; p<0.0001). These rates were even higher when possible molecular AMR cases with all AMR phenotype scores >0.3 (n = 38) were included (59% vs. 10% at 5 years). This difference was significant in all histologic groups by Banff 2022, except for probable AMR (p = 0.2). Higher mixed rejection phenotype scores (R3, p = 0.003) and higher all AMR phenotype scores (p = 0.044) were independent predictors of the combined endpoint among cases with molecular AMR.

Conclusions: The presence of molecular AMR is associated with higher rates of kidney allograft loss and eGFR decline in the new subgroups of AMR, DSA-negative MVI, and probable AMR. Additionally, molecular findings below the threshold may have clinical significance. Molecular rejection phenotype scores, especially the mixed rejection score and all AMR score predict outcomes independently.

OC 42

Non-HLA antibodies in the diagnosis of antibody-mediated rejection without circulating HLA donor-specific antibodies: biopsy-based transcript diagnostics perspective

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Background: Kidney transplant biopsies with at least moderate microvascular inflammation (MVI) without human leukocyte antigen (HLA) donor-specific antibodies DSAs and with negative C4d staining represent a phenotype of unknown cause and prognosis. Autoreactive non-HLA antibodies may play a role in some of these cases, and biopsy-based transcript diagnostics may help in understanding these lesions.

Methods: We identified 22 cases of MVI, DSA-negative, C4d-negative. We performed biopsy-based transcript diagnostics by Molecular Microscope Diagnostic System (MMDx) and measured non-HLA antibodies – angiotensin II type 1 receptor (AT1R-Ab) and endothelin type A receptor antibody (ETAR-Ab) – in all cases.

Results: Molecularly, the MVI, DSA-negative, C4d-negative group encompassed 9 (41%) cases of antibody-mediated rejection (AMR), 4 (18%) cases of T-cell-mediated rejection (TCMR), 2 (9.1%) cases of mixed rejection, 1 (4.5%) unspecified rejection and 6 (27%) "no rejection" cases. Applying a cut-off of 17 U/l (strong antibody binding), 4 (36%) patients showing molecular AMR were positive for AT1R-Ab and 3 (27%) positive for ETAR-Ab – 3 cases were double positive. None of the 6 cases without molecular rejection showed strong binding for either antibody. The median [IQR] titer for AT1R-Ab was higher in the molecular AMR cases (14 U/l [9.9-20]) compared to "no-rejection" cases (9.6 U/l [8.0-11], p = 0.08). Similarly, the ETAR-Ab titer was higher in molecular AMR cases (16 U/l [11-20]) compared to "no-rejection" cases (9.4 U/l [8.7-10], p = 0.04). We observed higher median phenotype rejection scores indicative of late AMR in cases with strong binding compared to intermediate and low binding both for AT1R (p = 0.16) and ETAR (p = 0.03).

Conclusion: In the MVI, DSA-negative, C4d-negative cases, non-HLA AT1R and ETAR autoreactive antibodies were more frequently positive in molecular AMR cases and mostly negative in "no-rejection" cases, suggesting a potential pathophysiological role for these antibodies in rejection.

OC 43

Population genetics meets precision-cut kidney slices: Nephrotoxicity modelled ex vivo in the founder strains of the BXD mouse consortium

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Background: Genome-wide association studies of patients receiving platinum chemotherapy nephrotoxicity have identified genetic variants associated with acute kidney injury. However, the genetic predisposition to acute nephrotoxicity inducible by agents such as calcineurin inhibitors is unclear. Here, we eval-

uated if the parental strains of the BXD mouse consortium harbor strain differences in several nephrotoxicity phenotypes in order to justify using this source of genetic diversity for nephrotoxicity research.

Methods: Precision-cut kidney slices (PCKS) were established from C57BL/6 and DBA/2 mice. PCKS were treated with different doses of Ciclosporin A to mimic acute calcineurin inhibitor toxicity, tunicamycin to induce endoplasmatic reticulum stress, or modelled ischemia and reperfusion injury by 18h of cold storage at 21% O2 followed by incubation at 95% O2 at 37°C. Tissues were analyzed by hematoxylin & eosin staining and histopathological scoring of tubular injury. Renal adenosine triphosphate (ATP) tissue content was measured. Finally, we performed RNAseq and estimated cell viability using linear models of transcriptional signatures of cell death.

Results: Histological scores of renal tubular injury and renal ATP release were increased by nephrotoxins compared to control condiitons and were overall higher in C57BL/6 than DBA/2. RNAseq analyses revealed that most transcriptional differences occurred after tunicamycin treatments over 24h, and in the modelled ischemiareperfusion injury of PCKS. Transcriptome-inferred renal cell viability was lowest in ischemic C57BL/6 kidney, low under modelled reperfusion injury in both strains, and overall worse in PCKS of C57BL/6 compared to DBA/2 mice.

Conclusion: Altogether, there were several strain differences in renal tissue phenotypes induced by nephrotoxins or ischemia-reperfusion injury modelled ex vivo, between the two parental strains of the BXD consortium. These data indicate that the genetic heterogeneity of BXD recombinant-inbred mice could be harnessed together with PCKS and nephrotoxins as a promising approach to perform genetic association studies for nephrotoxicity.

OC 44

Safety and effectiveness of prolonged calcineurin inhibitor-exposure during belatacept late conversion

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Background: De novo belatacept-based immunosuppression protocols and late conversion from a calcineurin inhibitor (CNI)- to a belatacept-based regime have been associated with a higher risk of rejection, especially T cell-mediated rejection (TCMR) in kidney transplant recipients (KTRs). Previous groups showed to overcome the increased risk for TCMR with a prolonged CNI-exposure in de novo protocols. In response to this, we revised our late conversion protocol to include an extended duration of concurrent CNI-administration.

Methods: From 03/2022-05/2024, 39 KTRs, transplanted at least 12 months prior, were converted to belatacept with a concurrent CNI-exposure of 3 months (n = 5) or 6 months (n = 34) post-conversion, based on individual immunological risk assessments. CNIs were tapered to low trough levels (2-4 µg/l) after 1 month. CMV-, EBV- and BKV-replication were routinely screened at month 3, 6 and 12 after conversion, with other infections documented at occurrence. Anti-HLA donor-specific antibodies (DSA) were screened at baseline and after 12 months, or during an indication biopsy. All patients were followed for 12 months after conversion, with documentation of infections, de novo DSA (dnDSA) and biopsy-proven acute rejections (BPAR).

Results: 5/39 (12.8%) patients had infections associated to conversion, needing medical treatment, including 1 case of CMV-associated diarrhea, 3 cases of bacterial pneumonia and 1 case of cellulitis. There were no other relevant CMV-, BKV-, or EBV-replications, and no fungal infections. At 1 year post-conversion 7/39 (17.9%) patients showed development of dnDSA, 2 against HLA-Class I dnDSA, and 5 against HLA-Class II dnDSA, with a mean fluorescence intensity (MFI) between 500-1000 (median 602, interquartile range 527-610). No BPAR was objectified in the first year post-conversion.

Conclusions: Our revised belatacept conversion protocol demonstrated a moderate rate of associated infections, comparable to previous studies. No dnDSA with an MFI >1000 and no BPAR were observed. Further investigation is needed to assess long-term outcomes.

OC 45

Social media call to search for an altruistic kidney donor.": ethical or not

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Background: Social media calls for altruistic organ donors remain controversial and ethically complex. Despite concerns, platforms like Facebook and Instagram for community reachout have become common, including for individuals with serious health conditions, such as kidney disease. Here, we report on an independent social media request by a young patient seeking a living kidney donor for preemptive transplantation. Her plea was widely shared, and several potential donors came forward.

Methods: This monocentric retrospective study took place at the nephrology division of Inselspital, Bern. After potential donors expressed interest via social media, they were sent a 2-page anonymized electronic questionnaire to better understand their motivations for altruistic donation. The patient's medical records provided her baseline characteristics.

Results: Out of 16 altruistic donors, 11 (68.7%) responded to the questionnaire. Their social media use and altruistic behaviors are summarized in Table 1. To compare, the same questionnaire was sent to all living kidney donors since 2017, and the responses are under ongoing evaluation.

Conclusion: This case illustrates the growing role of social media in connecting patients with potential organ donors but also highlights significant ethical concerns. Privacy, consent, and the possibility of exploitation are major issues as patients increasingly turn to these platforms. The lack of a clear legal and ethical framework necessitates careful consideration of the risks and opportunities involved in using social media for organ donation. As more patients seek donors through these channels, this case emphasizes the need for guidelines to protect both donors and recipients.

	Donor Candidates		
Characteristic	Altruistic n = 11	Directed Donor n = 11	p-value
Age (years)	38 (31, 49)	62 (56, 64)	**0.002**
Gender (Male)	1 (9.1%)	5 (45%)	0.15
Medication (yes)	3 (27%)	4 (36%)	>0.9
BMI (kg/m2)	24.91 (21.23, 26.26)	22.99 (22.36, 24.61)	0.6
Smoking (yes)	5 (45%)	2 (18%)	0.4

	Donor Candidates		
	Altruistic n = 11	Directed Donor n = 11	p-value
Social Media (yes)	10 (91%)	8 (73%)	0.6
Online Shopping (yes)	8 (73%)	5 (45%)	0.4
Online Banking (yes)	10 (91%)	7 (64%)	0.3
Online Media (yes)	7 (64%)	7 (70%)	>0.9
Print Medien (yes)	3 (27%)	2 (20%)	>0.9

OC 46

Sparsentan vs irbesartan in patients with immunoglobulin A nephropathy (IgAN): Subgroup analyses of 2-year results from the pivotal Phase 3 PROTECT trial

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Background: In the PROTECT trial, a phase 3, global, randomised, double-blind, parallel-group, active-controlled trial of sparsentan vs irbesartan in patients with IgAN, sparsentan met the primary endpoint with a significantly greater geometric mean percent reduction in urine protein-to-creatinine ratio (UPCR) vs active comparator irbesartan at the interim 36-week analysis (−49.8% vs −15.1%, respectively; *P*<0.0001) (Heerspink et al. *Lancet*. 2023). Here we present key efficacy results from the final analysis of the PROTECT double-blind period (≈2 years).

Methods: A total of 404 patients ≥18 years old with biopsy-proven IgAN, urine protein excretion of ≥1.0 g/day, and estimated glomerular filtration rate (eGFR) of ≥30 mL/min/1.73 m^2 were randomised 1:1 to receive sparsentan 400 mg/day (n = 202) or irbesartan 300 mg/day (n = 202) for up to 110 weeks.

Results: At final analysis, sparsentan showed sustained reductions in UPCR over 110 weeks, with a 40% relative reduction vs irbesartan at 110 weeks and long-term kidney function preservation vs irbesartan. Absolute change in eGFR from baseline to week 110 was lower with sparsentan vs irbesartan (**Table**); results consistently favoured sparsentan across subgroups, with larger effects seen with higher baseline proteinuria. In the total study population, sparsentan treatment led to a statistically significant reduction in the rate of eGFR decline over weeks 6 to 110 (chronic slope) vs irbesartan (difference = 1.1 mL/min/1.73 m^2/year; *P* = 0.037). The difference in the rate of eGFR decline from day 1 to week 110 (total slope) with sparsentan vs irbesartan was 1.0 mL/min/1.73 m^2/year (*P* = 0.058). Sparsentan was generally well tolerated; the overall safety profile was consistent between sparsentan and irbesartan.

Conclusions: The final analysis of the phase 3 PROTECT trial showed that sparsentan had a clinically meaningful benefit on long-term kidney preservation, with absolute change in eGFR and rate of eGFR change favouring sparsentan vs irbesartan across baseline proteinuria subgroups over 2 years.

Table. Subgroup analysis of the mean absolute change from baseline to Week 110 and mean annualised rate of eGFR change over 110 weeks

Mean absolute change in eGFR from Day 1 to Week 110 (95% CI), mL/min/1.73 m²	Sparsentan	Irbesartan	Difference
Total population	−5.8 (−7.38 to −4.24)	−9.5 (−11.17 to −7.89)	3.7 (1.45-5.99)*
Baseline UPCR quartiles			
<0.80 g/g†	−3.7 (−6.28 to −1.06)	−5.4 (−8.57 to −2.20)	1.7 (−2.41 to 5.84)
≥0.80-<1.25 g/g‡	−4.7 (−6.96 to −2.51)	−7.3 (−9.39 to −5.27)	2.6 (−0.44 to 5.63)
≥1.25-<1.80 g/g§	−4.6 (−7.06 to −2.21)	−10.6 (−13.09 to −8.04)	5.9 (2.43-9.43)
≥1.80 g/g‖	−8.9 (−11.48 to −6.22)	−14.0 (−16.98 to −10.97)	5.1 (1.12-9.11)
Mean annualised chronic eGFR slope from Weeks 6 to 110 (95% CI), mL/min/1.73 m²/year	**Sparsentan**	**Irbesartan**	**Difference**
Total population	−2.7 (−3.43 to −2.05)	−3.8 (−4.60 to −3.07)	1.1 (0.07-2.12)¶
Baseline UPCR quartiles			
<0.80 g/g#	−1.9 (−3.44 to −0.31)	−3.3 (−5.21 to −1.43)	1.4 (−1.01 to 3.90)
≥0.80-<1.25 g/g**	−2.3 (−3.44 to −1.22)	−2.8 (−3.79 to −1.82)	0.5 (−1.02 to 1.96)
≥1.25-<1.80 g/g††	−2.9 (−4.27 to −1.62)	−4.4 (−5.68 to −3.03)	1.4 (−0.46 to 3.28)
≥1.80 g/g‡‡	−4.3 (−5.88 to −2.82)	−6.2 (−7.94 to −4.38)	1.8 (−0.53 to 4.16)
Mean annualised total eGFR slope from Day 1 to Week 110 (95% CI), mL/min/1.73 m²/year	**Sparsentan**	**Irbesartan**	**Difference**
Total population	−2.9 (−3.58 to −2.24)	−3.9 (−4.59 to −3.13)	1.0 (−0.03 to 1.94)§§
Baseline UPCR quartiles			
<0.80 g/g#	−2.1 (−3.61 to −0.58)	−3.3 (−5.11 to −1.48)	1.2 (−1.17 to 3.57)
≥0.80-<1.25 g/g**	−2.4 (−3.46 to −1.28)	−2.6 (−3.52 to −1.59)	0.2 (−1.27 to 1.64)
≥1.25-<1.80 g/g††	−3.0 (−4.28 to −1.79)	−4.3 (−5.57 to −3.08)	1.3 (−0.47 to 3.05)
≥1.80 g/g‡‡	−4.7 (−6.27 to −3.13)	−6.7 (−8.52 to −4.90)	2.0 (−0.39 to 4.40)

CI, confidence interval; eGFR, estimated glomerular filtration rate; UPCR, urine protein-to-creatinine ratio.
*P=0.001. †Sparsentan, n=45; irbesartan, n=30. ‡Sparsentan, n=40; irbesartan, n=45. §Sparsentan, n=39; irbesartan, n=35. ‖Sparsentan, n=35; irbesartan, n=28. ¶P=0.037. #Sparsentan, n=54; irbesartan, n=39. **Sparsentan, n=47; irbesartan, n=64. ††Sparsentan, n=49; irbesartan, n=53. ‡‡Sparsentan, n=52; irbesartan, n=46. §§P=0.058.

OC 47

Structure and function analysis of NPHS1 and NPHS2 missense variants

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Background: The identification of monogenic causes of steroid-resistant nephrotic syndrome (SRNS) has highlighted the glomerular podocyte as central to its pathogenesis. *NPHS1*, the gene encoding nephrin, was the first gene identified to cause SRNS. Nephrin builds a specialised podocyte junction, the slit diaphragm (SD) and interacts *inter alia* with podocin (*NPHS2*), thereby building a signalling platform for dynamic interactions between the SD, the actin cytoskeleton, and focal adhesions. Variants of *NPHS2* are the most common cause of monogenetic-associated SRNS.

Over 200 disease-causing variants in *NPHS1/2* have been identified to date, most of them being missense variants leading to proteinuria with a wide range of ages at onset. The pathomechanisms of missense variants are incompletely understood.

Methods: Therefore, systematic structure-function analysis of nephrin and podocin missense variants, all likely pathogenic *in vivo,* was performed using HEK-293T and MDCKII cells. Cells stably expressing wildtype or missense variants were analysed by Western blot (WB) and immunofluorescence (IF) microscopy, as well as live-cell imaging. Furthermore, *Drosophila melanogaster* nephrocytes were used as an *in vivo* model.

Results: Cell culture experiments revealed a correlation between the expression and localization of nephrin, as the wildtype and variants presented in a double band in WB localize to the plasma membrane whereas variants displaying only the lower band do not exhibit membrane targeting. IF and live-cell imaging of podocin wildtype and missense variants revealed retention in the ER for most of the variants. Additionally, we showed that the loss of the nephrin orthologue sticks and stones (*Sns)* can partly be rescued with integrated wild-typic *NPHS1* in *Drosophila* nephrocytes. Moreover, Mec-2, the fly orthologue of podocin, was examined for its effect on the function and integrity of the nephrocyte diaphragm.

Conclusion: This study paved the way to establish models useful in predicting the disease severity of variants of unknown pathogenicity.

OC 48

Successful Targeting of the Alternative Complement Cascade with Iptacopan for the Treatment of IgA Nephropathy: A Case Report

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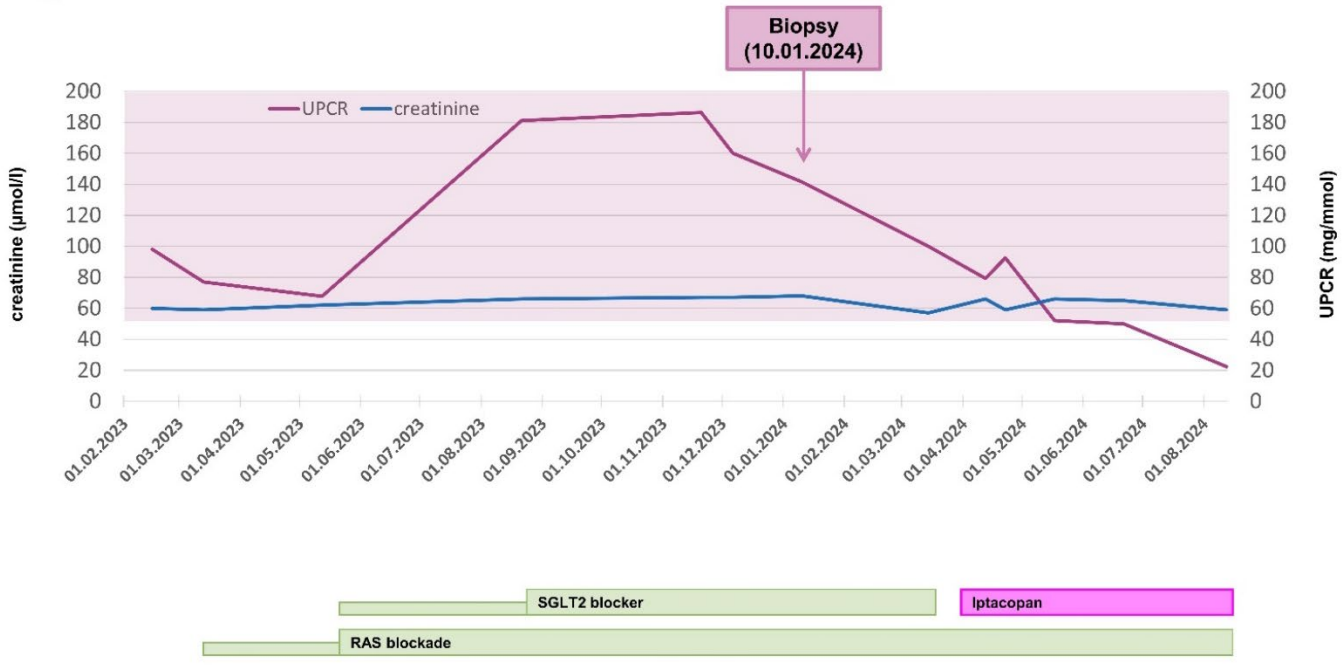
Background: Nowadays, there exist no approved disease-specific therapies for patients with immunoglobulin A nephropathy (IgAN). According to the 2024 KDIGO guidelines, the current treatment focus on reducing proteinuria and nephron loss with nephroprotective regimens consisting of renin-angiotensin-system (RAS) blockade, sodium-glucose cotransporter-2 inhibitors (SGLT-2i), and the dual endothelin angiotensin receptor antagonist Sparsentan. In addition, systemic glucocorticoids and a delayed-release formulation of budesonide are therapeutic options to reduce IgAN-specific drivers of nephron loss. However, their use has been associated with adverse side effects even with budesonide, and there remains weighing the benefit of these therapies against the risk of treatment-emergent toxicity. This highlights the ongoing need to identify more effective and safer therapies for the treatment of IgAN. Over the last years, increasing understanding of the pathogenetic role of alternative complement pathway (AP) dysregulation in the onset/progression of IgAN led to the development of new complement-targeting therapies. Iptacopan is an oral inhibitor of the complement factor B that effectively blocks the AP.

Case Presentation: We report the first successful treatment of a 40-year-old female patient with IgAN with iptacopan in Switzerland. In this patient, despite maximal tolerated RAS blockade and fully dosed SGLT-2i, we failed to achieve the aimed reduction of proteinuria <0.5g/day. Proteinuria persisted at a level >1g/day despite a reached blood pressure goal of

Fig. 1



≤120/70mmHg. Impressively, within three months after initiation of iptacopan, we could already see a reduction of proteinuria to 0.5g/day and after six months we reached our goal of proteinuria <0.3g/day (Figure 1). The medication was well tolerated.

Conclusion: To the best of our knowledge, our case report is the first in Switzerland to show that selective inhibition of the AP in IgAN results in significant reduction of proteinuria after six months and therefore, supports the innovating concept of targeting the AP with iptacopan to treat IgAN.

OC 49

Successful use of mycophenolate mofetil (MMF) in the treatment of acute checkpoint inhibitor-induced interstitial nephritis

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Background: Acute interstitial nephritis (AIN) is a frequent cause of acute kidney injury (AKI). Immune checkpoint inhibitors are nowadays widely used in cancer treatment and AIN is a typical complication. Treatment of drug-induced AIN consists of stopping the offending agent and if necessary, a course of corticosteroids. Alternative treatment options are only based on case series.

Case description: A 56-year-old man presented with an AKI stage 3 one month after the first cycle of therapy with pembrolizumab, pemetrexed and carboplatin for treatment of metastasized pulmonary adenocarcinoma. The initial clinical and laboratory examination revealed a truncal rash, a normal blood pressure, a CRP of 98 mg/l, and a serum creatinine of 334 µmol/l (baseline creatinine 90 µmol/l). Furthermore, he showed a mixed proteinuria of 1 g/day and glomerular microhematuria. The treating oncologist withheld cancer treatment immediately and started high dose intravenous corticosteroids on the assumption of pembrolizumab-associated AIN. No improvement of renal function was seen after 13 days and renal biopsy was performed which showed acute tubulointerstitial nephritis, and concomitant IgA nephropathy. Due to the steroid refractory course, MMF 500 mg twice daily was added to the treatment. 2 days later, kidney function started to improve. MMF was continued and prednisone was tapered. Kidney function further improved, and prednisone was stopped after 6 weeks. We continued MMF for another two weeks and stopped treatment completely after 2 months. Four weeks later, creatinine remained stable at about 160 µmol/l without specific therapy. Pembrolizumab was stopped permanently.

Learning points/conclusion: In this case, MMF proved to be effective in the treatment of pembrolizumab-induced AIN. Thus, along with other case reports on AIN, MMF can be a useful treatment alternative in steroid refractory AIN or in patients with contraindications to corticosteroids.

OC 50

The dilemma of CKD and ESKD following pre-eclampsia: a literature review and meta-analysis

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Background: Pre-eclampsia (PE) is a pregnancy-related multisystem syndrome, particularly characterized by sudden-onset hypertension (>20 weeks gestation). Although most studies and detailed analysis of previous reviews found an association between PE and chronic kidney diseases (CKD) / end-stage kidney disease (ESKD) later in life, it is still unclear whether this is causative. Furthermore, most of the research performed until now did not exclude women with chronic hypertension and/or CKD prior to pregnancy, indicating a possible selection bias. Therefore, we undertook a systematic review of updated literature on renal outcome in healthy women prior to pregnancy, who suffered from post–preeclampsia.

Methods: We selected articles from Pubmed-MEDLINE and Embase published between January 2000 and October 2023 in English, French, German and Italian. We included retrospective and prospective studies with healthy women affected from PE, follow-up of 5 years or more and outcome of CKD or ESKD.

Of the 2'422 titles originally considered, 9 papers were selected, providing information on 190'301 cases and 5'972'336 controls. We used a random meta-analytic model for the statistical analysis.

Results: We found a statistically significant increase in risk of CKD and ESKD after PE (meta-analytic risk ratios (95% confidence interval): 1.83 (1.16-2.89) and 4.28 (1.21 – 15.16) respectively), with high statistical heterogeneity. However, in the only prospective study there was no relationship between PE and CKD.

Conclusions: Although we found a significant association between PE and CKD later in life, the clinical significance and causality remain unclear. Medical investigations in the post-partum period of women who suffered from PE is mandatory, but long-term follow-up for women with no underlying pathologies after PE may not be indicated.

Future prospective studies and/or specific registers are needed to establish the relationship between PE and CKD later in life in healthy women who were healthy prior to pregnancy.

OC 51

The nephrin-associated phospho-protein network is essential for filtration at the slit diaphragm.

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Introduction: Minimal Change Disease (MCD) is characterized by nephrotic syndrome. In a subset of patients, antibodies targeting the slit-diaphragm protein nephrin, encoded by the *NPSH1* gene, have been detected in blood and biopsy samples. Nephrin plays a critical role in maintaining slit-diaphragm structure and transmits signals to the actin cytoskeleton of podocyte foot processes, presumably stabilizing their morphology. Therefore, analyzing the nephrin signalosome is promising for identifying potential therapeutic targets in MCD.

Methods: Antibody-mediated nephrin clustering in cultured podocytes established tyrosine-dependent signaling as a model

for MCD. Functional roles of the identified proteins were investigated using a knockdown approach followed by *in vivo* filtration assays in Drosophila nephrocytes. To explore C3G's role in mammalian podocytes, we created a C3G knockout (C3G-KO) in the metanephric mesenchyme of C57BL/6 mice using the Cre/*loxP* system.

Results: Phospho-proteome analysis after nephrin clustering identified approximately 180 differentially phosphorylated peptides. Pathway analysis indicated among others an enrichment in the biological process of 'actin cytoskeleton organization'. Many of these proteins are essential for filtration *in vivo* as has been shown using the Drosophila nephrocyte model. RAPGEF1 (C3G), an activator of the small GTPase Rap1, was one of the differentially phosphorylated proteins and is critical for filtration in Drosophila nephrocytes. C3G KO in mice, like *NPHS1* KO, resulted in an early onset of nephrotic syndrome and MCD / focal segmental glomerulosclerosis (FSGS). RNA sequencing of C3G-KO mouse glomeruli revealed significant alterations in genes related to cell signaling, adhesion and extracellular matrix organization. Immunofluorescence analysis confirmed changes in glomerular basement membrane (GBM) and focal adhesion (FA) composition, along with substantial podocyte loss in C3G-KO mice.

Conclusion: We identified numerous novel proteins in the nephrin signalosome essential for filtration *in vivo*. Loss of the nephrin signaling intermediary C3G alters FA and GBM composition, leading to podocyte loss.

OC 52

Time is kidney – Acute renal artery syndrome as a rare cause of high blood pressure

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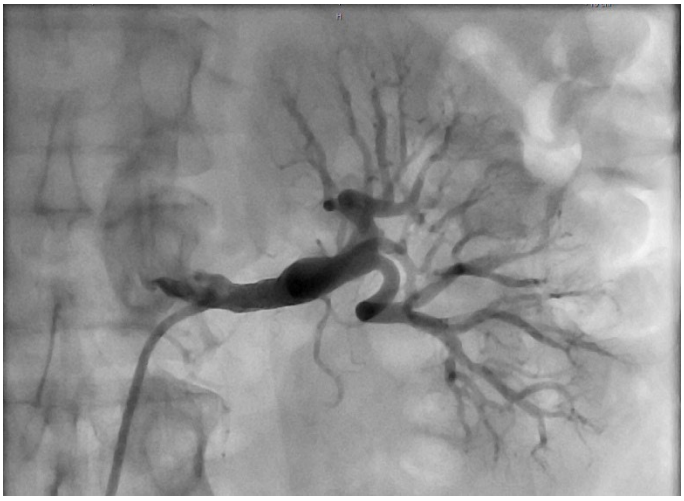
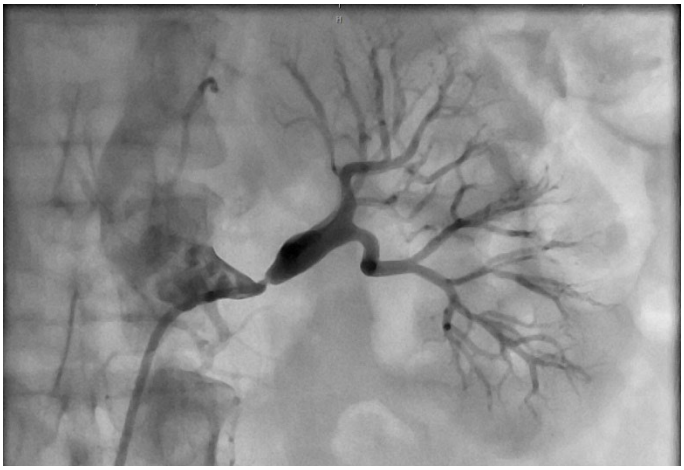
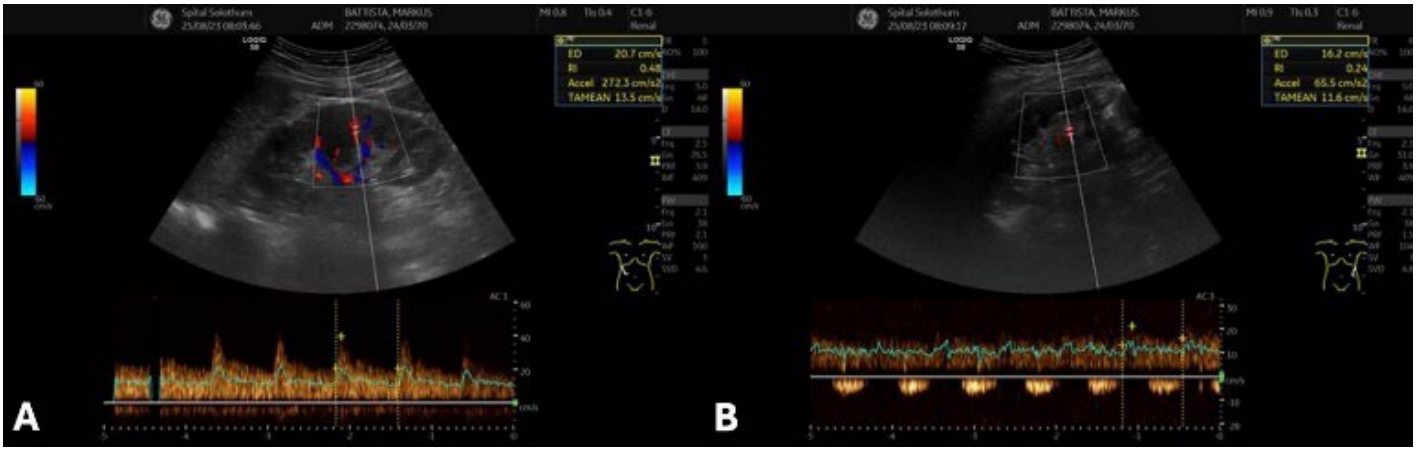
A renal infarction is a rare condition caused by a sudden restriction of renal blood flow. The prevalence in emergency departments is about 0.003%, while autopsy studies report a prevalence of up to 1.4%. The main causes are atherosclerosis, dissections, and aneurysms. Hypertensive crises and acute renal failure are often present at the time of diagnosis. An abnormal duplex sonography can support the suspected diagnosis, while CT angiography remains the gold standard in diagnostics. In this case report, a 53-year-old patient presented after a syncope with hypertensive emergency and subacute cardiovascular insult. After duplex sonography and subsequent CT angiography, an acute high-grade left renal artery stenosis was diagnosed. The following renal angiography revealed an unstable soft plaque in the middle part of the renal artery, which was treated with stent implantation. Post-intervention, blood pressure normalized. This case highlights the need for rapid, interdisciplinary investigation and treatment of secondary causes of hypertension. Early intervention can prevent severe complications. This case is particularly noteworthy due to the rare combination of acute renal artery stenosis with an atypical lesion location in a relatively young patient.







OC 53

Tocilizumab Reduces Injury-Repair-Associated Transcripts Compared to Standard Immunosuppression in Chronic-Active Antibody-Mediated Rejection

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Background: Chronic-active antibody-mediated rejection (caAMR) is a leading cause of late allograft failure in kidney transplant recipients (KTRs), with limited effective treatment options. Tocilizumab (TCZ), an interleukin-6 monoclonal antibody, has been proposed as a potential therapy improving long-term outcome. We examined gene expression changes in follow-up biopsies after TCZ treatment in comparison to optimized standard immunosuppression (sIS) alone.

Methods: KTRs with biopsy-proven caAMR >6 months post-transplantation and available follow-up biopsies were included. Biopsy-based transcriptomics were assessed using the Molecular Microscope Diagnostic System (MMDx). Six KTRs received monthly TCZ (8 mg/kg IV) plus optimized sIS (tacrolimus/mycophenolic acid/prednisone), and three KTRs received sIS only.

Results: In the TCZ group, there was a decrease in injury and repair-associated transcripts (IRAAT, median 0.24; 0.03) and a slight decrease in atrophy-fibrosis transcripts (IFTA, median 0.65; 0.51). Rejection classifier scores (median 0.66; 0.6) and AMR classifier scores (median 0.51; 0.58) remained stable, with a marginal decrease in all AMR score (median 0.92; 0.81). The rejection archetype cluster significantly evolved from early-stage AMR (R4 score, median 0.53; 0.23; p = 0.004) to fully developed AMR (R5 score, median 0.27; 0.47; p = 0.041). In contrast, in the sIS group, IRAATs (median -0.11; 0.40) and IFTA (median 0.22; 0.60) increased. Rejection classifier (median 0.81; 0.65) and AMR classifier scores (median 0.79; 0.45) decreased, with no change in AMR archetypes.

Conclusions: TCZ compared to sIS alone did not improve molecular AMR activity or halt progression from early to fully developed AMR. However, it reduced IRAAT scores, which are linked to graft failure, suggesting potential benefits. Further investigation in a larger cohort is needed to determine whether IRAAT scores could serve as early markers of treatment response.

OC 54

Transcriptomic analysis of kidney allograft biopsies may allow early detection of rejection, precise rejection typing, and dynamic treatment monitoring

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Background: The Molecular Microscope Diagnostic System (MMDx) was validated for various histological scenarios and was highlighted in the 2022 *Banff* Meeting Report. However, its effectiveness in the follow-up remains underexplored. Previous studies suggested that MMDx could (1) detect molecular signatures of rejection earlier than conventional histopathology, (2) more accurately differentiate between rejection types, and (3) offer measurable indicators of treatment response.

Methods: We examined 70 kidney transplant recipients with 155 allograft biopsies evaluated by histology and MMDx. This resulted in 85 biopsy-series (each with 2 consecutive biopsies), which were analyzed regarding (1) the correlation of histology and MMDx, (2) the time and type of rejection diagnosis, and (3) the measurability of treatment effects.

Results: 33, 4, and 10 of the baseline biopsies showed histological AMR/MVI, TCMR, and mixed rejection, respectively. Molecular rejection by pure molecular interpretation or archetypes was found in 70%/79%, 75%/75% and 80%/90%, respectively. Follow-up biopsies were obtained after a median of 8 months (IQR 4, 17). 13/38 (34.2%) of cases without histological rejection in the baseline biopsy showed rejection in the follow-up biopsy, and had significantly higher rejection classifier scores (median 0.17 vs. 0.03, p = 0.01), AMR classifier scores (median 0.13 vs. 0.04, p<0.001) and all AMR archetype scores (0.23 vs. 0.09, p = 0.007), than the 25/38 (65.8%) without rejection in the follow-up biopsy. 4/5 (80%) of cases which were AMR/MVI by histology at baseline but molecular mixed AMR/TCMR by MMDx were confirmed in the follow-up biopsies. Treatment responses to anti-rejection interventions with pulsed steroids and active AMR protocols reflected in significant changes in the molecular classifier but not archetypal scores.

Conclusion: Biopsy-based transcript diagnostics may detect rejection sooner and identify rejection types precisely, which might reduce the need for repeat biopsies and support treatment decisions. Molecular diagnostics may also depict treatment outcomes more comprehensively through follow-up biopsies.

OC 55

TrkC Deficiency in Nephrons Exacerbates Tubular Kidney Injury in Mice.

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Background: Acute tubular injury often progresses to chronic kidney disease (CKD). The neurotrophic tyrosine kinase receptor C (TrkC) regulates neuronal differentiation and survival. In murine kidney, TrkC is expressed in podocytes and specific tubular segments, including the cortical collecting duct and thick ascending limb. Loss of TrkC in nephrons (TrkC-KO) leads to proteinuria and focal segmental glomerulosclerosis (FSGS), while the tubules remain histologically unaffected. However, TrkC expression varies in CKD biopsy samples across different etiologies. This study aims to investigate TrkC's role in tubular injury.

Methods: Three-month-old nephron-specific TrkC-KO mice and littermate controls were fed either a 0.2% adenine-enriched diet or a control diet for 8 days. Weight and blood urea nitrogen (BUN) levels were measured. Kidney tissue was analyzed using histology, electron microscopy, and immunofluorescence. HEK293T cells were treated with adenine to assess TrkC signaling *in vitro*.

Results: The adenine-enriched diet caused crystal deposition, tubular injury, inflammation, and fibrosis. TrkC-KO mice on the adenine diet experienced greater weight loss and higher BUN levels than controls. Histological analysis revealed more severe tubular damage in TrkC-KO mice. Immunofluorescence showed increased NFκB and Ki67 expression in distal tubules of TrkC-KO mice, along with elevated leukocyte and macrophage infiltration in the kidney cortex. *In vitro*, HEK293T cells overexpressing TrkC displayed enhanced TrkC phosphorylation and downstream signaling when treated with adenine.

Conclusion: Loss of TrkC worsens adenine-induced tubular injury and increases tubulo-interstitial inflammation. These results suggest that TrkC signaling may have a protective role in the kidney during acute tubular injury, with potential implications for CKD progression.

OC 56

Usability of Machine Learning Algorithms based on Electronic Health Records for the Prediction of Acute Kidney Injury and Transition to Acute Kidney Disease: a Proof of Concept Study

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Importance: Acute kidney injury(AKI) and acute kidney disease(AKD) are common complications during hospitalization, leading to poorer outcomes and increased healthcare costs. These conditions are often underrecognized and untreated in a timely manner.

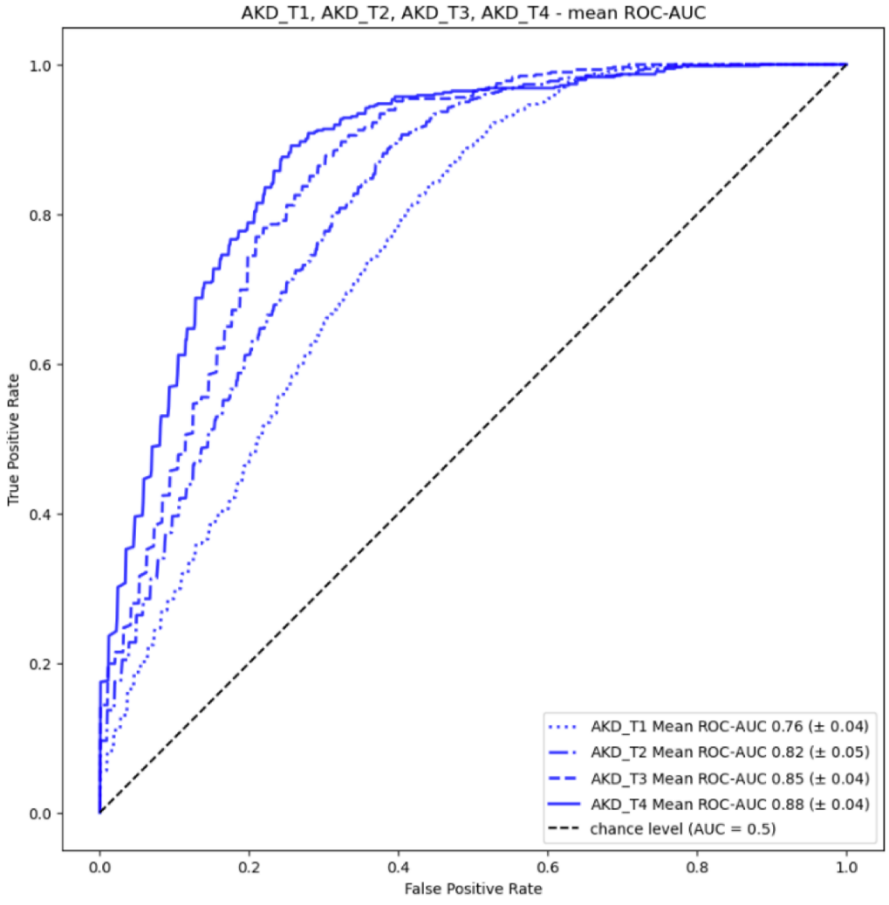
Objective: This study explores the potential of artificial intelligence (AI) using electronic health records (EHR) to diagnose AKI and AKD during hospital stays.

Design: We retrospectively analyzed EHR from all patients admitted to our public hospital network in 2022. AKI and AKD were defined according to international guidelines (Figure 1). The database was split into training and validation sets. Machine Learning (ML) algorithms were implemented with cross-validation, and diagnostic accuracy was assessed.

Results: We analyzed 34,579 hospitalizations (mean age of 60 years, 50% females) (Table 1). Baseline renal function was available in ~50% of cases. AKI and AKD complicated 10% and 1.5% of hospitalizations. Most AKI episodes (77%) occurred within the first three days of hospitalization, with >50% of AKI patients discharged before complete renal function recovery. ML accurately predicted AKI during hospitalization (AUC-ROC 79%) using data available before and at hospital admission. For patients with AKI on the first day and extended hospital stays, the ML accuracy for predicting the transition from AKI to AKD improved (AUC-ROC from 76% to 88%) (Figure 2) by incorporating data accumulated during the hospitalization. Consistently, the negative predictive value(NPV) progressively increased from 94% to 98%. Shapely additive explanations analysis documented that age, urgent hospital admission, AKI severity, and baseline renal function were associated with AKI. In contrast, renal function trajectory during the initial days of hospitalization was the most relevant predictor of AKD.

Conclusions and Relevance: ML algorithms utilizing EHR before and during hospitalization show an adequate level of accuracy in early prediction of AKI and AKD. The high NPV indicates its potential to rule out renal failure risk, personalize patient care, and optimize healthcare resource allocation.

Receiving Operator Curve(ROC) of the ML models to predict the risk of AKD transition at day 1,2,3, and 4



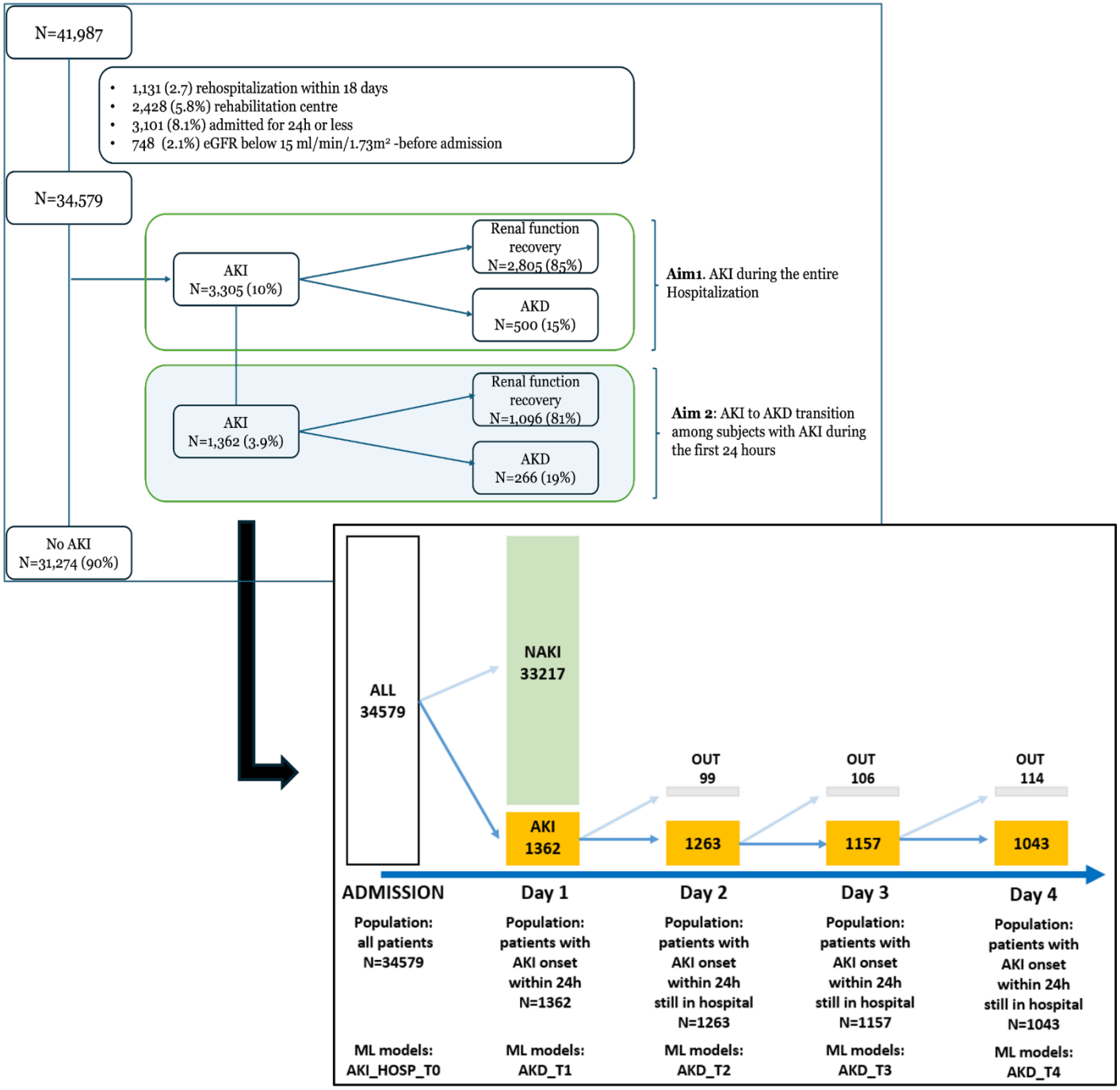


Table 1: demographic, administrative, and laboratory data of the entire study cohort

Variable	ALL (N=34,579)	NAKI (N=31,274)	AKI (N=3,305)	AKI_NAKD (N=2,805)	AKI_AKD (N=500)
Entire cohort					
Age, Mean ± SD	60.82 ± 25.37	59.40 ± 25.85	74.17 ± 14.62	74.15 ± 14.52	74.32 ± 15.16
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Female sex, %	50%	51%	40%	40%	40%
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Medical Speciality Medicine, %	31%	29%	53%	52%	59%
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Medical Speciality Urology, %	6%	6%	9%	9%	5%
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Urgency admission, %	62%	59%	85%	85%	84%
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Elective admission, %	33%	35%	14%	14%	14%
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Institute Emergency Medicine, %	6%	5%	16%	17%	11%
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Institute Surgery, %	35%	36%	26%	26%	20%
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
sCr baseline, Mean ± SD	88.48 ± 35.67	85.98 ± 32.38	105.28 ± 49.57	107.69 ± 47.90	96.37 ± 54.44
Missing	17938 (52%)	16789 (54%)	1149 (35%)	1108 (40%)	41 (8%)
sCr 1st, Mean ± SD	96.98 ± 58.24	87.34 ± 35.10	158.62 ± 113.17	153.04 ± 99.63	189.95 ± 166.95
Missing	10155 (29%)	10155 (32%)	0 (0%)	0 (0%)	0 (0%)
Estimated GFR 1st, Mean ± SD	73.12 ± 26.24	77.23 ± 24.17	47.27 ± 23.88	47.50 ± 23.19	45.94 ± 27.47
Missing	10670 (31%)	10644 (34%)	26 (1%)	20 (1%)	6 (1%)

ELEVATOR PITCH

OC 57

A critical appraisal of current criteria to diagnose the syndrome of inappropriate antidiuresis (SIAD)

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Background: Since its first description, the syndrome of inappropriate antidiuresis (SIAD) has been a diagnosis of exclusion. Current reviews and guidelines recommend a series of essential and supplemental criteria for its diagnosis. We hypothesized, that these criteria wrongfully exclude many cases of inappropriate antidiuresis, and still do not rule out other etiologies of hypotonic hyponatremia.

Methods: We used patient data (n = 298) from a previous prospective, observational study. Diagnostic criteria of SIAD were assessed as defined by the European guideline on hyponatremia (Spasovski G et al. Nephrol Dial Transplant. 2014). First, we determined the prevalence of all 6 essential and 5 of 7 supplemental criteria and their combinations. We then cross-checked them against the presence of factors known to be associated with inappropriate antidiuresis. Finally, we analyzed whether the different criteria did exclude other etiologies of hypotonic hyponatremia.

Results: All essential criteria of SIAD were fulfilled by 20.8% of patients. The addition of the supplemental criteria reduced the prevalence of SIAD to only 4.7%. The two most restrictive essential criteria were 'no [thiazide] diuretics' and 'euvolemia', being met in 56% and 58.1% of patients respectively. In 22.1% and 12.4% of cases, they were the singular excluding essential criterion. In contrast, we found that factors associated with inappropriate antidiuresis were present in 63.8% of patients. Importantly, their prevalence was very similar irrespective of the essential criteria of volume status, urine sodium concentration, kidney disease, and diuretic therapy. Additional etiologic factors of hypotonic hyponatremia were present in 71.9% of patients who fulfilled all essential criteria of SIAD.

Conclusion: Most patients with attributes of inappropriate antidiuresis are excluded from a diagnosis of SIAD by current criteria. Very often, the same criteria fail to rule out other etiologies of hypotonic hyponatremia.

OC 58

Aurantiasis cutis in a 60-year-old patient undergoing dialysis

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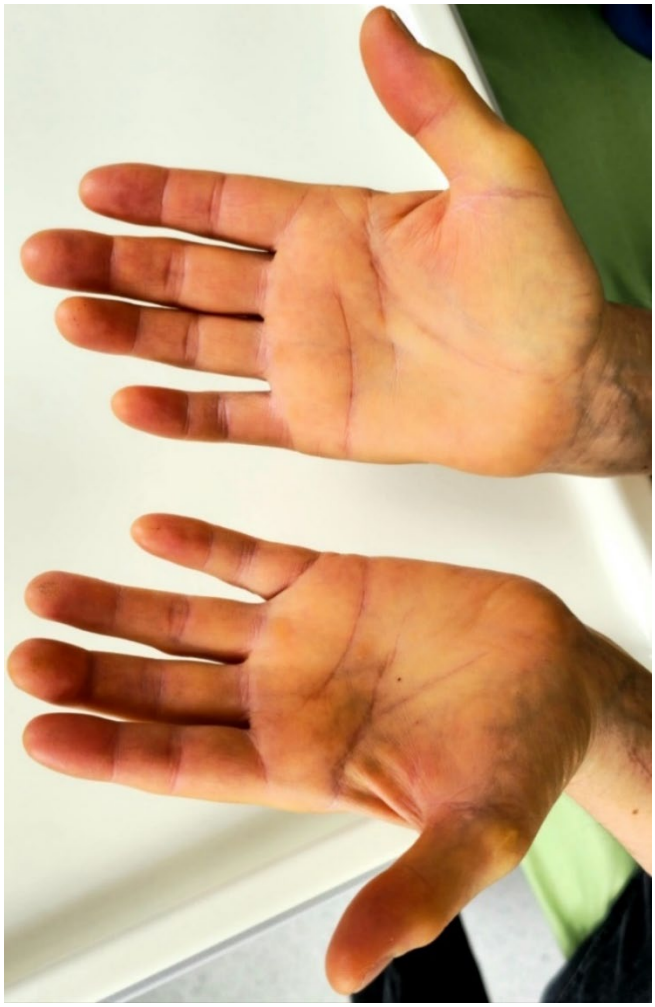
Background: Vitamins are known to the general population as being beneficial in health and development. Dialysis and ESKD-patients are at risk of side effects or even hypervitaminosis, especially in cases of selfmedication. Case Report: A sixty-year-old patient with end stage kidney disease (ESKD) due to diabetic nephropathy in need of chronic dialysis, presented with intensively yellow to orange discoloration of hands and face with exemption of sclera with stronger tint palmar(Picture 1). The initial questionnaire didn't show changes in medication or eating habits or risk for viral infection or cholestatic hepatopathy, thus the suspected diagnosis initially was a probable iron overload due to regular intravenous supplementation. As symptoms worsened without serological signs of iron overload another thorough questionnaire was done. It showed, that the patient after eye surgery, containing pars plana vitrectomy, intraocular lense explantation and implantation of a new lense started to take beta-carotene tablets as selfsupplementation to help eye-recovery. He reported feeling as if the beta-carotene improved his vision and thought taking three times the recommended dose could improve it further. Fearing liver toxicity, we initiated laboratory testing which showed no elevation of liver enzymes or bilirubin or cholestase parameters or elevated Vitamin A-levels (Figure 1). We actually had no indication of acute vitamin A toxicity. Nevertheless we diagnosed Aurantiasis cutis due to oversupplementation of beta-carotene in combination with anuric ESKD. After stopping supplementation the yellow discoloration faded away over four weeks.

Conclusion: Thorough case history remains one of the most important tools available to clinicians. Vitamin- or even precursors selfsupplementation can lead to side effects though they are not perceived as potentially dangerous by the general population or even by clinicians. Even though beta-carotene supplementation is not strongly toxic patients with ESKD, and diabetes mellitus are at higher risk of amaurosis cutis.



Bilirubin	10.9 µmol/l	<21 µmol/l
ASAT	15 U/l	< 50U/l
ALAT	6 U/L	< 50U/L
GGT	15 U/L	< 66U/L
Vitamin A(Retinol)	2.32 µmol/l	1.33 -3.42 µmol/l

OC 59

Bicentric validation of the diffusion-weighted magnetic resonance imaging as a noninvasive tool to assess fibrosis level

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Background and Aims: Renal cortical interstitial fibrosis is a well-established prognostic marker for renal health, traditionally assessed via biopsy. Advances in diffusion-weighted MRI have enabled the measurement of cortico-medullary apparent diffusion coefficient difference (ΔADC), which we previously demonstrated to inversely correlate with histologically confirmed interstitial fibrosis. This study aims to validate these findings, assess reproducibility across institutions, and evaluate their relevance in specific subgroups, particularly comparing allograft recipients and native kidney patients.

Method: Between 2014 and 2023, a prospective cohort study was conducted involving 309 patients with chronic kidney disease (n = 106) or renal allografts (n = 203). Each patient underwent a biopsy followed by multimodal MRI within the subsequent weeks. Patients were recruited from the University Hospitals of Geneva (HUG) and Lausanne (CHUV), Switzerland. The primary objective was to evaluate the correlation between ΔADC and biopsy-confirmed renal fibrosis. Subgroup analyses were conducted by institution and kidney type (native vs. allograft), and linear regression models were applied to examine these associations.

Results: Of the 309 participants, 270 were recruited from Geneva and 39 from Lausanne. Across the entire cohort, a significant negative correlation was observed between ΔADC and the degree of fibrosis (R = -0.41, p <0.001). Subgroup analyses revealed similar findings at both Geneva (R = -0.43, p <0.001) and Lausanne (R = -0.35, p <0.001). The negative correlation was also significant in both native kidneys (R = -0.48, p <0.001) and allograft kidneys (R = -0.38, p <0.001).

Conclusion: These results confirm the inverse relationship between ΔADC and renal fibrosis, demonstrating consistency across centers and kidney types (native and allograft). This supports the potential use of diffusion MRI as a reliable noninvasive tool for assessing renal fibrosis.

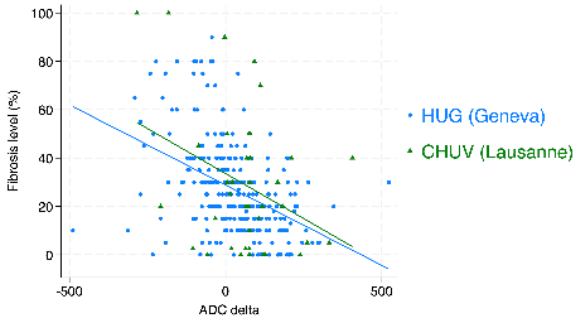

Figure 1: Correlation between fibrosis and apparent diffusion coefficient's cortico-medullar difference (ΔADC) for HUG's (blue circle) and CHUV'S (green triangle) cohorts with their respective regression line (R= -0.43 with p<0.001 for the HUG, R= -0.35, p<0.001 for the CHUV).

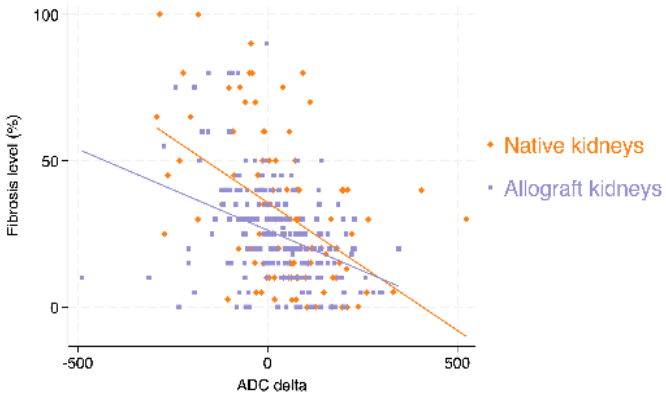

Figure 2: Correlation between fibrosis and apparent diffusion coefficient's cortico-medullar difference (ΔADC) for native kidneys (orange diamond) and kidney allografts (purple square) with their respective regression line (R= -0.48 with p<0.001 for native kidney, R= -0.38, p<0.001 for allograft).

OC 60

Cobalamin C deficiency associated atypical HUS

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Background: Cobalamin C (CbI-C) deficiency as origin of atypical hemolytic uremic syndrome is rare. Cobalamin C disease is multisystemic: failure to thrive, muscular hypotonia, multiple central nervous symptoms, retinopathy, megaloblastic anemia and around 10% of patients develop hemolytic uremic syndrome. Specific treatment consists of substitution of hydroxycobalamin, betaine (methylcobalamin), carnitine and folic acid.

Case: A ten-year-old female patient developed emesis and abdominal pain during her holiday in the United States of America. She had an uneventful medical history. She then suffered a tonic-clonic status epilepticus and hypertensive crisis with systolic blood pressure of 220mmHg. Cerebral imaging was normal and laboratory exams revealed renal insufficiency with creatinine at 506µmol/l, intravascular hemolysis (hemoglobin 63g/l), thrombocytopenia (min. 100 G/l), hematuria and proteinuria. Atypical hemolytic uremic syndrome was suspected (diarrhea negative) and eculizumab was administered. She was on intermittent hemodialysis and hypertension was treated with amlodipine and clonidine patches. Renal biopsy showed thrombotic microangiopathy and genetic testing resulted in two mutations in the MMACHC gene consistent with a cobalamin C deficiency. Subsequent treatment was hydroxycobalamin, betaine, L-carnitine and folic acid. After repatriation in Switzerland she still required dialysis and had a relapse of hypertensive crisis despite stable metabolic values and controlled fluid management. Hypertension required a five-fold regimen and she was on renal replacement therapy for ten weeks. She recovered well by now; the latest renal function (eGFR) was at 63ml/min/1.73m^2 (Schwartz formula) and she has no evident neurologic sequelae.

Learning points: Patients with atypical hemolytic uremic syndrome, especially of younger age (e.g. <30 years), should be screened biochemically for treatable cobalamin C deficiency. An inclusion into Swiss newborn screening, as in other countries, should be considered to detect presymptomatic patients and prevent severe complications of cobalamin C disease such as hemolytic uremic syndrome.

OC 61

Deconvoluting the distal convoluted tubule – a mouse population genetics approach

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Background: The cellular composition of the kidney is determined by organ development but its determinants remain largely elusive, including at the distal-convoluted tubule (DCT) responsible for many hormone-regulated active cellular transport mechanisms. Here, I determined which genomic loci and gene variants are associated with the abundance of DCT cells in murine kidney.

Methods: I performed transcriptome reanalyses of microarrays from males of 36 strains and females of 51 strains of the BXD consortium of recombinant inbred mice. After a reanalysis of single-cell RNAseq data from 7 healthy mice by R/Seurat as a reference, I applied cell-type decomposition by R/Bisque to the transcriptome data. I then used the log-transformed fraction of inferred DCT cells as a computed phenotype for quantitative trait locus (QTL) analysis by R/qtl2. I determined p-value thresholds of QTLs by 1000 permutations and assessed candidate genes in comparison with genome-wide association study data and the GeneNetwork2 computational resource.

Results: Among the assessed strains, the DCT cell abundance was 3.9% ± 4.8% in males and 3.4% ± 4.4% in females (mean ± standard deviation). QTL analysis revealed one suggestive locus associated with DCT cell abundance on chromosome 18 in males but none in females. The identified locus contains 10 genes. Among the genes in this QTL, the potentially causative candidates for this association include *Ppp1r39* and *Prelid2* involved in urothelial or renal cancer and *Ppp2r2b*, the human ortholog of which has a variant that is associated with urate levels in humans.

Conclusion: Overall, the present data reveal a potential for combining advanced transcriptome analysis methods with the systems genetics approach of studying associations between phenotypes and genomic loci in genetically diverse mice consortia. Abundance of cells of the DCT segment has a potential association with gene variants to be further investigated by experimental study.

OC 62

Early onset end-stage renal disease in a patient with a pkd2 deletion

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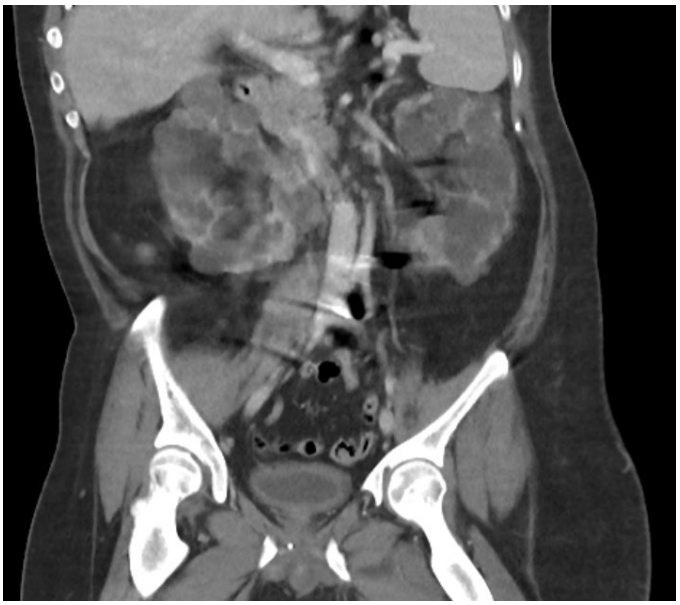
Background: Autosomal dominant polycystic kidney disease (ADPKD) results from a pathogenic variant in *PKD1* or *PKD2* in most patients. *PKD2* variants generally lead to a milder disease course. Affected patients rarely require renal replacement therapy before the age of 70 years, if at all. We report the case of a patient with a *PKD2* deletion who started haemodialysis at the unusually young age of 29 years.

Case Description: A 23-year-old man was referred to our renal clinic because of enlarged kidneys with multiple bilateral cysts. He suffered from a severe developmental disorder with mental retardation, facial dysmorphism and was unable to walk or to speak. He had also required a correction of a severe scoliosis of his spine at the age of 21 years. None of his parents or his 3 siblings had any renal cysts. The patient started haemodialysis at the age of 29 years. Two years later he received a deceased donor kidney transplant. Genetic testing revealed a large heterozygous pathogenic deletion 4q21.2q22.1 spanning 15 Mb with 89 genes including *PKD2*. The deletion contains the critical region of the so-called 4q21 deletion syndrome which is associated with a severe developmental disorder like in our patient. No other (likely) pathogenic variant was found in the analyzed gene panel including over 150 kidney-disease-related genes. We can speculate that other genes in the deleted region may have an impact onto the renal function, leading to a more severe phenotype than expected by the solely loss of *PKD2*. To our knowledge, all the reported cases of 4q21 deletion syndrome have been de novo.

Learning Points: As demonstrated by our case report as well as others, *PKD2* variants can in rare situations lead to early onset ESRD. This might be the case with larger deletions or with biallelic hypomorphic mutations of *PKD2*.



OC 63

High level of psychosocial distress in a dialysis population: A single center cross-sectional observation. Time for an integrated nephropsychological service?

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Background: Psychosocial problems and psychological disorders are very common among dialysis patients. However, these are not systematically assess in practice. It can therefore be assumed that patients with end stage kidney disease undergoing renal replacement therapy do not receive the psychological support and therapy they need.

Methods: We performed a cross-sectional study among patients undergoing chronic renal replacement therapy (hemodialysis (HD) or peritoneal dialysis (PD)) from 1st of July until 31st of August 2024 at the two dialysis centers of the Hospital cantonal of Baselland. The aim was to assess the psychosocial distress levels of patients on dialysis and the need for psychological support. We used an adapted questionnaire of the National Comprehensive Cancer Network Distress Thermometer screening Tool Version 2.2022, which is used to screen cancer patients for their overall psychosocial and physical distress levels and need for psychological support.

Results: The response rate of the questionnaire was 60% (57/94). Overall, we found a high psychosocial distress level in the population with a mean level of 6.4. The distress level in PD patients with a mean of 7.25 was higher compared to the mean level in HD patients with 6.24. A level of >4, indicating the need for further psychological assessment and support, was found in 63% of patients. The most common psychosocial and physical complaints were fatigue (65%), pain (42%), muscle cramps (40%), limited mobility (39%) and symptoms of depression (35%).

Conclusion: There is an overall high distress level in patients on dialysis. At least 1/3 of dialysis patients would qualify for professional psychological assessment and support. This fact points to the need for a nephropsychological service.

OC 64

Mimicry and mystery – subacute kidney failure in a man with lymphadenopathy

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Background: IgG4-related disease is a multisystem lymphoplasmatic fibro-inflammatory disease, whose histological characteristics include dense lymphoplasmocytic infiltrates, rich in IgG4-positive plasma cells and fibrosis, often in a storiform pattern. Renal manifestations comprise tubulointerstitial nephritis, obstructive uropathy secondary to retroperitoneal fibrosis and membranous nephropathy.

Case: We present the case of a 69-year-old male, who initially presented with fatigue, malaise and shortness of breath and weight loss of 5 Kg within a few weeks. Moderate anaemia and elevated creatinine (260 µmol/l) were noted. A CT-scan revealed bilateral hilar lymphadenopathy. Subsequent pulmonary follow-up included bronchial lavage and lymph node fine needle biopsy, which could neither confirm, nor rule out the suspected diagnosis of sarcoidosis. Renal impairment was not followed up on at that time. Over the next weeks, and after a short hospitalisation due to pneumonia, kidney function declined and he developed arthritis in his ankles. Further work-up showed elevated IgG4 levels, as well as significant hypocomplementemia. Kidney biopsy revealed tubulointerstitial nephritis with sclerosis and infiltration of inflammatory cells comprising lymphocytes and numerous IgG4-positive plasma cells, with an elevated ratio of IgG4-positive to IgG-positive plasma cells. Subsequently the diagnosis of IgG4-related disease was established and high dose glucocorticoid treatment initiated. At follow up 4 weeks after begin of treatment, kidney function was improved.

Teaching points: This case highlights a rare, but treatable cause of tubulointerstitial nephritis and kidney failure. Early biopsy in unexplained kidney failure is essential to ensure diagnosis and to facilitate timely treatment decisions.

OC 65

Osmotic nephropathy secondary to L-proline-stabilized intravenous immunoglobulins

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Background: Acute tubular necrosis (ATN) is a well described complication of the sucrose containing intravenous immunoglobulins (IVIG). It is thought to be mediated by the reabsorption and toxic accumulation of sucrose in proximal tubular cells (PTC), with a histological pattern of vacuolization of PTC and improperly termed as « osmotic nephropathy (ON)». It is much rarer with sucrose-free formulations of IVIG, and the underlying mechanisms aren't clearly understood.

Case description: We describe the case of a 67 years old male hospitalized for Guillain-Barré syndrome (GBS) two weeks after a SARS-CoV 2 infection, who was severely dysautonomic and had wide variation of blood pressure. He was treated with sucrose-free IVIG, stabilized with L-proline (Privigen®), for four consecutive days (20g/dose, administered in 3h), and developed a sudden anuric acute kidney injury (AKI). The immune assessment was negative, C3 and C4 levels were in the normal range, and there was no proven hemolysis. The kidney biopsy showed vacuolization of tubular cells, confirming the diagnosis

of ATN secondary to ON. There was no glomerular involvement. Immunostaining was negative. The evolution was favorable with diuretics and hemodialysis was not needed.

Learning point: L-proline stabilized IVIG can induce AKI, but most of the reported cases are in the setting of hemolysis. They rarely induce ON, and several hypothetical mechanisms are suspected such as transient impaired lysosomal activity and intravacuolar crystallization of immunoglobulins. Toxicity of IVIG might be favorized by hemodynamic instability.

Conclusions: ON secondary to IVIG – irrespective of their sugar content – must be suspected in a patient with AKI following IVIG treatment.

OC 66

Patients' quality of life and care satisfaction on a Swiss dialysis ward

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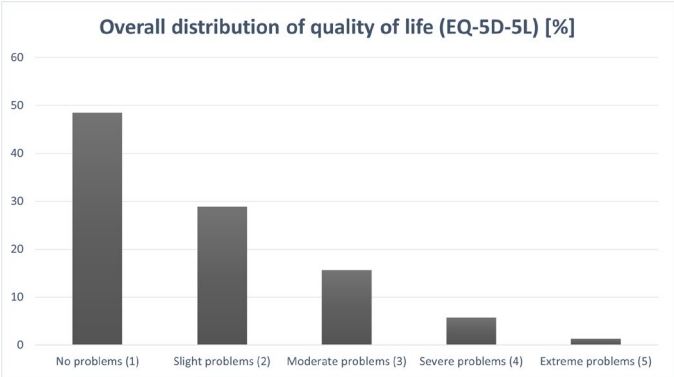
Introduction: End-stage kidney disease requires renal replacement therapy, either dialysis or a kidney transplant, to survive. Due to limited availability of organs for donations haemodialysis is the therapy of interest. Since 2002, the number of haemodialysis patients is annually increasing by 4% in average. Because of the increasing age of patients, heamodialysis patients need more support with respect to the complexity of the therapy and their high symptom burden. In this regard an advanced practice nurse is implemented.

Methods: For evaluation of the initial situation a cross-sectional survey was obtained amongst a sample of chronic hemodialysis patients (n = 62) during two weeks at the beginning of September 2024. Regarding patient experience care satisfaction and quality of life (eq5d5l); using two different assessment instruments and a visual analogue scale. Informed consent in all patients was obtained.

Results: Patients' average age was 67 years and 74% were male. Patients' satisfaction with the care they received was rated high with 1.38 (of a scale from 1 to 5); across five parameters and the average visual analogue score was high with 87.3 (of 100). The average quality of life score (eq5d5l) was high with 1.7 (of a scale from 1 to 5); but the visual analogue scale score was medium with 66.5 (of 100).

Conclusions: This cross-sectional survey indicates a high patients' satisfaction compared to a lower quality of life score. Quality of life could be affected by the timely, efficient, and patient-centered delivery of quality health care. Implementation of an advanced practice nurse to increase continuity of care may aid in improving patients' quality of life.



OC 67

Plasma-derived Fetuin-A as a potential patient-specific biomarker for predicting acute kidney injury associated with cardiovascular surgery: interim analysis results from the PEAK study

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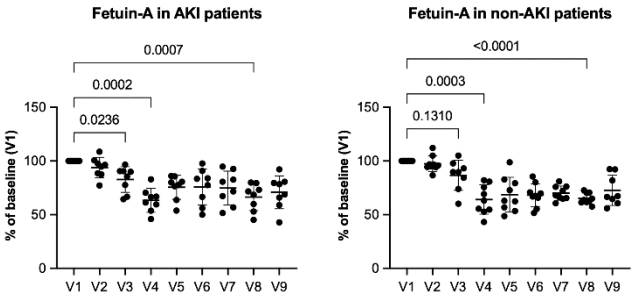
Background: Acute kidney injury (AKI) is one of the most common and life-threatening complication following cardiovascular surgery (CVS) with incidence rates of up to 60% among critically ill and elderly patients, leading to significantly increased mortality, longer hospital stays, and a higher risk of progression to chronic kidney disease (CKD). Recently, we identified the liver-derived glycoprotein Fetuin-A (FA) as a crucial tissue chaperone in mice, where its supplementation improved outcomes in renal ischemia-reperfusion injury. However, the relationship between FA and CVS-associated AKI in patients remains largely unexplored.

Methods: PEAK is a prospective, observational, non-interventional study conducted at the University Hospital Bern, Switzerland, designed to evaluate in elective CVS patients the association between FA and AKI in blood and urine samples, as well as by frailty assessment as patient-reported outcome measures (PROM).

Results: This interim analysis includes the first 30 patients (10 females and 20 males), with a mean age of

65.5±7.3 years. Among them, 9 patients (30%) developed AKI, with 2 requiring dialysis within the first postoperative week. In the AKI group, the highest recorded CRP value was 271±112 mg/L, compared to 172±65 mg/L in the non-AKI group. Serum FA levels showed a biphasic drop in all patients, reaching their lowest point (35% below baseline) 4–9 hours after surgery, and on postoperative day 3 (Figure 1). Notably, patients who developed AKI had significantly reduced FA levels as early as 1–2 hours into surgery, a change not observed in the non-AKI group.

Conclusion: This preliminary analysis provides promising results, supporting our hypothesis that rapid FA depletion may serve as a crucial patient-specific biomarker for predicting AKI and poorer clinical outcomes in CVS patients. Secondary outcomes, including correlations with established inflammatory markers, the incidence of CKD, and PROM at 90 days, will be analyzed at the end of the study period.



OC 68

Primary aldosteronism unmasked by pregnancy: a case report and literature review

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Background: Primary aldosteronism (PA) is a neuroendocrine disorder and it is one of the most frequent causes of secondary hypertension (HT). PA may affect hypertensive pregnancies and its frequency is underestimated because of its unusual presentation. In pregnancy, because of renin-angiotensin system activation and lack of hypokalemia, due to physiologic pregnancy-related metabolic acidosis and anti-mineralcorticoid effect of progesterone, the diagnosis of PA may be challenging.

Case Report: A 46yrs old woman attended our renal outpatient clinic at 8 weeks gestation (SGD) of a FIV-ET pregnancy under treatment with estrogens, steroids and LMW-heparin, because of high blood pressure (BP 138/94mmHg). The obstetric history is characterized by a spontaneous abortion, 3 failed embryo transfers and by several hormonal stimulations. The patient is known for Hashimoto disease, breast cancer and HT, diagnosed 2 years prior to the current pregnancy.

Results: At 10 weeks gestation BP increased to 180/115 mmHg. Renal parenchymal/vascular diseases were excluded. With Labetalol therapy, BP normalized during all pregnancy. Laboratory data showed normal renal function, normal potassium and a light metabolic acidosis. At $38^{6/7}$ SGD, Caesarian Section and birth of 3350g boy. Because of post-partum HT, we performed a screening for PA, including a recumbent saline suppression test according to our standard protocol and after a medications wash-out period (>2 weeks). The results listed below confirm the diagnosis of PA. No adrenal gland anomalies were seen at MRI. Aldosterone and direct renin were determined by chemiluminescent immunoassay technology (DiaSorin®).

Conclusions: In hypertensive pregnancies, especially before 20 weeks gestation, secondary forms of HT should be ruled out. Even in absence of hypokalemia and metabolic alkalosis, PA should be excluded. Since diagnostic criteria for PA in pregnancy are not well defined and its diagnosis would not change the management of HT in pregnancy, the screening tests should be performed post-partum.

Post-partum Variables	**Plasma aldosterone** *pmol/l*	**Plasma direct renin** *ng/l*	**Aldosterone-to-renin ratio** *pmol/ng*	**Plasma K^+** *mmol/l*
Baseline	487 *(N 32-654)*	2.4 *(N 1.7-23.9)*	**203** *(N <55)*	4.2 *(N 3.5-5)*
After NaCl suppression test	***247*** *(N <140)*			

OC 69

Primary membranoproliferative glomerulonephritis (MPGN): natural history, complement system and renal outcome

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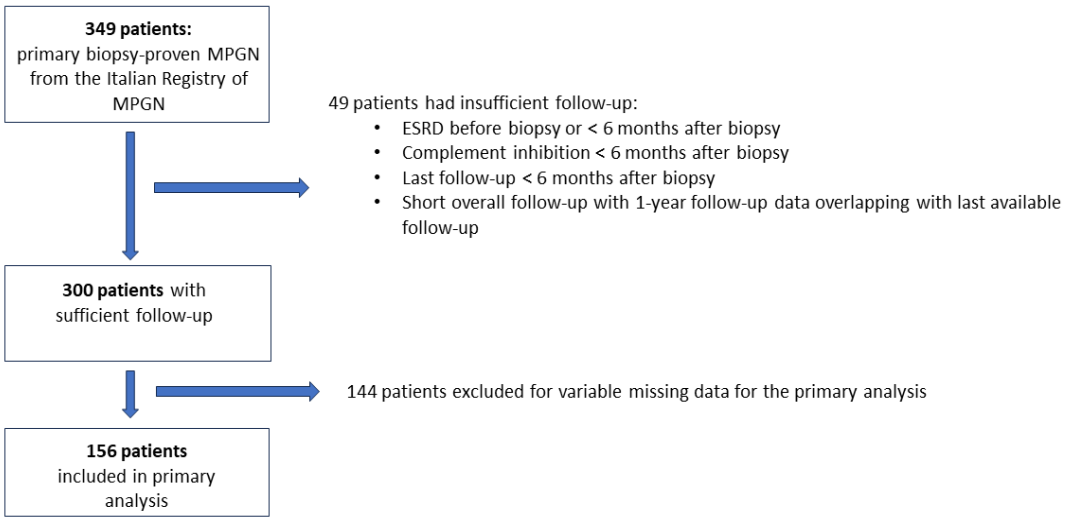
Membranoproliferative glomerulonephritis (MPGN) is a rare nephropathy, affecting predominantly children and young adults and defined by a typical histopathological pattern of mesangial hypercellularity, endocapillary proliferation and duplication of the glomerular basement membrane. While clinical presentation and outcome are variable, the overall prognosis is poor. Our aim was to describe the natural history of primary MPGN and to explore the relationship between proteinuria and renal outcome. Subjects with biopsy-proven primary MPGN were selected from the Italian Registry of MPGN (https://www.marionegri.it/eng/mpgn-c3g-registry). Parameters were collected at onset, at baseline (defined as the time of the first diagnostic biopsy), at 1-year follow-up (with an accepted range of 6 to 18 months) and at the last available follow-up.

Exclusion criteria for the primary analysis were:
- Follow-up <6 months after baseline
- End-stage renal disease (ESRD) before baseline or <6 months thereafter
- Complement inhibition <6 months after baseline
- Missing data

The primary analysis included the correlation between 24h-proteinuria at one year after baseline and a composite renal outcome including ESRD (eGFR <15 ml/min/1.73m^2, dialysis or preemptive kidney transplantation), doubling of creatinine at last follow-up (except for children <18) or death from renal causes. Our population consisted of 349 subjects. Around 30% of patients progressed to ESRD. Average follow-up was over 7 years. In the 156 patients included in the primary analysis, there was a statistically significant correlation ($p = 0.0011$) between the 1-year 24h-proteinuria and the composite endpoint. In conclusion, this study on patients with primary MPGN demonstrated a statistically significant correlation between a higher proteinuria one year after diagnosis and an unfavorable renal outcome, supporting the possibility of considering proteinuria as a predictor of long-term renal outcome in primary MPGN.

Figure 1: flowchart of patients' selection for the primary analysis



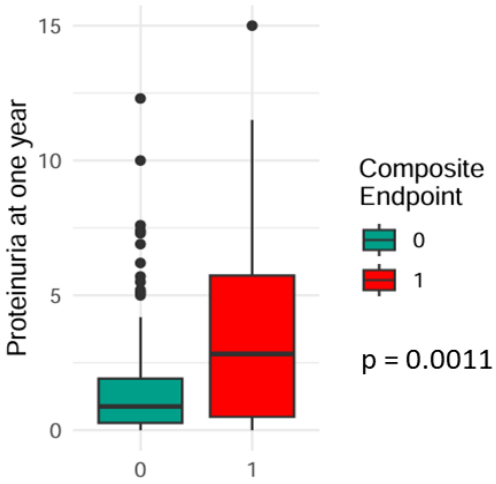


Figure 2: proteinuria at one year by composite endpoint

Table 1: full cohort description

	Primary MPGN total (n=349)	IC-MPGN (n =141)	C3G (n= 208)	p-value	DDD* (= 40)	C3GN (n=140)	p-value
Females % (n)	41.0 (143)	43.3 (61)	39.4 (82)	0.5065	37.5 (15)	40.7 (57)	0.8550
Age at onset years; median (IQR) (n=346)	15.0 (9.9-24.6)	16.2 (10.4-32.7)	13.4 (9.5-21.8)	0.1193	12.6 (9.7-16.1)	14.7 (9.4-19.0)	0.6371
Age at diagnosis (years)	21.9 (0-72)	23.2 (3-72)	21.1 (0-72)	0.2530	17.8 (1-62)	21.6 (0-72)	0.1284
Children <12 years old % (n)	30.9 (108)	29.1 (41)	32.2 (67)	0.5571	40.0 (16)	32.1 (45)	0.3519
Adolescents 12-17 years old % (n)	24.6 (86)	22.0 (31)	26.4 (55)	0.3769	25.0 (10)	24.3 (34)	1
Delta between onset and diagnosis (months) (n=345)	26.1 (0-605)	21.3 (0-378)	29.5 (0-605)	0.1863	25.7 (0-208)	34.6 (0-605)	0.3898
Clinical presentation at onset:							
Hematuria % (n) (n=340)	84.7 (288)	81.5 (110)	86.8 (178)	0.2179	84.6 (33)	87.7 (121)	0.5966
Nephrotic-range proteinuria % (n) (n=279)	44.8 (125)	57.8 (63)	36.5 (62)	*0.0006	45.7 (16)	34.9 (38)	0.3159
eGFR (ml/min/1.73m²) (n=217)	81.5 (10.2-187.8)	82.5 (13.4-175.3)	80.9 (10.2-187.8)	0.7345	91.9 (29.1-187.8)	79.7 (11.9-163.5)	0.0987
Rapidly progressive renal failure % (n)	1.2 (3)	0 (0)	1.9 (3)	0.2857	0 (0)	3.0 (3)	0.5718
Arterial hypertension % (n) (n=339)	41.6 (141)	47.8 (65)	37.4 (76)	0.0719	35.9 (14)	38.2 (52)	0.8529
Complement biochemical and genetic profile:							
Low C3 at first measure % (n) (n=347)	84.4 (293)	81.4 (114)	86.5 (179)	0.2283	92.5 (37)	85.6 (119)	0.2979
sC5b-9 at first measure (ng/mL; norm 140-280) (n=323)	960.1 (15.4-5880)	1009.0 (75.3-5880)	927.1 (15.4-5517)	0.5250	637.9 (79-4145)	1068.9 (15.4-5517)	*0.0110
Positive C3NeF at first investigation % (n) (n=335)	38.8 (130)	42.0 (58)	36.5 (72)	0.3622	75 (30)	27.9 (38)	*<0.00001
Rare functional variant in complement genes % (n) (n=346)	15.3 (53)	12.9 (18)	17.0 (35)	0.3619	12.5 (5)	18.8 (26)	0.4788
Rare variant gene:							
CFH % (n)	32.1 (17)	33.3 (6)	31.4 (11)	1	40 (2)	30.8 (8)	1
CFI % (n)	11.3 (6)	0 (0)	17.1 (6)	0.0846	20 (1)	15.4 (4)	1
C3 % (n)	32.1 (17)	27.8 (5)	34.3 (12)	0.7603	20 (1)	42.3 (11)	0.6236
CFB % (n)	7.5 (4)	22.2 (4)	(0) 0	*<0.0104	0 (0)	0 (0)	1
THBD % (n)	11.3 (6)	5.6 (1)	14.3 (5)	0.6510	20 (1)	7.7 (2)	0.4216
MCP % (n)	1.9 (1)	5.6 (1)	(0) 0	0.3396	0 (0)	0 (0)	1
Structural variant % (n)	3.8 (2)	5.6 (1)	2.9 (1)	1	0 (0)	3.8 (1)	1
Clinical parameters at biopsy (baseline):							
Proteinuria (g/24h) (n=313)	4.2 (0-33)	5.4 (0.15-33)	3.4 (0-28.3)	*0.00041	4.2 (0.12-20.0)	3.3 (0-28.3)	0.2028
eGFR (ml/min/1.73m²) (n=317)	83.3 (10.2-247.3)	79.9 (13.4-186.0)	85.5 (10.2-247.3)	0.1936	94.9 (27.8-170.7)	84.3 (11.5-247.3)	0.0902
Albuminemia (g/dL) (n=254)	3.2 (1.4-4.9)	3.1 (1.4-4.5)	3.4 (1.4-4.9)	*0.00031	3.1 (1.5-3.1)	3.5(1.6-4.9)	0.0210
Histological parameters:							
Fraction of sclerotic glomeruli (%) (n=337)	10 (0-94)	10 (0-94)	9.0 (0-71)	0.5146	6.0 (0-71)	9.5 (0-69.8)	0.2427
Fraction of crescents (%) (n=334)	5.5 (0-100)	6.6 (0-100)	4.8 (0-84)	0.3181	7.8 (0-75)	4.0 (0-66)	0.2417
Degree of mesangial proliferation (0-3) (n=339)	2.0	2.1	1.9	*0.0286	1.9	1.8	0.7683
Degree of endocapillary proliferation (0-3) (n=333)	1.3	1.4	1.2	0.0658	0.9	1.2	0.2995
Degree of interstitial inflammation (0-3) (n=339)	0.8	0.8	0.7	0.2748	0.8	0.65	0.5139
Degree of interstitial fibrosis (0-3) (n=335)	0.6	0.7	0.6	0.2559	0.3	0.6	*0.0215
Degree of arterial sclerosis (0-3) (n=330)	0.3	0.4	0.3	0.71157	0.2	0.3	0.2709
Proteinuria at 1 year (g/24h) (n=228)	1.9 (0-15)	2.7 (0-15)	1.4 (0-6.8)	*0.00053	1.8 (0.1-6.8)	1.2 (0-5.2)	0.0787
Outcome:							
eGFR at last follow-up (ml/min/1.73m²) (n=233)	93.2 (17.1-190.0)	90.4 (20.7-190.0)	94.4 (17.1-161.0)	0.3074	103.5 (31.2-161.0)	93.8 (19.9-159.8)	0.1891
ESRD % (n) (n=347)	29.4 (102)	34.8 (49)	25.7 (53)	0.0733	30.8 (12)	25.2 (35)	0.5387
Death % (n)	3.2 (11)	3.5 (5)	2.9 (6)	0.7618	5.0 (2)	2.1 (3)	0.3081
Follow-up duration (months) (n=339)	91.6 (0-529)	92.3 (0-440)	91.0 (0-529)	0.8858	128.6 (1-328)	88.0 (0-529)	*0.0121
Treatment:							
RAAS inhibition before or during first year after biopsy % (n) (n=339)	72.9 (247)	76.3 (103)	70.6 (144)	0.2637	72.5 (29)	69.9 (95)	0.8449
Immunosuppression before or during first year after biopsy % (n) (n=343)	71.7 (246)	81.2 (112)	65.4 (134)	*0.0015	56.4 (22)	63.8 (88)	0.4561
Corticosteroids only % (n)	47.6 (117)	43.8 (49)	50.7 (68)	0.3060	68.2 (15)	46.6 (41)	0.0953
Corticosteroids and MMF % (n)	26.4 (65)	22.3 (25)	29.9 (40)	0.1943	0 (0)	34.1 (30)	*0.0004
Corticosteroids and others % (n)	26.0 (64)	33.9 (38)	19.4 (26)	*0.0129	31.8 (7)	19.3 (17)	0.2492
Complement inhibition at any time % (n) (n=348)	16.1 (56)	15.6 (22)	16.4 (34)	0.8827	25.0 (10)	16.5 (23)	0.2495
Complement inhibition at any time in patients with follow-up extending after 2010 % (n) (n=292)	18.5 (54)	19.3 (22)	17.9 (32)	0.8773	30.0 (9)	18.0 (22)	0.2038

*180 of 208 C3G patients had available electronic microscopy

Quantitative variables are expressed as means unless otherwise specified.

IQR: interquartile range. Hematuria: microscopic or macroscopic. Nephrotic-range proteinuria: ≥ 3.5 g/24h, +++ or ≥ 300 mg/dL. eGFR: estimated glomerular filtration rate, calculated using the FAS equation (Pottel et al., 2016). Arterial hypertension: as reported by the referring physician. Low C3: <90 mg/dL. Rare pathogenic variant: MAF ≤0.001 and CADD pathogenic score ≥10. 24-hour proteinuria: measured on 24h urine sample when available or estimated from a random spot urine using Hogan's equation (Hogan et al., 2016). Proteinuria at 1 year: between 6 and 18 months after biopsy. ESRD: end-stage renal disease, defined as dialysis, preemptive transplantation, or eGFR < 15 ml/min/1.73m² at last available follow-up. Histological score: degrees of mesangial proliferation, endocapillary proliferation, interstitial inflammation, interstitial fibrosis, and arterial sclerosis were graded using a scale of 0-3 (absent (0), trace (0.5), mild (1-1.5), moderate (2-2.5), severe (3)). Follow-up duration: from biopsy until ESRD or last-available follow-up. RAAS: renin–angiotensin–aldosterone system. MMF: mycophenolate mofetil. Immunosuppression: others: calcineurin inhibitors, cyclophosphamide, azathioprine.

OC 70

Renal handling of Selenium and Manganese in persons with and without chronic kidney disease and their associations with renal function decline and renal tissue oxygenation

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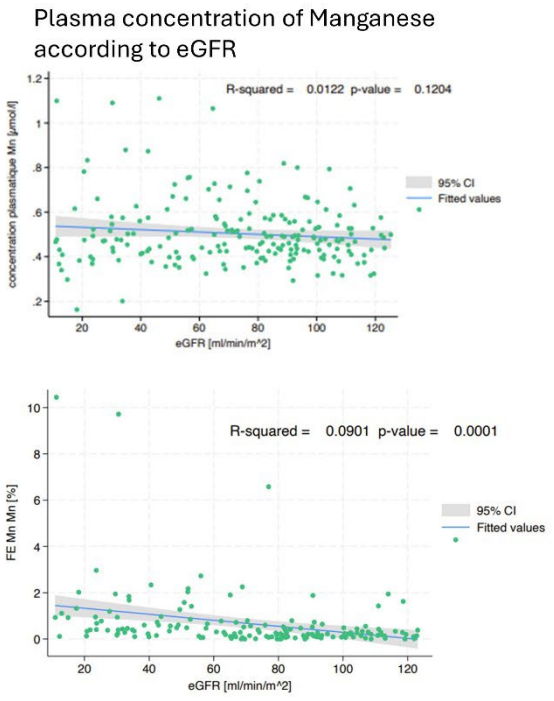
The trace-elements Selenium (Se) and Manganese (Mn) play an important role in mitochondrial functioning. Patients suffering from chronic kidney disease (CKD) are characterized by a dysregulation in several trace-elements and chronic hypoxia. This study aimed to assess the role of Se and Mn in renal oxygenation and CKD progression in humans.

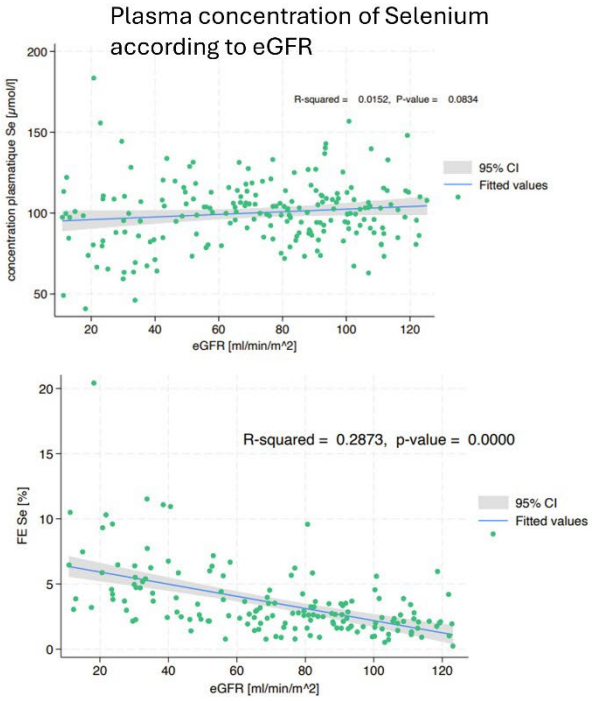
Methods: Plasma and urinary levels of Se and Mn were measured in 108 patients with CKD and 81 controls with preserved renal function. All participants underwent blood oxygenation level dependent (BOLD) MRI at baseline to assess renal oxygenation. Trace elements were measured by inductively coupled plasma mass spectrometry, and yearly changes in estimated glomerular filtration rate (eGFR) were based on prospectively measured serum creatinine values over a three-year period.

Results: Baseline eGFR and annual decline in eGFR were 56±30 ml/min/1.73m² and -2.0 ±6.0 ml/min/1.73m²/year in CKD versus 93±15 ml/min/1.73m² and 0.2±5.1 ml/min/1.73m²/year in controls. There were no significant differences in plasma Se and Mn levels across the stages of CKD, whereas the fractional excretions (FE) of Se and Mn were significantly higher at lower eGFR values (see figure). In multivariable regression analysis, cortical R2* was positively associated with albuminuria and the FE of Se (β 0.54, p = 0.001), indicating lower renal oxygenation at higher Se and albumin excretion. The FE of Se (β -0.48, p = 0.036) and Mn (β -1.07, p = 0.010) were both associated with yearly decline in eGFR.

Conclusions: Se and Mn remained stable across CKD stages, but their fractional excretions increased at lower eGFR and were associated with lower renal oxygenation and faster renal function decline. These results suggest that altered homeostasis of these trace elements may contribute to CKD progression through mechanisms involving impaired renal oxygenation. However, further research is needed to disentangle the underlying mechanisms and to assess the potential of Se and Mn supplementation in CKD.



Fractional excretion of Manganese vs eGFR



Fractional excretion of Selenium vs eGFR

OC 71

T1 mapping magnetic resonance imaging predicts renal function decline

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Background and Aims: Renal cortical interstitial fibrosis, typically assessed by biopsy, is a critical predictor of kidney function decline. Magnetic resonance imaging (MRI) has emerged as a promising non-invasive method for evaluating fibrosis, with T1 mapping showing a significant correlation with renal fibrosis. This study aimed to evaluate whether T1 mapping could predict rapid renal function decline (RRFD). Secondly, we aim to assess whether incorporating T1 mapping into an existing predictive model based on diffusion-weighted MRI, estimated glomerular filtration rate (eGFR), and proteinuria improves the model's predictive accuracy.

Method: Data were analysed from 197 patients, including those with chronic kidney disease (n = 42) and allograft kidneys (n = 155). Each patient underwent a biopsy and multiparametric MRI within a week. The median follow-up period was 2.2 years, during which laboratory data were recorded. The primary outcome was rapid renal function decline (RRFD), defined as a reduction in eGFR by more than 30% or initiation of dialysis. Univariable and multivariable Cox regression models were used, incorporating MRI parameters (ΔADC, cortical T1, ΔT2), eGFR, and proteinuria.

Results: RRFD occurred in 54 patients after a median time of 1.1 years (IQR 0.9–2.1). Univariable analysis identified cortical T1 (Figure 1) as the best predictors of RRFD. Patients with high cortical T1 values (≥1617 x10^{-6}mm^2/s) had 3.1 more risk of RRFD. However, adding cortical T1 to our predictive model, which already included ΔADC, eGFR, and proteinuria did not significantly improve the hazard ratio (from 4.62 [95% CI: 1.56– 13.67] to 4.36 [95% CI: 1.46–13.02]) and only marginally increased Harrell's C-index (from 0.77 to 0.79).

Conclusion: High cortical T1 values can predict kidney function decline and the initiation of dialysis. However, the inclusion of T1 or T2 MRI sequences did not significantly enhance the predictive accuracy of the composite model based on diffusion-weighted MRI, eGFR, and proteinuria for predicting RRFD.

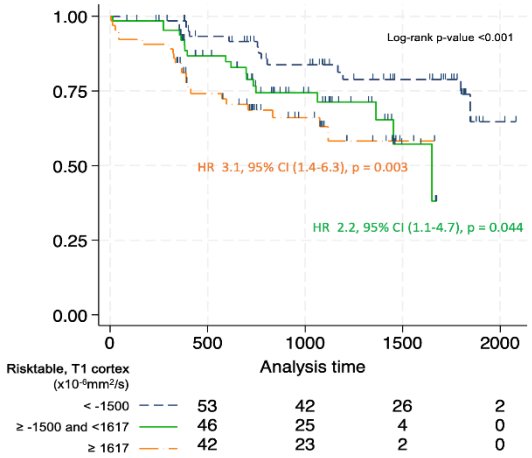

Figure 1: Kaplan-Meier survival curve for rapid kidney function decline, stratified according to cortical T1 categories (tertile).

Multivariable model	Coefficient β	HZ (95% CI)[a]	P value
ΔADC[b] ≥0 & ≤100	0.67	1.96 (0.69 – 5.57)	0.208
ΔADC[b] <0	1.47	4.35 (1.45 – 13.09)	**0.009**
Cortical T1[b] ≥-1500 & <1617	0.70	2.00 (0.90 – 4.48)	0.091
Cortical T1[b] ≥ 1617	0.54	1.72 (0.76 – 3.93)	0.196
eGFR[c] ≥30 & <60	0.14	1.15 (0.54 – 2.46)	0.721
eGFR[c] <30	1.04	2.65 (1.10 – 7.24)	**0.031**
Proteinuria[d] ≥0.3 & <3.0	1.10	3.00 (1.43 – 6.31)	**0.004**
Proteinuria[d] ≥3.0	0.98	2.65 (1.05 – 6.71)	**0.039**

[a] Hazard Ratio (HZ), Confidence Interval (CI)
[b] Units MRI: x10^{-6}mm^2/s
[c] Units eGFR: ml/min/1.73m^2
[d] Units proteinuria; g/24h

Figure 2: Composite score including ΔADC, eGFR, and proteinuria and cortical T1 to predict the renal function decline.

OC 72

The price of beauty

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Background: The NELL1 antigen is after PLA2R the second most common antigen in membranous nephropathy (MN) and is identified in primary MN, but it is also associated with malignancies and drugs esp. indeginous or lightening creams containing mercury. In these cases IgG1 is the dominant IgG subtype.

The case: 36y old woman presented with nephrotic syndrome (Serum-albumin 21g/L, Proteinuria 6,5 g/d, hyperlipidemia, peripheral edema for 6 weeks), preserved renal function and blunt urinary sediment. No signs, symptoms or serology compatible with systemic lupus erythematosus. No history of recent drugs. The biopsy showed a MN with diffuse positivity of PLA2R in the immunohistochemistry (IHC) but not in the immunofluorescence, no findings suggesting a secondary MN. PLA2R-Ab (ELISA and IIF) and THSD7-Ab were and remained negative. She started on anticoagulation and Tacrolimus. She went into complete remission four months later. Extended screening revealed no malignancy. Three months after stopping tacrolimus she relapsed (Serumalbumin 12g/l, Proteinuria >7g/d). The IHC of the initial biopsy showed an IgG1 dominance with negative IgG4. Due to IgG1 dominance the initial biopsy was stained for NELL1 and it was found to be positive. The initial PLA2R in IHC was regarded as false positive. Given the NELL1 positivity, during further discussion with the patient, she reported the use of an imported unregulasted skin cream for acne during the presentation and the relapse. Tacrolimus and anticoagulation were restarted. The mercury levels in urine and blood were elevated. There were no extrarenal manifestations of mercury poisoning. As per toxicology consultation no chelation therapy was given. The cream analysis revealed 35% mercury. The mercury levels and the proteinuria (0,8 g/d) gradually reduced.

Conclusion: This case highlights i) the importance of IgG subtype and antigen reveal and ii) the consideration of mercury exposure, probably unrecognised and underreported, in PLA2R/THSD7A negative MN cases.

Type of Analysis	13.03.24	23.03.24	25.04.24	27.08.24	Limits
Hg in Blood	**50,8 nmol/L** (10,2 µg/L)	**33,3 nmol/L** (6,6 µg/L)		7,4 nmol/L (1,5 µg/L)	HBM I * < 5µg/L HBM II**< 15µg/L
Urine	Spot-Urine	Spot-Urine	24h-Urine (2,8 Lt)	Spot-Urine	
Hg	1197,2 nmol/L	95,2 nmol/L	92,5 nmol/L	13,9 nmol/L	
Hg/Creatinine	**47,5 nmol/mmol**	**45,8 nmol/mmol**	**27 nmol/mmol**	6,1 nmol/L	SUVA: < 14,3 nmol/mmol (< 25 µg/g) HBM I* < 2,9 nmol/mmol (5,0 µg/g) HBM II **: < 11,4 nmol/mmol (< 20 µg/g)
Creatinine	25,2 mmol/L	2,1 mmol/L	3,75 mmol/L	2,28 mmol/L	
Creatinine/24h			10,49 mmol/24h		

Source www.umweltsbundesamt.de
* = Suggested values
** = Above these values health issues can occur. Vigilance for exposure is needed

OC 73

The spectrum and characteristics of acute renal dysfunction at the university hospital basel

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Background: The spectrum and characteristics of patients with acute kidney injury (AKI) at the university hospital Basel are not known. The aim of this study is to evaluate epidemiology, causes, frequency, and evaluation of AKI in all admitted patients.

Methods: Retrospective, descriptive cohort study of all in-patient nephrology consultations with AKI at the University Hospital Basel between 01.01.2022 and 30.04.2024.

Results: 528 patients fulfilled the inclusion criteria of AKI, 59.3% males, and 40.7% females. Mean age was 68.51 years (range: 18 to 95 years). Age and gender distribution are shown in figure 1. Mean BMI was 25.9 in male, and 25.8 in female patients. Main referring clinics are shown in figure 2. Systolic blood pressure at the time of first consultation was low (<100 mmHG) in 24% (mean: 87.6mmHg), normal (100-139) in 54% (mean: 117.5mmHg), and high (>140 mmHG) in 22% (mean: 154.6mmHg). 50% of AKI were classified as prerenal, 46% as renal, and 4% as postrenal, respectively. Initial and final classification into the pre-, renal, and post-renal groups was identical in 91.5% and showed the same distribution in patients with a biopsy proven diagnosis. The most frequent cause of AKI in the

renal group was acute tubular necrosis (38%), drug-toxic (27%) and interstitial nephritis (13%). Overall mortality rate was 25.4%. Kidney function fully recovered in 10%, partially recovered in 55%, and did not improve in 35%, and 1.7% remained on long-term RRT.

Conclusions: Prerenal etiology was the main reason of AKI and most often observed in ICU patients. Accordance of initial und final classification of patients with AKI by a board-certified nephrologist was very high and correlated very well with the subgroup of biopsied proofed diagnoses. 5 out of 123 patients with AKI finally had ESRD.

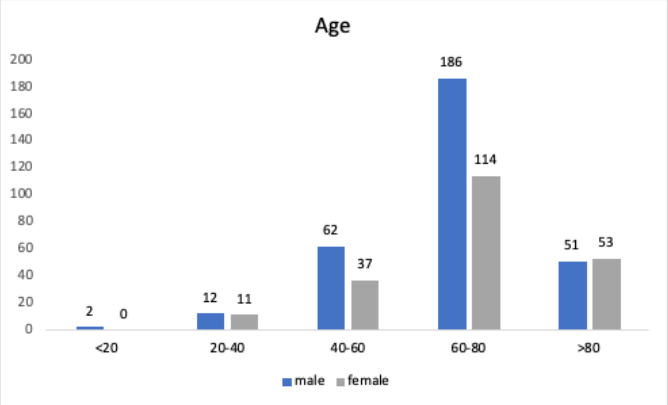

figure 1: Age and gender distribution of patients with AKI

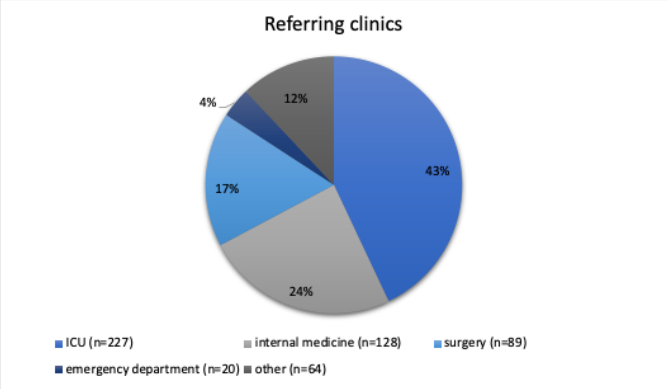

figure 2: Referring clinics of the consults of patients with AKI

OC 74

Unexpected proteinuria in a patient with alkaptonuria

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Background: Alkaptonuria is a rare disorder of the phenylalanine and tyrosine metabolism. It is an inherited genetic disease caused by a mutation in the HGD gene coding for the enzyme homogentisate 1,2-dioxygenase. Consequently, homogentisic acid cannot be degraded and accumulates in blood and tissue (primarily cartilage, heart valves). Homogentisic acid may also precipitate and cause kidney stones. In addition, there is a typical dark color of the alkalinized urine in these patients.

Case: We report the case of a 39-year-old woman with known alkaptonuria who was referred to us by her family doctor because of unexplained microhematuria. In addition to painful degenerative spine changes, she had suffered two episodes of uncomplicated urolithiasis in 2010 and 2013. She was being treated with nitisinone, a drug known to diminish the accumulation of homogentisic acid. Blood pressure was normal at 110/68 mmHg, and renal function preserved with a creatinine of 62 µmol/l. Urin microscopy did not show any microhematuria. In addition, renal ultrasound was unremarkable. However, a urine protein/creatinine ratio of 27.5 mg/mmol was noticed. Interestingly, differential analysis of the urine proteins did neither show albuminuria nor an increase of tubular proteins (alpha1-microglobuline, retinol-binding protein). False proteinuria was suspected. The initial measurement of proteinuria by determination of the protein/creatinine ratio was carried out using the benzethonium chloride method, which relies on precipitation of urinary protein by benzethonium chloride in an alkaline medium. We therefore re-measured the same sample with the photometric biuret method, which revealed an unremarkable result. In literature, we found few case reports describing the same phenomenon, namely an interference of the benzethonium chloride method, in patients with alkaptonuria.

Conclusion: Detection of proteinuria in a patient with alkaptonuria warrants caution in interpretation since false proteinuria caused by interference with the commonly used benzethonium chloride method may occur.

OC 75

Unlocking kidney protection: the antiproteinuric impact of sglt2 inhibitors in transplant recipients

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Introduction: Nephrotoxicity and non-immunologic long-term allograft failure is a frequent complication in kidney transplant (KT) recipients. Therefore, nephroprotective treatments are key in management of such patients. Recently, sodium-glucose cotransporter-2 (SGLT-2) inhibition has been shown to reduce cardiovascular morbidity and preserve kidney function in diabetic and non-diabetic patients with kidney disease without KT. Aim of the study was to explore the antiproteinuric activity of SGLT2 inhibitors in patients who had undergone KT.

Methods: Retrospective, single center study (Bern, Switzerland) from September 2020 to December 2027, including all KT recipients. With a stringent selection, we identified the following subgroup: KT recipient with significant albuminuria (>30 mg/mmol). Primary endpoint was the percentage change of albuminuria from baseline to a follow-up period of at least one month.

Results: Among 627 patients at risk, 38 patients exposed to SGLT2 inhibitors were identified. Among those, 15 albuminuric patients were selected for the analysis. At baseline, patients had the following characteristics: eGFR 50 ml/min/1.73m2 (interquartile range [IQR]: 23-65), albuminuria 153 mg/mmol (IQR: 58-879), transplant history 3.2 years (IQR: 0.2-6.1), diabetes mellitus 67%, ACE Inhibitor treatment 80%. All patients received Dapagliflozin 5-10 mg daily. The total follow-up under SGLT2 inhibitor was 0.3 years (IQR: 0-1.19). After 1 month, albuminuria was reduced in 64% of patients with a median change of -48% (IQR: -75 – +2%). Sensitivity analysis revealed that all subgroups profited from treatment: long-term KT recipients (>1 year at exposure), albuminuria >100 mg/mmol, ACE exposed patients, CNI-free regiment (Belatacept).

Conclusions: Exposure to SGLT2 inhibitor leads to a relevant reduction of albuminuria in proteinuric KT recipients and the effect extends to a wide range of patient subgroups. Information about long-term sustainability and nephroprotection is needed.

OC 76

Zoo in the belly – a furry cause of peritoneal dialysis (PD) peritonitis

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Background: PD peritonitis is a major complication in PD treatment and contributes to patient mortality and PD failure. The most common pathogens are gram positive pathogens entering the peritoneal cavity by contamination due to insufficient sterile technique or by exit site and tunnel infections of the PD catheter. Gram negative or fungal infections are less common.

Case description: A 47-year-old man on automated peritoneal dialysis (APD) presented with a first episode of abdominal pain and cloudy dialysate. Analysis of the dialysate revealed a leucocyte count of 11.5 G/l confirming the clinical suspicion of PD peritonitis. Cultures of the dialysate were obtained, and the patient was started on an empirical peritonitis treatment with cefazolin and amikacin i.p. He experienced rapid clinical improvement. The cultures finally grew *Neisseria zoodegmatis*, gram-negative bacteria found in the saliva of dogs and cats. Extended history revealed that the patient had recently acquired two kittens for his children, and he had seen bite marks on his dialysis tubing a couple of days prior to the onset of symptoms. After consulting our colleagues of the infectious disease department, antibiotic therapy was switched to ceftriaxone i.p. Antibiogram testing showed a low minimal inhibitory concentration for ceftriaxone, thus sensitivity was assumed, and therapy was continued for two weeks. Leucocyte count in the dialysate normalized by day 5 of treatment and the patient tolerated the therapy well.

Learning points/Conclusion: Pets are a rare source of PD peritonitis. Detection of atypical gram-negative pathogens warrants a closer examination of the PD environment. Patient education to ensure proper hygiene and keeping pets away from dialysis equipment is important to prevent pet-related PD peritonitis.

YSN AWARD (PECHA KUCHA)

OC 77

Effect of felzartamab anti-CD38 treatment on the molecular phenotype of antibody-mediated rejection in kidney transplant biopsies

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A recent randomized controlled trial demonstrated that treatment with CD38 monoclonal antibody felzartamab suppressed antibody-mediated rejection (ABMR) in kidney transplant patients but with recurrence post-treatment in some patients. This study examined the molecular effects of 6-months felzartamab treatment on biopsies from the trial using genome-wide microarray analysis, comparing pre-treatment, end-of-treatment (24 week) and post-treatment (week 52) biopsies from 10 felzartamab and 10 placebo patients. Felzartamab reduced molecular ABMR activity scores in all 9 patients with baseline ABMR activity, selectively suppressing interferon gamma (IFNG)-inducible and natural killer (NK) cell transcripts, with minimal effect on ABMR-induced endothelial transcripts an no effect on T cell transcripts (Fig. 1A,B). Suppression was often incomplete when ABMR activity was intense, and molecular recurrence was nearly universal by week 52. In genome-wide transcriptome analysis, felzartamab impacted 58 genes between baseline and week 24. (Fig 2A). Ten of the top 20 differentially expressed genes were decreased, including those associated with ABMR activity. Functional enrichment analysis confirmed the suppression of 12 ABMR-related pathways, reflecting downregulation of NK- and IFNG-induced genes. No significant pathways were associated with the increased genes at week 24, suggesting suppression of ABMR activity. Of the top 20 differentially expressed genes, 10 were increased. These genes likely represented normal parenchymal genes previously suppressed by ABMR activity, all of which decreased after therapy as ABMR activity returned by week 52 (Fig. 2B). Felzartamab suppressed both IFNG-inducible and NK-expressed ABMR activity genes (Fig 2C/D). From baseline to week 52, felzartamab affected 166 genes (Fig. 3). 17 of the top 20 genes were injury-inducible and decreased by week 52, indicating lasting recovery from ABMR-related parenchymal injury after 24 weeks of therapy. Felzartamab selectively suppressed IFNG-inducible and NK cell transcripts, providing parenchymal benefits and potentially slowing future progression to kidney failure despite near-universal molecular recurrence by week 52.

Figure 1

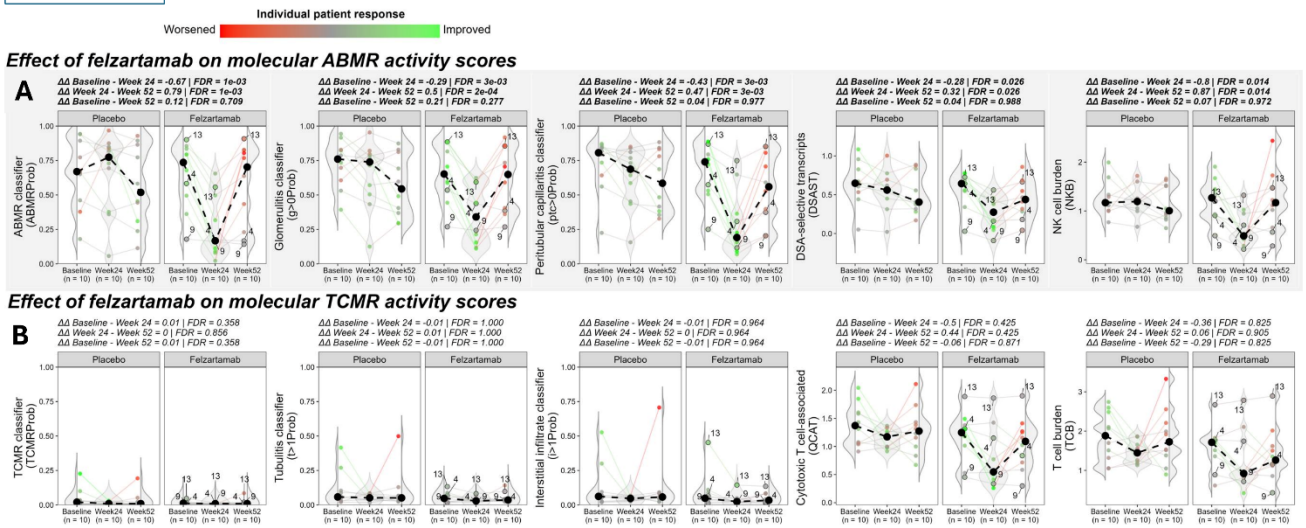
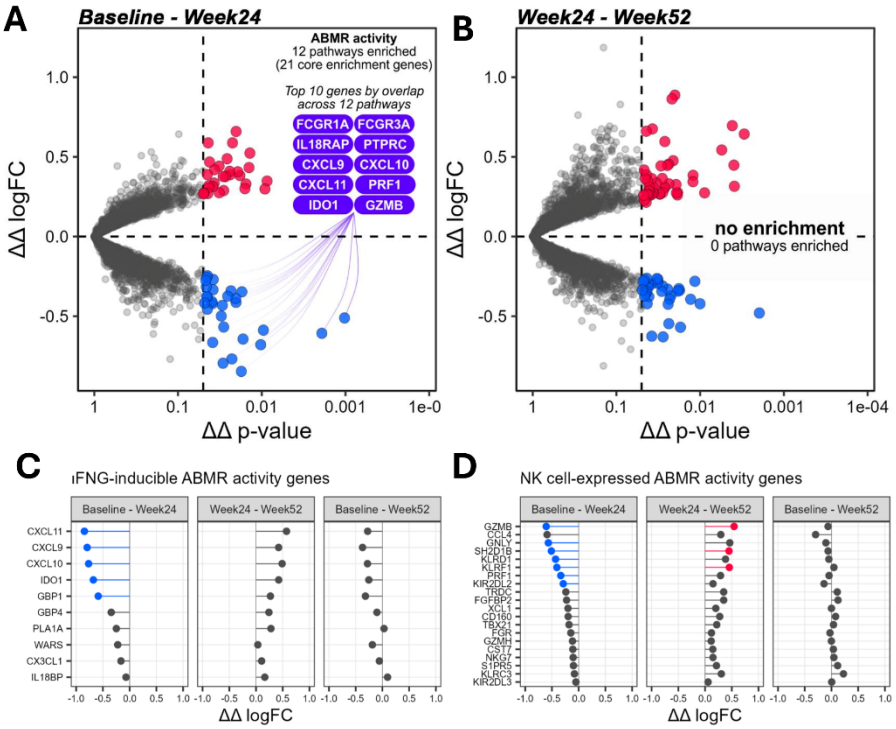


Figure 2



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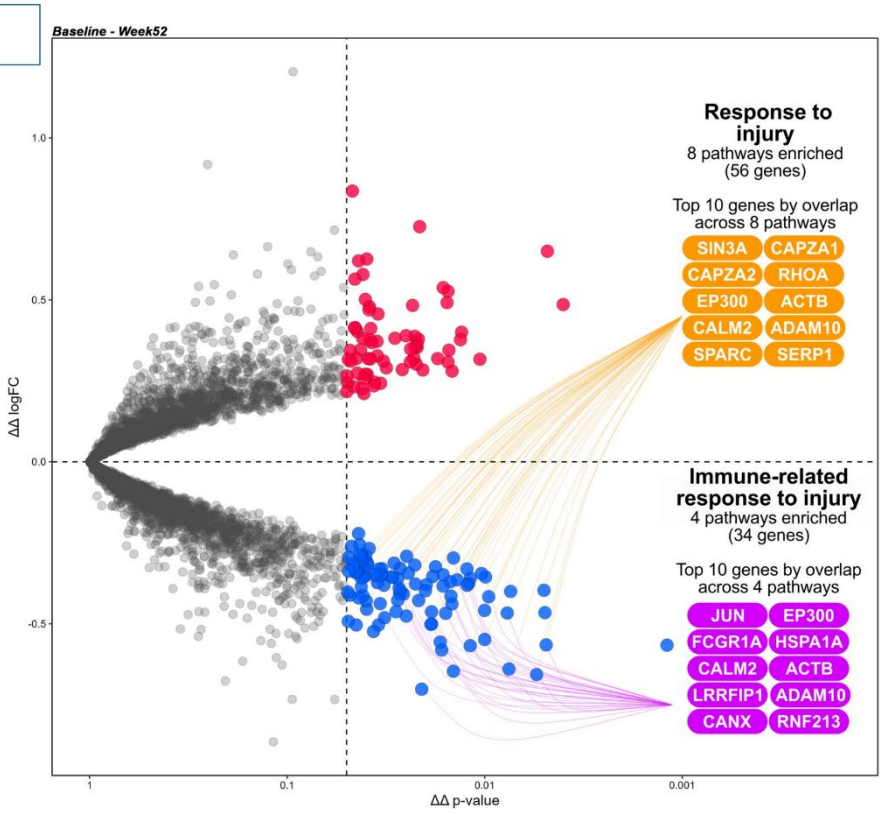

OC 78

Practice patterns of routine blood sampling in Swiss hemodialysis centers

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Background: Routine blood sampling is performed at regular intervals in hemodialysis patients to monitor complications of kidney failure and guide their treatment. However, there is minimal evidence on the optimal frequency and timing of such testing, i.e. early-week (sampling after the long dialytic interval) vs. mid-week, and current guidelines lack evidence-based recommendations.

Methods: A questionnaire was sent to all hemodialysis centers contributing to the Swiss renal registry and quality assessment program (SRRQAP) to inquire about their current practice and its rationale. Data from the returned questionnaires were analysed by descriptive statistics.

Results: Questionnaires were sent to 100 centers treating 3757 chronic hemodialysis patients (prevalence on 31.12.2023). 57 centers (57%) treating 2850 patients (76%) returned the questionnaire and were included in the analysis. 41 centers (72%) perform routine blood sampling after the long dialytic interval (i.e. early-week) and 16 (28%) mid-week with a striking east-west-difference (Figure 1). The intended interval between routine blood tests was highly variable between centers, ranging from every 2 weeks to every 2 months. Moreover, actual intervals were quite variable within centers even if regular intervals were intended. As reason for their current routine (multiple answers were possible), most nephrologists specified that they kept following either previously established procedures of their center (52.6%) or the practice they were trained (64.9%). Fewer based their practice on physiological considerations (28.1%) or scientific evidence (15.8%).

Conclusions: We found a wide variability of routine blood sampling practice among Swiss hemodialysis centers regarding both, the time of the week and the frequency of testing. This likely reflects the lack of scientific evidence and guideline recommendations. Further analyses are planned to test whether differences in practice patterns correlate with laboratory parameters and patient outcomes.

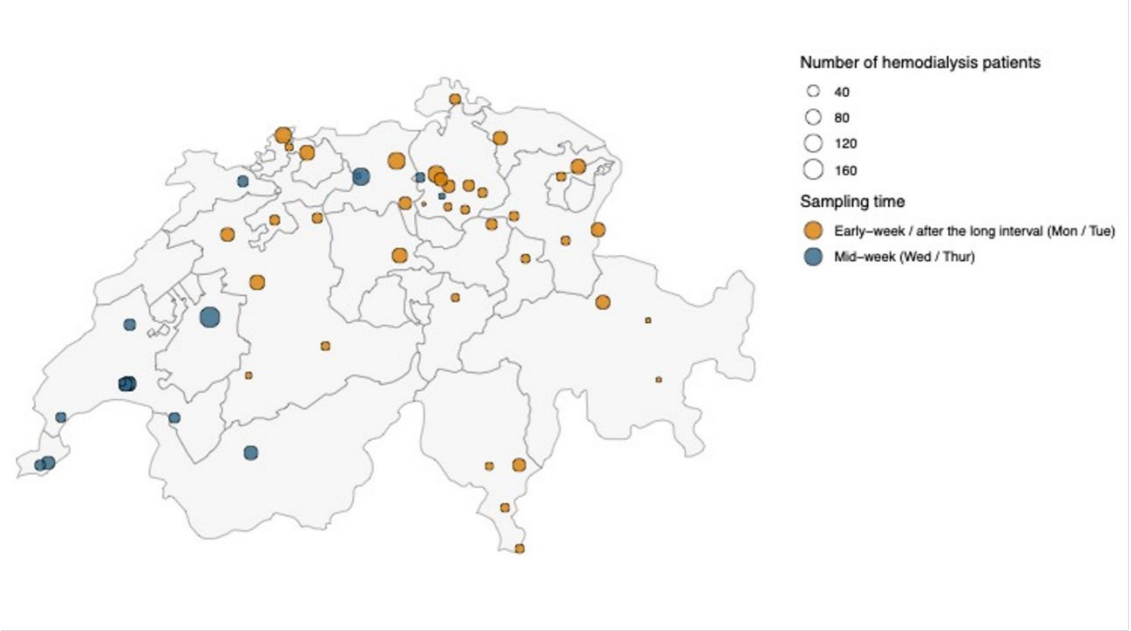

Figure 1: Map of Switzerland. Orange dots represent hemodialysis centers performing early-week (after the long dialytic interval) blood draws, blue dots centers performing mid-week blood draws. The size of the dots corresponds to the number of patients treated per center.

OC 79

Renal cell carcinoma after kidney transplantation: observational cohort study from University Hospital Zurich

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1. Department of Nephrology, University Hospital Zurich

Background: The incidence of renal cell carcinoma (RCC) increases after kidney transplantation (KT) and is about 5-10 times higher than in the general population, with most cancers found in the native kidneys. Clinical trial data on RCC screening are lacking, and most guidelines do not recommend routine screening for RCC in kidney transplant recipients (KTRs), although screening might be beneficial in high-risk groups.

Methods: We enrolled patients who received KT at the University Hospital of Zurich or the Children's Hospital Zurich between January 1, 2002, and December 31, 2021. The main cohort consisted of 1282 KTRs. 604 KTRs underwent evaluation of their native kidneys post-transplant via CT, MRI, PET/CT, or histology – most of these KTRs had data on acquired cystic kidney disease (ACKD) available.

Results: We identified 27 RCCs, corresponding to an incidence rate of 2.65 cases per 1000 person-years in the entire cohort and 6.62 per 1000 person-years in the subgroup with native kidneys evaluation post-transplant (excluding asymptomatic cases). RCC was diagnosed at a median time of 5.8 years (IQR: 2.7-11) after KT and

7.9 years (IQR: 5.4-15) after the initiation of dialysis. RCC risk was significantly elevated for KTRs with glomerulonephritis (hazard ratio [HR] 4.09) compared to all other kidney diseases combined, and for KTRs with high-risk CMV status (HR 4.6) compared to intermediate- or low-risk status. In the subgroup of 604 patients, ACKD was associated with significantly increased risk of RCC (HR 3.9). The proportion of KTRs with ACKD doubled from 17% to 37% by the time of native kidneys evaluation, which occurred at a median of 5.7 years (IQR: 2.2-11) after the first KT.

Conclusion: Glomerulonephritis, high-risk CMV status, and ACKD are associated with increased risk of RCC in the Zurich kidney transplant cohort. Screening should be considered for these high-risk groups.

OC 80

Trough-level guided dosing is reliable for mycophenolate mofetil but not for enteric-coated mycophenolate sodium in kidney transplant recipients

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1. Department of Nephrology, University Hospital Zurich (USZ), Department of Nephrology, City Hospital Waid, 2. Department of Nephrology, University Hospital Zurich (USZ), Department of Nephrology, Cantonal Hospital Lucerne, 3. Department of Nephrology, University Hospital Zurich (USZ), 4. Department of Nephrology, University Hospital Zurich (USZ), Switzerland

Background: While trough level (TL) guided dosing is common for calcineurin inhibitors, mycophenolic acid (MPA) was marketed as a one-size-fits-all drug. TL has been reported to be a poor surrogate marker of MPA exposure due to complex pharmacokinetics. Measurement of area under the curve (AUC) remains the gold standard for MPA dosing.

Methods: We measured MPA TL and AUC in 298 KTRs at the University Hospital of Zurich. KTRs with agreement between TL and AUC target range of 40-60 mg/Lxh were compared to KTRs without agreement between TL and AUC for differences in baseline characteristics and co-medication.

Results: For mycophenolate mofetil (MMF, n = 218), a high correlation between TL and AUC was observed ($p<0.0001$, $r = 0.85$), while correlation was low for enteric-coated mycophenolate sodium (EC-MPS, n = 81) ($p = 0.002$, $r = 0.34$). However, a high correlation between MPA level 4 hours after EC-MPS intake (c4L) and AUC was found ($p<0.0001$, $r = 0.94$). ROC analysis defined an MMF-TL range of >2.05 mg/l (sensitivity 68%, specificity 89%) and <3.05 mg/l (sensitivity 70%, specificity 81%) correlating with an AUC of 40-60 mg/Lxh. Lack of proton pump inhibitors (PPI) use was significantly associated with incorrect classification (n = 71/218, $p = 0.04$). for EC-MPS c4L, a range of >1.25 mg/l (sensitivity 98%, specificity 100%) and <4.4 mg/l (sensitivity 93%, specificity 91%) was defined for an AUC of 40-60 mg/Lxh. Here, non-tacrolimus-based immunosuppression was significantly associated with incorrect classification (n = 7/81, $p = 0.01$).

Conclusion: MMF dosing according to TL highly correlates with AUC, especially in KTRs treated with PPI. In contrast EC-MPS dosing according to c4L is recommended highly correlating with AUC in context of tacrolimus-based immunosuppression.

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