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Swiss Medical Weekly

Formerly: Schweizerische Medizinische Wochenschrift
An open access, online journal • www.smw.ch

Supplementum 256
ad Swiss Med Wkly
2021;151
December 7, 2021

53rd Annual Meeting of the Swiss Society of Nephrology

Interlaken (Switzerland), December 9–10, 2021

EMH Media
SCHWEIZERISCHER ÄRZTEVERLAG
EDITIONS MEDICALES SUISSES

53RD ANNUAL MEETING

OF THE SWISS SWISS SOCIETY OF NEPHROLOGY (SGN-SSN)

INTERLAKEN, DECEMBER 9–10, 2021

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ORAL COMMUNICATIONS – BASIC SCIENCE / GENETICS / EXPERIMENTAL NEPHROLOGY & NCCR KIDNEY.CH

OC 1

Interim analysis of a Phase 2 dose ranging study to investigate the efficacy and safety of iptacopan in primary IgA nephropathy

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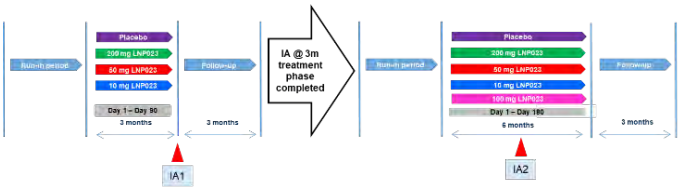
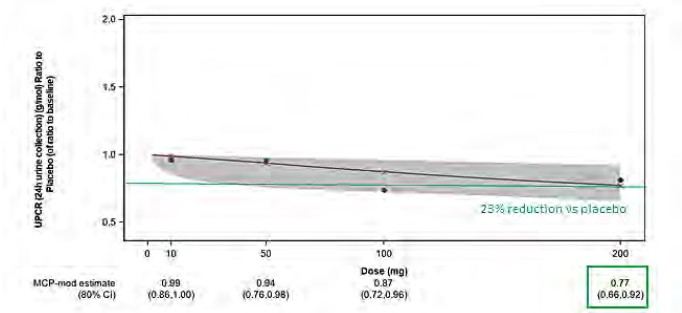
Background: IgA nephropathy (IgAN) is a major cause of chronic kidney disease and kidney failure. There are multiple lines of evidence suggesting a role for alternative complement pathway (AP) activation in driving IgAN. Iptacopan is a first-in-class, orally administered, potent and highly-selective inhibitor of factor B. We conducted a randomized, double-blind, placebo-controlled, dose-ranging phase-2-study of iptacopan in IgAN patients (NCT03373461).

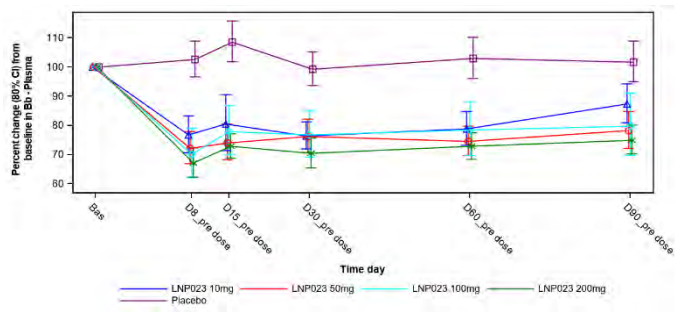
Methods: In Part 1, 46 patients were randomised to three doses of iptacopan or placebo for 90 days treatment. Guided by the Part1 interim analysis, additional 66 patients were randomised to four doses of iptacopan or placebo in Part2 (Fig 1). The final primary endpoint data from Part1 and Part2 up to Day 9 were pooled and evaluated in the second IA (IA2), reported here.



Results: 112 patients were randomised in this study. The primary analysis yielded a significant dose-response effect (1-sided p = 0.038) of iptacopan versus placebo, and suggested a 23% UPCR 24h reduction (80% confidence interval 8-34%) in the 200 mg b.i.d. arm vs placebo at Day90 (Figure 2).



In parallel, iptacopan treatment was associated with a dose-dependent reduction in serum levels of Wieslab assay, and fall in urine excretion of soluble C5b-9 (creatinine-normalized) and plasma levels of Bb (Figure 3).



Most treatment-emergent adverse events (AE) were mild (92%) or moderate (8%). No severe AEs and no deaths were reported. The most common AEs were headache, back pain, diarrhoea, nasopharyngitis and vomiting with no evidence of relation to the dose taken.

Conclusions: This is the first study to report the safety and efficacy of selective AP inhibition in IgAN. Iptacopan treatment was well tolerated and resulted in a dose-dependent inhibition of AP activity. Inhibition of AP with iptacopan was associated with a significant dose-dependent reduction in UPCR and a trend to eGFR stabilization. These data support evaluating iptacopan in IgAN in the Phase-3 APPLAUSE-trial (NCT04578834).

OC 2

24p3 receptor (24p3R) knockout reduces kidney fibrosis and inflammation during proteinuric kidney disease*

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Background: Albuminuria is associated with chronic kidney disease (CKD) progression. In normal condition, albumin is reabsorbed in the kidney by the proximal tubule through the megalin/cubulin complex. In pathological condition, the proximal tubule is saturated and the distal nephron is exposed to high concentrations of albumin. The lipocalin receptor (also named 24p3R) is located in the distal nephron and is able to bind and reabsorb albumin. The aim of our study is to better understand the role of 24p3R during CKD progression in proteinuric and non proteinuric conditions.

Methods: We generated 24p3R kidney tubular specific knockout mice (24p3RKO/KO) using the PAX8 promoter. 24p3RKO/KOmice were then submitted to two different models of CKD, a proteinuric model (POD-ATTAC) and a non-proteinuric model (unilateral ureter obstruction : UUO). We measured glomerular filtration rate (GFR) through sinistrin-FITC clearance and we scored kidney damages by histological staining. Protein and mRNA expressions of inflammation and fibrosis markers (*MCP1, Rantes, Fibronectin and*α*SMA*) were measured.

Results: At baseline, there was no difference in GFR measurement, histological observation or creatinine value between 24p3RWT/WT and 24p3RKO/KO mice. In proteinuric induced CKD (POD-ATTAC), 24p3R knockout presented a higher GFR, lower expression of α*SMA, Fibronectin, Rantes and MCP1*mRNA and protein compared to 24p3RWT/WT mice.24p3RKO/KO mice displayed less fibrosis and chronic lesions by Masson's trichrome staining. In opposition, in non-proteinuric chronic model of fibrosis (UUO), 24p3RKO/KO mice were not protected against fibrosis and chronic injury.

Conclusions: Our results suggest that the 24p3R may play a role in proteinuria induced CKD, and may thus be an interesting therapeutic target.

*YSN paper

OC 3

Fetuin-A attenuates fibrotic remodeling and improves renal function in a mouse model of ischemia reperfusion injury

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Background: Ischemia-reperfusion is a leading cause of acute kidney injury in hospitalized patients and contributes to increased morbidity and mortality. Fetuin-A is a circulatory, liver-derived glycoprotein that beyond its role as a systemic calcification inhibitor was recently shown to counteract hypoxic tissue damage in the fetal kidney. Here we addressed the

question, if fetuin-A administration improves renal function and tissue recovery in an ischemia reperfusion mouse model.

Methods: Ischemia reperfusion injury (IRI) was performed in 10-12 weeks old C57BL/6N mice (ischemia time 20 min). Mice were treated with human plasma derived fetuin-A or PBS either before (prophylactic approach) or after (therapeutic approach) IRI. Blood, urine and kidney samples were analyzed for markers of renal dysfunction using standard molecular methods, including RT-qPCR, histology and ELISA. Glomerular filtration (GFR) was assessed in mice subjected to bilateral IRI.

Results: Following surgery, endogenous fetuin-A levels dropped in the serum, and inflammatory and kidney injury markers increased in urine, renal tissue and systemically. Both, prophylactic as well as therapeutic administration of fetuin-A diminished not only the expression of those markers upon IRI, but also attenuated the expression of several fibrotic markers in injured kidneys in the long term. Consistently, renal function was improved in treated mice compared to untreated mice.

Conclusions: A wide range of biological functions have been proposed for fetuin-A based on its structural similarities to other proteins or physical interactions with biogenic molecules. We have shown herein that fetuin-A administration has anti-inflammatory, anti-damage and anti-fibrotic properties in a mouse models of pre-renal injury. Based on these findings, fetuin-A administration appears to be a promising approach to improve renal function and mitigate fibrotic remodeling related to ischemic insults, which is principally applicable to all tissues.

OC 4

Claudin-4 is involved in chloride retention of nephrotic syndrome (NCCR project)*

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Background: Nephrotic syndrome is a common disease characterized by massive proteinuria, hypoalbuminemia and edema due to renal sodium chloride retention. The mechanism of sodium retention in nephrotic syndrome (NS) has been extensively studied, but the mechanism of increased chloride reabsorption has not been elucidated.

Methods: We assessed the expression levels of both paracellular and transcellular components of chloride transport in the CD of POD-ATTAC mice and PAN rats, two rodent models of NS, as well as in biopsies from human nephrotic kidneys. We also used cultured mouse cortical collecting duct cells to see how overexpression or silencing of claudin-4 affect paracellular permeability.

Results: We demontrate that the tight junction protein claudin-4 expression significantly increased in transgenic mice with podocyte apoptosis-induced NS (POD-ATTAC mice) and rats with puromycin-aminonucleoside-induced NS (PAN rats), two well characterized rodent models of NS. Plasma membrane Pendrin, which exchanges chloride for bicarbonates in B-IC, declined along with the time-course of NS in POD-ATTAC mice. We also observed a significant decrease in pendrin mRNA and protein expression in PAN rats compared to controls. Furthermore, we found that claudin-4 was expressed at very low levels in normal human kidneys and dramatically increased along the lateral membranes of CD cells in human nephrotic kidneys (focal and segmental glomerulosclerosis). *In vitro*experiments using claudin-4 over-expression or silencing in mCCDcl1 cells confirmed that claudin-4 functions as a paracellular chloride pore.

Conclusions: Our study uncovered that paracellular chloride pore claudin-4 abundance increased in both rodent and human NS. These results suggest that on progression of NS, transcellular Cl-/ HCO3 - transport decreases while paracellular chloride transport increases in the CD. This increased paracellular chloride permeability may constitute a Cl- shunt that favors Na+ reabsorption and prevents K+ secretion along the CD in NS.

* YSN paper

OC 5

Urinary cystathionine protects from calcium oxalate nephropathy

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Background: Deposition of calcium oxalate (CaOx) in kidneys leads to tubulointerstitial injury, diminished kidney function and end-stage kidney disease. Increased urinary oxalate excretion and CaOx deposits in kidney allograft are also associated with worse kidney outcomes. We recently reported that mice deficient in cystathionine-gammalyase (CSE), an experimental model of cystathioninuria (rare AR hereditary disorder), are protected from CaOx nephropathy. These mice excrete large amounts of cystathionine in urine. To differentiate systemic from local, renal effects, we employed inducible, kidney-specific CSEdeficient mice.

Methods: *Cse flox/flox, Pax8 tg/+, LC1 Cre/+* mice (kKO) were treated with doxycyclin for 10 days to induce a nephronspecific CSE deficiency. After a wash-out period, the mice were treated for 3 weeks with diet enriched with calcium (1.5%) and hydroxyproline (1.5%) to induce CaOx nephropathy. Animal experiments were complemented with *in chemico* crystallization assay.

Results: After doxycycline treatment in kKO mice, CSE was completely depleted in the kidneys, but its expression was not affected in the liver. kKO mice did not morphologically, biochemically, and kidney-histologically differ from their WT littermates. kKO mice were not protected from CaOx nephropathy – they showed the same amount of CaOx deposits and the same degree of kidney failure and injury as their WT littermates. *In chemico* crystallization assay indicated an inhibitory effect of cystathionine on CaOx crystallization.

Conclusions: Deficiency of CSE in nephron did not protect mice from oxalate nephropathy. We hypothesize a similar level of cystathioninuria in kKO and WT mice. Systemic CSE-deficiency protects from oxalate nephropathy most likely by increased cystathionine urinary excretion — cystathionine inhibits calcium oxalate crystallization *in chemico*. Increasing cystathionine urinary content might be a promising strategy in the prevention of oxalate nephropathy.

OC 6

Glomerular proteomic profiling of kidney biopsies with hypertensive nephropathy reveals a signature of disease progression

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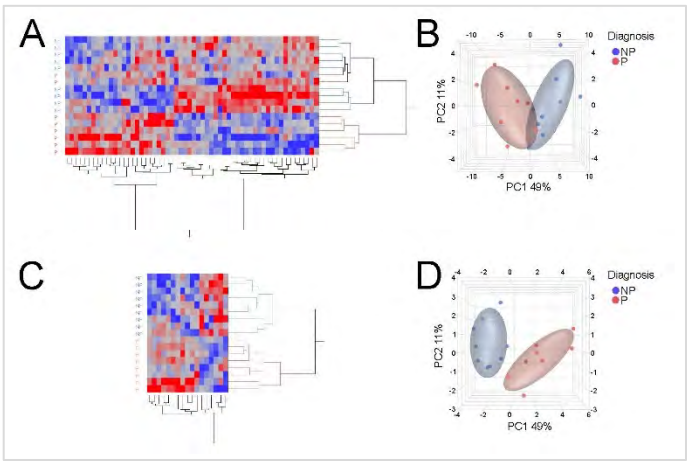
Background: Hypertensive nephropathy (HN) requires kidney biopsy as the diagnostic gold-standard but histological findings are unspecific and specific prognostic markers are missing. We hypothesized that we can identify candidate prognostic markers based on glomerular protein signatures.

Methods: We studied adult patients (n = 17) with an eGFR >30 ml/min/1.73 m^2 and proteinuria <3 g/d from the Norwegian Kidney Biopsy Registry (NKBR), including stable non-progressing patients (n = 9) and patients progressing (n = 8) to end-stage renal disease (ESRD) within 20 years. Glomerular cross-sections from archival kidney biopsy sections were microdissected and processed for protein extraction. Proteomic analyses were performed using Q-exactive HF mass spectrometer and relative glomerular protein abundances were compared between progressive and non-progressive patients.

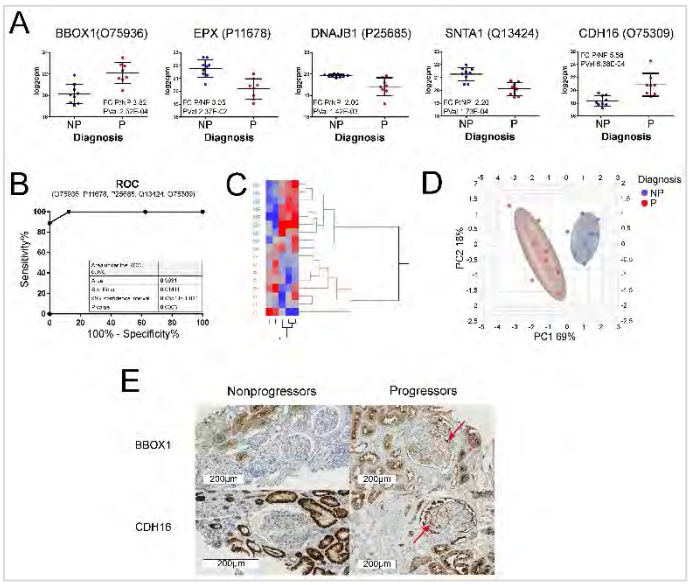
Results: Amongst n = 1870 quality filtered proteins, n = 58 were differentially expressed in progressive and nonprogressive glomerular samples, with absolute fold changes ≥1.5, p ≤0.05. However, only by using the n = 17 glomerular proteins with absolute fold changes ≥2 and p ≤0.05, the hierarchical clustering and principal component analysis effectively separated progressors and non-progressor patient samples (Figure 1A-B).

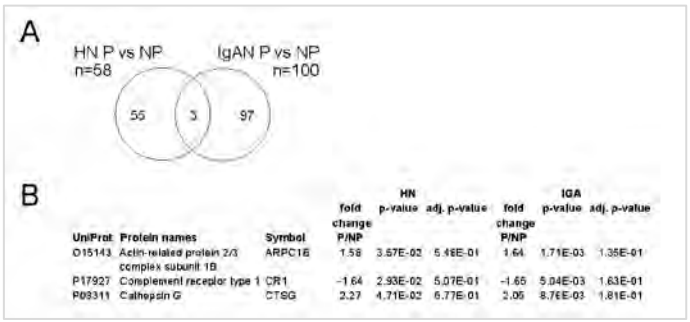


Supervised classifier analysis (K nearest neighbour) identified a set of five proteins, including Gamma-butyrobetaine dioxygenase (BBOX1, O75936) and Cadherin 16 (CDH16, O75309), overexpressed in progressors, and Eosinophil peroxidase (EPX, P11678), DnaJ homolog subfamily B member 1 (DNAJB1, P25685) and Alpha-1-syntrophin (SNTA1, Q13424), overexpressed in non-progressive glomeruli, correctly classifying 16/17 samples. Respective results and immunohistological confirmation of BBOX1 and CDH16 are shown in Figure 2A-E.

Geneset Enrichment Analysis (GSEA) showed that metabolic pathways were enriched in progressors, and structural cell pathways in non-progressors. We then evaluated protein signatures associated with HN progression with those associated with IgA nephropathy progression from our published dataset *(Paunas T. Clin Proteom 2017)*. The expression of only three proteins was altered in a similar direction in both datasets (Figure 3A-B).

Conclusions: Glomerular proteomic profiling from renal biopsies can be used to discriminate progressive from nonprogressive patients with HN.





			HN			IGA	
UniProt	Protein names	Symbol	fold change P/NP	p-value	adj. p-value	fold change P/NP	p-value	adj. p-value
O15143	Actin-related protein 2/3 complex subunit 1B	ARPC1B	1.58	3.57E-02	5.46E-01	1.64	1.71E-03	1.35E-01
P17927	Complement receptor type 1	CR1	-1.64	2.93E-02	5.07E-01	-1.65	5.04E-03	1.63E-01
P08311	Cathepsin G	CTSG	2.27	4.71E-02	6.77E-01	2.05	8.76E-03	1.81E-01

ORAL COMMUNICATIONS – TRANSPLANTATION

OC 7

Successful tolerance induction by combined kidney and hematopoietic stem cell transplantation

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Background: Induction of immunological tolerance has been the holy grail of transplantation immunology for decades. The only successful approach in the clinical situation has been a combined kidney and hematopoietic stem cell transplantation from the same living donor. Here, we report the first three patients included in this first European trial to induce tolerance by mixed lymphohematopoietic chimerism.

Methods: The protocol followed previous studies at Stanford University: kidney transplantation was performed on day 0 including induction with anti-thymocyte globulin followed by conditioning with 10x1.2 Gy total lymphoid irradiation and the transfusion of CD34+ stem cells together with a body weight-adjusted dose of donor T cells. Immunosuppression consisted of cyclosporin and steroids for 10 days, cyclosporin and mycofenolate mofetil for 1 month, and then cyclosporin monotherapy with tapering over 9–20 months.

Results: Two female and one male patients were transplanted with a kidney and peripherally mobilized hematopoietic stem cells from their HLA-identical sibling donor. No rejection or graft-versus-host disease occurred in these patients, which are currently off immunosuppression since 31, 18 and 6 months. Chimerism was stable in the first, but slowly declining in the other two patients. A molecular microscope analysis in patient 2 revealed the genetic profile of a normal kidney. No relevant infections were observed, and the quality of life in all three patients is excellent. During the SARS-CoV2 pandemic, all three patients were vaccinated with the mRNA vaccine, and they showed excellent humoral and cellular SARS-CoV2-specific immunity.

Conclusions: Combined kidney and hematopoietic stem cell transplantation is a feasible and successful approach to induce specific immunological tolerance in the setting of HLA-matched living kidney donation while maintaining immune responsiveness to a viral vaccine.

OC 8

Functionalised magnetic nanoparticles remove donor-specific antibodies (DSA) from patient blood. Preliminary data of an ex vivo feasibility and proof-of-principle study*

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Background: When anti-human leukocyte antigen antibodies (donor specific antibodies, DSA) are formed, the success of kidney transplantation is compromised due to antibody-mediated rejection (ABMR). Potential allograft loss might be prevented if DSA are specifically removed and ideally new formation of DSA is prevented. Magnetic nanoparticles were functionalised with human leukocyte antigen A1 (HLA-A1) to specifically remove anti-HLA-A1 antibodies.

Methods: Intact HLA-A1 protein was bound to magnetic nanoparticles. These functionalized nanoparticles were then incubated for 5-7 minutes with phosphate-buffered saline (PBS), with whole blood from healthy volunteers, both spiked with anti-HLA Class I antibodies (5µg/ml), or with patient plasma and patient whole blood from sensitised patients with anti-HLA-A1 antibodies. After incubation, nanoparticles were magnetically removed. Anti-HLA-A1 antibody levels were measured using the Luminex method (OneLambda, Thermo Fisher®). Mean fluorescent intensity (MFI) values before and after treatment were determined and evaluated with Students's t-test, $p < 0.05$ was considered significant.

Results: In antibody spiked PBS (n = 3), the MFI could be reduced by 93% ± 4%, $p < 0.001$ (raw MFI reduction from 7235 to 859, from 10134 to 446, and from 3120 to 136). In spiked blood from healthy volunteers (n = 2), the MFI could be reduced by 93% ± 4%, $p < 0.001$ (raw MFI reduction from 10266 to 1128 and from 5751 to 152). Two patients could be included so far. The MFI could be reduced by 96% and by 44% (raw MFI reduction from 4940 to 236 and from 11088 to 6219). The current results demonstrate the feasibility of a successful reduction of anti-HLA antibodies using custommade nanoparticles. This method might open the possibility to a specific removal of preformed or *de novo* DSA and hence a highly targeted desensitization with the potential to offer a treatment option for ABMR and to improve graft survival.

* YSN paper

OC 9

Outcome of husband-to-wife kidney transplantation with mutual children: single center experience using T cell-depleting induction

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Background: Only very few data on husband-to-wife transplantations with mutual children (H2W) exist in the current era. At our center, we regard H2W as immunological risk transplantations and treat them with T cell-depelting induction.

Methods: We investigated the outcome of H2W transplantations (n = 25) compared to women with prior pregnancies also receiving their first HLA-mismatched kidney transplant, but from a different donor source: (i) other living donor (n = 52) and (ii) deceased donor (n = 120).

Results: The median follow-up time was 5 years. Seventy-four percent of the women had ≥2 pregnancies. Deathcensored allograft survival was significantly lower in the H2W group compared to the other two groups ($p = 0.03$). Three of 4 graft losses in the H2W group were due to rejection. 5-year patient survival in the H2W group was high and similar compared to the other living donor group (100% vs 98%; $p = 0.28$). The incidence of (sub)clinical antibody-mediated rejection was higher in the H2W group (36% vs 20% vs 18%) ($p = 0.10$). The frequency of infections was similar among the 3 groups. No immunological parameter (i.e. number of pregnancies, presence of donor-specific antibodies, number of HLA mismatches) was predictive for rejection or graft loss in H2W transplantations.

Conclusions: H2W transplantation is a valuable option, but associated with a higher risk for allograft loss due to rejection despite T cell-depleting induction. Further research is required for better risk prediction on an individual patient level.

OC 10

Comparing methods for donor-derived cell-free dna quantification in plasma and urine from kidney and liver transplant recipients

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Background: In allograft monitoring of solid organ transplant recipients, there is an unmet need for diagnostic methods that are less invasive than tissue biopsies. In this context, liquid biopsy has emerged as a novel approach using quantification of donor-derived cell-free DNA (dd-cfDNA) in body fluids.

Methods: Different approaches were compared for the quantification of dd-cfDNA in urine and plasma of kidney and liver allograft recipients: A) Droplet digital PCR (ddPCR) using allele-specific detection of seven common HLA-DRB1 alleles and the Y chromosome; B) high-throughput sequencing (HTS) using a custom QIAseq DNA panel targeting 117 common polymorphisms; and C) a commercially available kit (AlloSeq® cfDNA, CareDx). Dd-cfDNA was quantified as fractional abundance (FA), and for ddPCR and HTS also as donor copies, utilizing unique molecular identifiers (UMIs).

Results: A total of 113 urine and plasma samples from kidney and liver recipients showed a strong linear correlation between ddPCR and HTS for the FA of dd-cfDNA (r = 0.98), donor copies/ml (τ = 0.78) and total copies/ml (τ = 0.73). In a subset of 40 plasma and urine samples (kidney and liver), dd-cfDNA FA also showed a strong correlation of ddPCR (r = 0.95) and HTS (r = 0.99) with AlloSeq® cfDNA. FA correlations had an intercept of -0.16 - 0.05 and a slope of 0.96 - 1.08, while a reduced slope was observed for HTS based quantification of donor copies/ml (0.62) and total copies/ml (0.53).

Conclusions: This first direct comparison of different dd-cfDNA quantification methods yielded comparable results with no indication of systematic bias for the dd-cfDNA FA. The strong correlation of absolute copies indicates the suitability of the presented custom HTS method for absolute dd-cfDNA quantification (copies/ml). These findings suggest that the definition of a method-independent diagnostic cutoff for dd-cfDNA FA may be feasible in the further evaluation of dd-cfDNA for non-invasive graft monitoring.

OC 11

Outcome of patients transplanted for glomerulonephritis in the Swiss kidney transplant cohort*

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Background: Despite having a rather low incidence compared to other type of nephropathies, glomerulonephritis (GN) account for 10 to 40% of end-stage renal disease (ESRD) cases. Moreover, recent international epidemiologic studies have demonstrated an increase of GN incidence. Consequently, one would expect an increase in ESRD patients due to GN who will require transplantation.GN transplanted patients (GN-KTx) are known to have a higher morbidity and an increased risk of graft loss due to the recurrence of the initial GN. However, data are scarce regarding the specific outcome of GN-KTx patients.

Methods: The purpose of our study is to provide such data, taking advantage of the prospective Swiss Transplant Cohort Study (STCS). We compared the rates of graft failure (composite endpoint of graft loss, eGFR <30 ml/min/m^2 or proteinuria >1 g/d, with time after transplantation) between GN-KTx, diabetic nephropathy (DM-KTx), ADPKD transplanted patients, and patients transplanted for other causes. Only kidney alone transplantation and first allograft recipients were included. Statistical differences between groups were assessed by Kaplan-Meier analysis.

Results: A total of 2621 patients were included in the analysis, of whom 782 were GN-KTx. We analyzed in detail baseline demographical and transplant-related data, comparing subgroups of patients based on the cause de nephropathy. 31% of patients reached the endpoint with a mean follow up of 5.5 years. Subgroup analysis showed statistically significant differences (Fig. 1A), with DM-KTx having the worse outcome (P <0.0001,OR1.5; 1.1 to 2) compared to GN-KTx.During follow-up,14% of GN-KTx had a recurrence (RGN-KTx). Compared to patients with absence of recurrence, RGN-KTx had significantly more acute rejection episodes (OR 1.9,1.3 to 3) and were twice more likely to reach transplant failure (Fig.1B). Interestingly, RGN-KTx had the same outcome as DM-KTx.

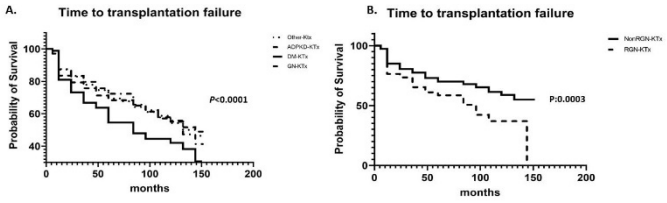

Figure 1. Kaplan-Meier analysis of time to transplantation failure. **A.** all groups; **B.** patients with absence of recurrence of glomerulonephritis and patients with recurrence (RGN-KTx).

Conclusions: The overall prognosis of GN-KTx in the STCS is good but recurrence leads to more acute rejection episodes and a significantly worse graft outcome.

* YSN paper

ORAL COMMUNICATIONS – CLINICAL NEPHROLOGY / HYPERTENSION / MINERAL / ELECTROLYTES

OC 12

Uromodulin, Blood Pressure and Chronic Kidney Disease: Assessing Causality Using Mendelian Randomization

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Background: *UMOD* variants associated with higher levels of urinary uromodulin (uUMOD) increase risk of CKD and hypertension. However, uUMOD levels also reflect functional kidney tubular mass in observational studies, questioning the causal link between uromodulin production and kidney damage.

Methods: We used Mendelian randomization (MR) to clarify causality between uUMOD levels, kidney function and blood pressure in individuals of European descent. The link between uUMOD and eGFR was first investigated in a population-based cohort (CoLaus, n = 3,851) using classical linear regression and one-sample MR. We next applied two-sample MR on 4 GWAS consortia to explore causal links between uUMOD and eGFR, CKD risk (n~500k) and blood pressure (BP, n~750k).

Results: In observational data, higher uUMOD associated with higher eGFR. Conversely, when using *rs12917707*as an instrumental variable in one-sample MR, higher uUMOD strongly associated with eGFR decline. Using two-sample MR, higher uUMOD levels significantly associated with lower eGFR, higher odds for eGFR decline or CKD, and higher SBP or DBP. Per 1 SD increase of uUMOD, log-transformed eGFR decreased by -0.15 SD (95% CI: -0.17 to -0.13) and log-odds CKD increased by 0.13 SD (95%CI: 0.12 to 0.15). Increase in 1SD of uUMOD increased SBP by 0.06 SD (95% CI: 0.03 to 0.09) and DBP by 0.08 SD (95% CI: 0.05 to 0.12). The effect of uUMOD on BP was mediated by eGFR, whereas the effect on eGFR was not mediated by BP.

Conclusions: Our data support that genetically-driven levels of uromodulin have a direct, causal and adverse effect on kidney function outcome in the general population, not mediated by blood pressure.

OC 13

Cardiovascular outcomes associated with achieved haemoglobin level and preliminary rate of rise of haemoglobin in pooled phase 3 studies of roxadustat in non–dialysis-dependent patients with anaemia

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Background: The relationship between achieved haemoglobin levels and haemoglobin rate of rise (ROR) and subsequent cardiovascular event incidence rates in patients with non–dialysis-dependent (NDD) chronic kidney disease (CKD) who received roxadustat remains uncertain.

Methods: We analysed pooled data from four phase 3 studies in patients with NDD-CKD (placebo-controlled: ALPS, ANDES, OLYMPUS; ESA-controlled: DOLOMITES) who received any dose of roxadustat. Incidence rates of adjudicated major adverse cardiovascular events (MACE: all-cause mortality [ACM], myocardial infarction, and stroke), MACE+ (MACE plus heart failure and unstable angina requiring hospitalisation), and ACM during the treatment period and within 7 days of last roxadustat dose were examined relative to most recent haemoglobin level before the event and preliminary data for haemoglobin ROR within the 4-week period prior to the event (>2 vs ≤2 g/dL/4 weeks). Patients with a decreasing haemoglobin were included in the haemoglobin ROR ≤2 g/dL/4 weeks subgroup.

Results: Overall, 2709 patients were randomised and received roxadustat. Incidence rates of MACE, MACE+, and ACM were 3- or 4-fold higher in patients with lower reported haemoglobin levels (haemoglobin <10 g/L) versus those who achieved haemoglobin ≥10 g/dL. Incidence rates of MACE, MACE+, and ACM were similar or lower in patients with a maximum haemoglobin rise of >2 g/dL within the 4-week period prior to the event versus those with a change of ≤2 g/dL within the same period (Table).

Table. Incidence Rates of Adjudicated MACE, MACE+, and ACM Events/100 PEY in Patients Receiving Roxadustat

	Achieved Haemoglobin Immediately Prior to Event[a]				Preliminary ROR of Haemoglobin[a,b]	
	<10 g/dL PEY=759.9	10 to <12 g/dL PEY=2835.7	12 to <13 g/dL PEY=984.3	≥13 g/dL PEY=129.9	≤2 g/dL/4 weeks PEY=4247.6	>2 g/dL/4 weeks PEY=142.3
MACE	17.4	5.1	5.0	6.2	7.2	2.8
MACE+	24.7	7.5	7.2	10.0	9.8	9.8
ACM	13.2	3.0	2.9	1.5	4.8	0.7

[a]Adjudicated events by haemoglobin level that occurred during the treatment period and within 7 days of the last dose of study medication in randomised subjects who took any dose of roxadustat.
[b]Preliminary haemoglobin ROR was defined as the maximum change at every moving 4-week window. Total PEY for the ROR >2 g/dL per 4 weeks category includes a union of all windows that contain ROR >2 g/dL; the complement set is defined as the PEY for ROR ≤2 g/dL per 4 weeks category.
Subjects with more than one event in each category were only counted once.
Incidence rate/100 PEY = 100 x number of subjects with events/PEY.
Abbreviations: ACM, all-cause mortality; MACE, major adverse cardiovascular events; MACE+, MACE plus heart failure and unstable angina requiring hospitalisation; PEY, patient-exposure years; ROR, rate of rise.

Conclusions: In this analysis of roxadustat-treated patients with NDD CKD, incidence rates of MACE, MACE+, and ACM were lower in patients who achieved target haemoglobin levels of 10-12 g/dL versus patients who achieved haemoglobin <10 g/dL. Risk of MACE, MACE+, or ACM did not appear to be associated with the proximal preliminary data for haemoglobin ROR; however, further characterisation of the haemoglobin ROR and ROR in relation to baseline haemoglobin are warranted.

OC 14

Urinary tetrahydroaldosterone is associated with circulating FGF23 in kidney stone formers

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Background: The spectrum of diseases with overactive renin-angiotensin-aldosterone system (RAS) or elevated circulating FGF23 overlaps, but the relationship between aldosterone and FGF23 remains unclarified. Here, we report that systemic RAS activation sensitively assessed by urinary tetrahydroaldosterone excretion is associated with circulating C-terminal FGF23.

Methods: Retrospective analysis in the Bern Kidney Stone Registry, a single-center observational cohort of kidney stone formers. Urinary excretion of the main aldosterone metabolite tetrahydroaldosterone was measured by gas chromatography – mass spectrometry. Plasma FGF23 concentrations were measured using a C-terminal assay. Univariable and multivariable regression models were performed to assess the association of plasma FGF23 with 24 h urinary tetrahydroaldosterone excretion.

Results: 314 participants were included in the analysis. Mean age was 47 ± 14 years and 73 % were male. Mean estimated GFR was 96 ml/min per 1.73 m^2. In unadjusted analyses, we found a positive association between plasma FGF23 and 24 h urinary tetrahydroaldosterone excretion (β: 0.0027; p = 4.2×10-7). In multivariable regression models adjusting for age, sex, body mass index and GFR, this association remained robust (β: 0.0022; p = 2.1×10-5). Mineralotropic hormones, 24 h urinary sodium and potassium excretion as surrogates for sodium and potassium intake or antihypertensive drugs did not affect this association.

Conclusions: Our data reveal a robust association of RAS activity with circulating FGF23 levels in kidney stone formers. These findings are in

line with previous studies in rodents and suggest a physiological link between RAS system activation and FGF23 secretion.

OC 15

Characteristics and outcomes of pregnancy-triggered atypical hemolytic-uremic syndrome (aHUS): global aHUS registry analysis

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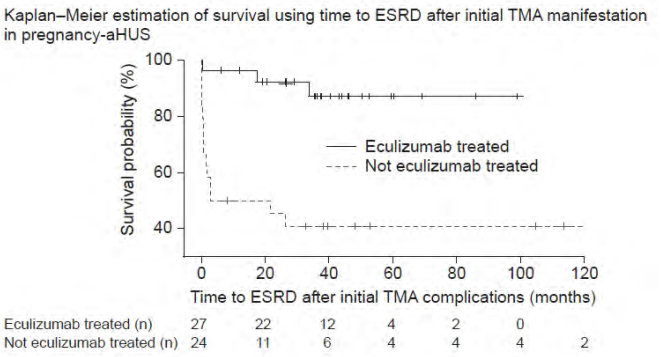
Background: Pregnancy-triggered aHUS (P-aHUS) accounts for 10–20% of aHUS diagnoses. Complement-mediated thrombotic microangiopathy (CM-TMA) may be associated with high maternal and fetal morbidity and mortality such as ESRD. The clinical characteristics of P-aHUS and survival probability in patients treated with the complement C5 inhibitor eculizumab are described, using the largest collection of P-aHUS data available in a single study.

Methods: Patients with a clinical diagnosis of aHUS were included in the global aHUS registry (NCT01522183). Patients with P-aHUS were selected as those with first TMA manifestations during pregnancy or within 60 days postpartum. Patients with other triggers of aHUS were excluded. Survival, based on time to ESRD, was calculated by the Kaplan-Meier method.

Results: In the registry, 51/1029 female patients were selected with P-aHUS and 27 received eculizumab. Mean ± SD age at pregnancy onset was 30.7 ± 5.9 years. P-aHUS occurred during pregnancy in 28 (54.9%) patients, with the remainder occurring postpartum. A diagnosis of pre-eclampsia or HELLP (hemolysis elevated liver enzymes low platelet count) syndrome was reported in 28 (54.9%) and 17 (33.3%) patients, respectively. A complement pathogenic variant was identified in 23 (45.1%) patients, of whom 3 (8.3%) also tested positive for anti-complement factor H antibodies. Mean ± SD eculizumab treatment duration was 1.8 ± 1.8 years. Survival probability was higher in eculizumab-treated patients compared with patients not receiving eculizumab (Figure).



Conclusions: Survival probability was higher in patients who received eculizumab compared with patients who did not receive eculizumab. Successful treatment with eculizumab, in addition to almost half of the patients having a complement pathogenic variant, confirms the appropriate classification of P-aHUS as a CM-TMA.

OC 16

Predictors of bone mineral density in kidney stone formers

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Background: Nephrolithiasis is associated with an increased fracture risk, but predictors of bone mineral density in stone formers remain poorly defined.

Methods: We conducted a retrospective analysis in the Bern Kidney Stone Registry, a single-center, observational cohort of kidney stone formers. Inclusion criteria were age ≥ 18 years and ≥ 1 past stone episode. Multivariable linear regression analyses, adjusted for age, sex, BMI, eGFR and tobacco consumption, were used to assess the association of blood and 24 h urine parameters and stone composition with bone mineral density at the lumbar spine and femoral neck.

Results: In the analysis, 504 participants were included, mean age was 46 years and 76 % were male. In multivariable analyses, fasting (β: -0.031; p = 0.042), post-load (β: -0.059; p = 0.0028) and Δ post-load minus fasting (β: -0.053; p = 0.0029) urine calcium/creatinine ratios after 1 week of restricted diet and calcium oxalate dihydrate stone content (β: -0.042; $p = 0.011$) were negatively associated with Z-scores at the lumbar spine. At the femoral neck, alkaline phosphatase (β: -0.035; $p = 0.0034$) and PTH (β: -0.035; $p = 0.0026$) were negatively associated with Z-scores, whereas 24 h urine magnesium (β: 0.043; p = 3.5×10-4) and potassium (β: 0.032; p = 0.012) correlated positively with Z-scores at the femoral neck.

Conclusions: In summary, our study reveals distinct predictors of bone mineral density at the lumbar spine and the femoral neck in stone formers. Commonly available clinical parameters, such as kidney stone composition results, can be used to identify stone formers at risk for low bone mineral density.

OC 17

Hypertensive patients have a decreased microperfusion response during a cold pressure test compared to healthy participants

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Background: Microcirculation is essential to supply oxygen and nutriments to tissue. Alteration in the microcirculation is often proposed as a mechanistic link between hypertension and target organ damage. Thanks to recent developments in contrast-enhanced ultrasonography (CEUS), quantification of renal microcirculation is now possible. The objective of this study was to compare the response in microcirculation during a cold pressure test (CPT) in hypertensive patients with those in healthy normotensive participants.

Methods: Hypertensive (HT) and normotensive (NT) participants underwent 2 separate CPT of 2 minutes. Doppler ultrasound was used to measure renal resistive index (RRI) and CEUS to measure the so called perfusion index (PI) as a proxy of renal tissue microcirculation. Renal Doppler and CEUS were performed before and during the CPT. We compared baseline measures and responses to CPT of HT and NT groups using a Wilcoxon test.

Results: Fourteen hypertensive and nineteen normotensive male participants were included. HT participants were older and had higher blood pressure and body mass index. Baseline RRI was similar in both group, but HT had lower PI (median with interquartile range) : 1177 U(515-1879) vs 2476 U(1411-3462)p = 0.016. The CPT decreased the RRI in NT and increased the RRI in HT, resulting in a different CPT response -0.041 [CI -0.066; -0.016, p = 0.004]. The CPT increased the PI in both groups but the increase was more marked + 650U±754 in healthy participants (p = 0.042).

Conclusions: Compared to healthy participants, hypertensive patients show a paradoxal RRI response and[MP1] a lower increase in perfusion index during CPT suggesting that microcirculation and possibly renal autoregulation is altered. This is the first demonstration that CEUS is able to detect differences in microcirculation between healthy participants and hypertensive patients.

ORAL COMMUNICATIONS – HEMODIALYSIS / PERITONEAL DIALYSIS

OC 18

Seroconversion, cellular response and persistence of immunogenicity following COVID-19 mRNA vaccination in a cohort of swiss hemodialysis patients

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Background: Patients receiving dialysis are at increased risk of COVID-19 related disease and mortality. Moreover, they may display a reduced humoral and cellular response after vaccination. Whereas high rates of seroconversion after two doses of mRNA vaccine have been reported for this population, little is known about persistence of immunogenicity in terms of antibody titers and cellular response during the following months after vaccination.

Methods: We conducted a prospective, single center study on swiss dialysis patients to evaluate the rate of seroconversion 1 month after two doses of BNT162b2mRNA (Pfizer/BioNTech) vaccine and the persistence of immunogenicity after 4 and 6 months by measurement of Serum IgGS1 antibodies. At 6 months cellular response was assessed by an interferon-gamma-release assay (IGRA). Furthermore, antibody-titers were compared to a group of healthy controls (HC) at 1 and 6 months.

Results: Out of 23 patients, n = 20 were negative for IgGS1 antibodies prior vaccination. Overall seroconversion at 1 month was 85% and in patients without taking immunosuppressive drugs (n = 17) 94%, respectively. Mean antibody titers declined during the study (1 month 692 ± 717 BAU/ml, 4 months 218 ± 289 BAU/ml, 6 months 99 ± 111 BAU/ml). However, at 6 months antibodies were still detectable in 73% of patients. When compared to HC, antibody titers of patients where significantly lower at 1 (2662 ± 678.9 BAU/ml vs 692.2 ± 721.4 BAU/ml) and 6 months (586.5 ± 703 BAU/ml vs 99 ± 111 BAU/ml). A positive IGRA test was observed in 62% of patients after 6 months. Risk factors for cellular non-response were low antibody titers, immunosuppressive drugs and older age.

Conclusions: Although seroconversion after two doses mRNA vaccination was high, in terms of antibody titers, antibody persistence and cellular response, dialysis patients may display impaired protection during and after a 6 months observation period.

OC 19

COVID-19 pandemic in dialysis patients: the Swiss experience

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Background: Chronic dialysis patients are classified as patients with increased risk for COVID-19. Knowledge about the incidence and survival of chronic dialysis patients infected with SARS-CoV-2 in Switzerland - a high-income country with high density of relatively small dialysis centers - is scarce. We present the findings regarding incidence, survival and regional differences, compared to those of the general population in Switzerland.

Methods: Information on chronic dialysis patients who tested positive for SARS-CoV-2 between February 24, 2020 and January 31, 2021 were reported to the Swiss dialysis registry by all 95 Swiss dialysis centers. Hereafter, these results were linked with clinical characteristics from the Swiss dialysis registry.

Results: Throughout the study period 573 dialysis patients tested positive for SARS-CoV-2 in Switzerland: 96 cases occurred in the first wave, 472 in the second wave and 5 in between. During the first wave, Italian-speaking Ticino was most severely affected, with a 7-fold higher incidence compared to the general Swiss population. In the second wave, the majority of cases were found in the French-speaking part of Switzerland, with a 2.5 times higher incidence versus non-dialysis patients. A total of 123 deaths were recorded, of which COVID-19 was the main cause of death in 100 patients. This corresponds to a highly increased overall mortality rate of 17.5% compared to 1.7% in the general population. None of the 40 patients with a history of renal transplantation died. Age was identified as the only independent risk factor for mortality in dialysis patients.

Conclusions: Chronic dialysis patients in Switzerland are more likely to be infected by SARS-CoV-2 than the rest of the population, with large regional differences. Mortality is significantly increased compared to non-dialysis patients, albeit slightly less than in some other European countries.

OC 20

Peritoneal dialysis (PD)-related peritonitis rate and microbiology spectrum: a ten-year single center cohort-study

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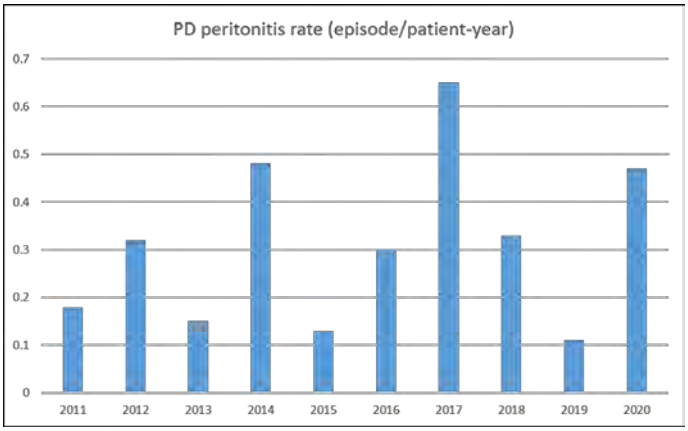
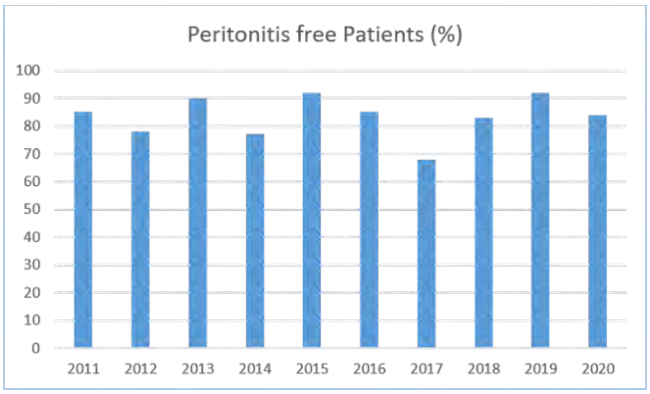
Background: Peritoneal dialysis-related peritonitis represents a quality outcome. We reviewed the incidence of PD peritonitis, microbiology and antibiotic resistance at our institution over 10 years. Our standards include culture from the dialysate in blood culture vials and culture from centrifuged dialysate. Empiric therapy was started according to the ISPD guidelines.

Methods: Retrospective analysis of prospectively collected data in the prevalent PD patient cohort from 1.1.2011 until 31.12.2020. Peritonitis rates are reported as episodes per patient-years on PD treatment as recommended by the ISPD. Culture results and antibiotic resistance data were assessed from the patient records.

Results: Overall, 46 peritonitis episodes were identified in 93 patients. 15 episodes (32%) occurred in patients with prior PD peritonitis (2 recurrent, 6 repeat, 7 new infections). The average peritonitis rate for the last 10 years was 0.30/patient-year and ranged from 0.11 to 0.65/patient-year (Fig.1).



Causative organisms were mostly Gram positive (46%), with fewer Gram negative and only one fungal and one pseudomonas infection. 33% of episodes were culture negative, which exceeds the recommended rate of less than 15%. Antibiotic resistance was noted in 12 cases (26%), 3 cases were resistant to cephalosporins and two were resistant to aminoglycosides. 61 patients (66%) remained completely peritonitis free throughout their PD time in the observed period. The yearly proportion of peritonitis-free patients ranged from 68% to 92% (Fig. 2). We observed no changes in the peritonitis pattern over the 10 years assessment time.



Conclusions: At our institution, the recommended PD peritonitis rate of less than 0.5 episodes per patient-year was achieved over the last 10 years. Resistance patterns do not suggest a selection towards increasing microbial resistance over time. A high rate of culture-negative cases warrants review and optimization of sampling and culture methods. This emphasizes that regular quality assessments are meaningful to improve standards of care.

OC 21

Management and outcomes of patients on maintenance dialysis during the first and second wave of the COVID-19 pandemic in Geneva, Switzerland

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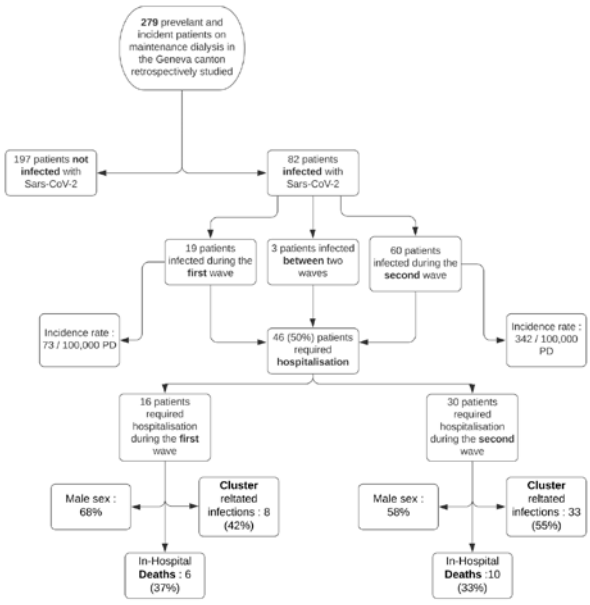
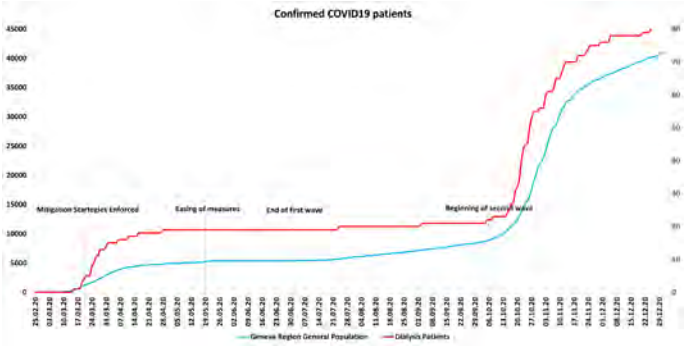
Background: Patients on maintenance dialysis are at high risk for serious complications from COVID-19 infec- tion, including death. We present an overview of local experience with dialysis unit management and reorgan- isation, local epidemiology and outcomes during the COVID-19 outbreak in Geneva, Switzerland, where SARS-CoV-2 incidence was one of the highest in Europe.

Methods: All SARS-CoV-2-positive outpatients on maintenance dialysis were transferred from their usual dialysis facility to the Geneva University Hospitals dialysis unit to avoid creation of new clusters of transmission. Within this unit, appropriate mitigation measures were en- forced, as suggested by the institutional team for prevention and control of infectious diseases.



Results: From 25 February to 31 December 2020, 82 of 279 patients on maintenance dialysis tested positive for SARS-CoV-2 during two distinct waves, with an incidence rate of 73 cases per 100,000 person-days during the first wave and 342 cases per 100,000 during the second wave, approximately four- to six-fold higher than the general population.

The majority of infections (55%) during both waves were traced to clusters. Most infections (62%) occurred in men. Sixteen patients (34%) died from COVID-19 relat- ed complications. Deceased patients were older and had a lower body mass index as compared with patients who survived the infection.



Conclusions: SARS-CoV-2 is associated with high infection and fatality rates in the dialysis population. Strict mitigation measures seemed to be effective in controlling infection spread among patients on maintenance dialysis outside of clusters. Large scale epidemiological studies are needed to assess the efficacy of preventive measures in decreasing infection and mortality rates within the dialy- sis population.

*In press SMW

OC 22

Computational nephrology part 1: hemodialysis*

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Background: Patients on hemodialysis require frequent monitoring of clinical and laboratory data. Laboratory results guide treatment of anemia, mineral and bone disorder, dialysis prescription and dietary recommendations. Single pool and standardized Kt/V calculations need many variables and are laborious. Electronic health records are not designed to facilitate hemodialysis adequacy assessment. We aimed to develop an accurate algorithm to help nephrologists taking care of patients on hemodialysis.

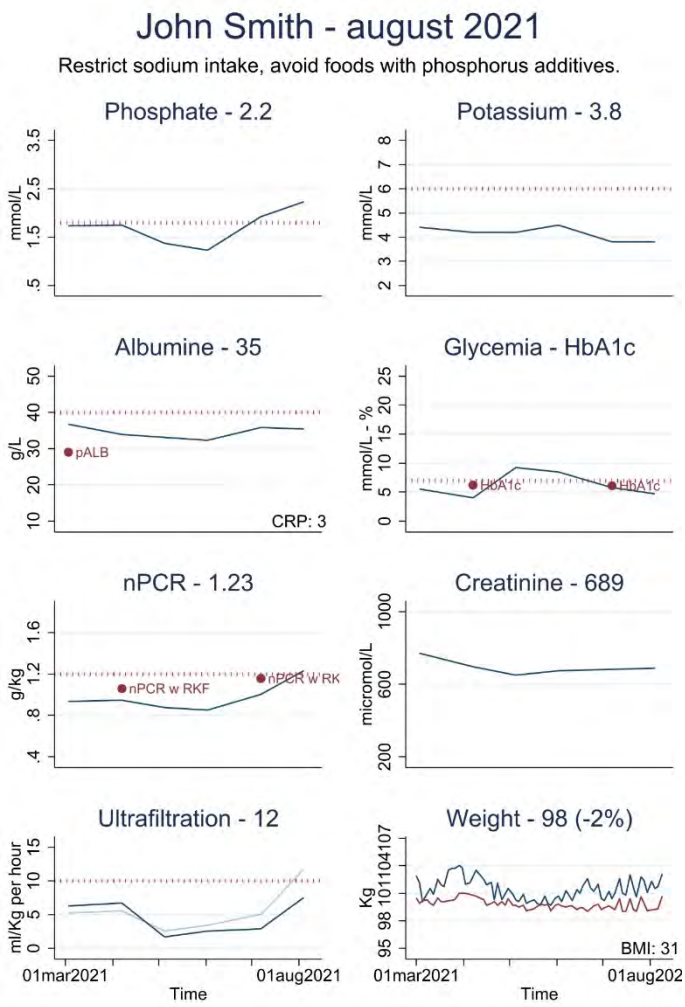
Methods: The algorithm consists of formulas, conditional statements, loops, graphs creation commands and linear regression models. For 40 patients, it needs approximately 3 minutes and analyses millions of observations.

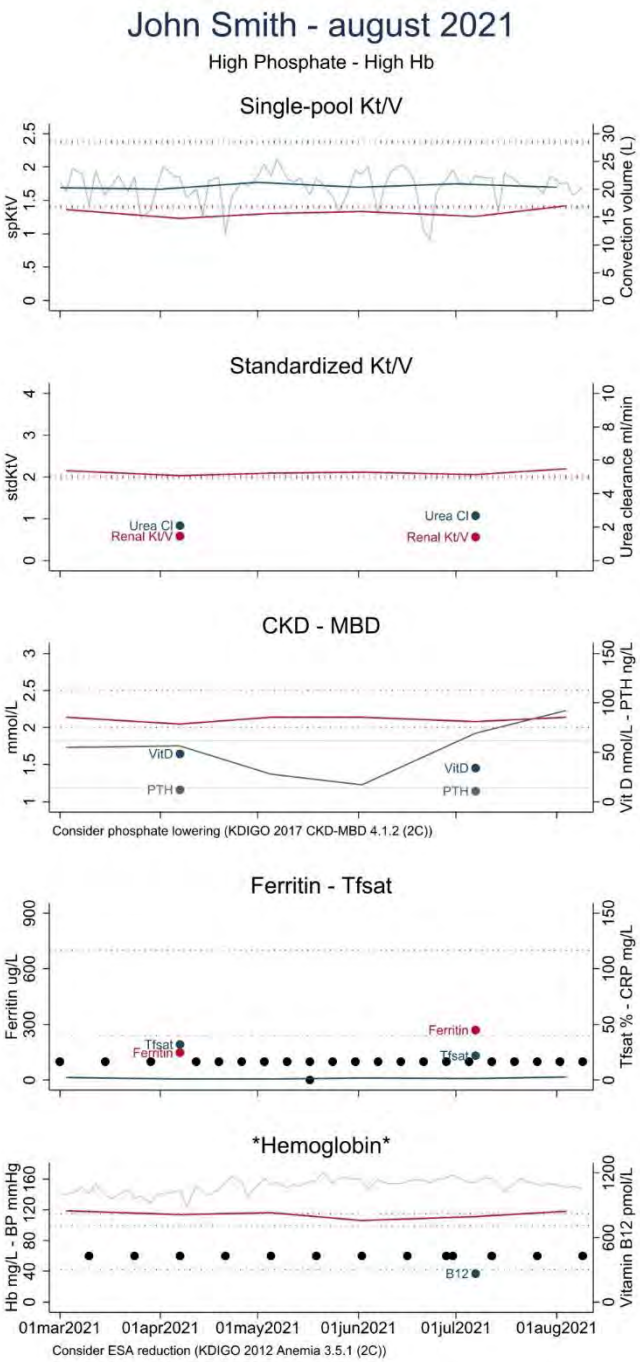
Inputs (automatically extracted):

- Laboratory Results
- Dialysis monitoring parameters (weight, BP, ultrafiltration, blood flow, convection volume…)
- Dialysis prescription (frequency, length, dialysis concentrate composition….)
- Medications given during hemodialysis sessions

Results: Outputs (user customizable):

- Off targets laboratory results or dialysis goals
- Graphic representation over 6 months of single pool KtV, standardized KtV and residual kidney function (Figure 1)
- Other graphs to guide prescription for CKD – MBD and to evaluate iron store and hemoglobin level.
- Recommendations based on KDIGO guidelines for treatment or dialysis prescription modification
- Other dedicated reports for the dietician (Figure 2 the nurse and the patient)





Conclusions: We developed a rapid algorithm to guide hemodialysis patient care. There is no need to prove that it saves time. Whether it improves user's satisfaction and reduce medical errors should be ascertain in further clinical trials. We will develop computational nephrology for other frequent clinical situations, like AKI, CKD and posttransplant follow up.

*YSN paper

ORAL COMMUNICATIONS – YOUNG SWISS NEPHROLOGY SESSION

OC 23

Humoral and cellular responses to mRNA vaccines against SARS-CoV2 in patients receiving anti-CD20 therapy*

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Background: B-cell depleting therapies increase COVID19 morbidity and mortality. For this specific population, evidencebased vaccination strategies are lacking. Here, we investigated humoral and cell mediated immune responses to SARS-CoV2 mRNA-based vaccines in patients receiving CD20-B-cell depleting agents for autoimmune disease, malignancy, or transplantation.

Methods: Patients at the Bern University Hospital with a treatment history of anti-CD20 depleting agents (rituximab or ocrelizumab) were enrolled for analysis of humoral and cell-mediated immune responses (by IFN-g release assay) after completing vaccination against SARS-CoV2. Primary outcome was the the anti-spike antibody response in anti-CD20-treated patients (n = 96) in comparison to immunocompetent controls (n = 29).

Results: Anti-spike IgG antibodies were detected in 49% of patients 1.79 months after the second vaccine dose (interquartile range, IQR: 1.16-2.48) compared to 100% of controls (p <0.001). SARS-CoV2 specific interferon-γ release was detected in 20% of patients and 75% of healthy controls (p <0.001). Only 11% of patients, but 75%of healthy controls showed positive reactions in both assays, respectively (p <0.001). Time since last anti-CD20 therapy (7.6 months), peripheral CD19+ (>27/µl), and CD4+ lymphocyte count (>653/µl) predicted humoral vaccine response (area under the curve [AUC]: 67% [CI 56-78], 67% [CI 55-80] and 66% [CI 54-79], (positive predictive value [PPV]: 0.78, 0.7 and 0.71).

Conclusions: This study provides evidence for blunted humoral and cell-mediated immune responses elicited by SARS-CoV2 mRNA vaccines in patients with CD20-depleting treatment history. Lymphocyte subpopulation counts including CD4+ T helper cell counts are associated with vaccine response in this highly vulnerable population.

*YSN paper

OC 24

Relevance of Deceased Donor Urine Findings for Kidney Transplantation: a Comprehensive National Cohort Study*

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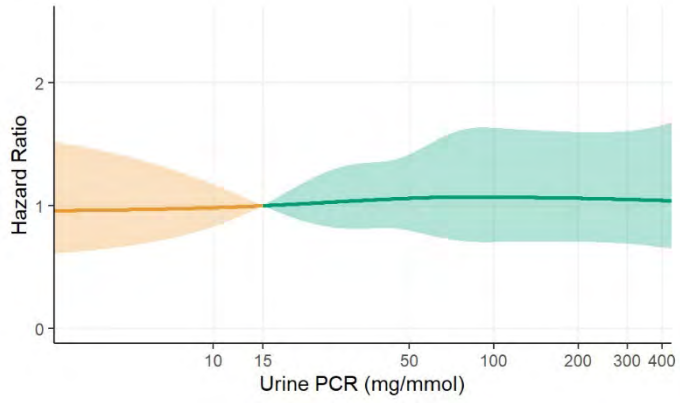
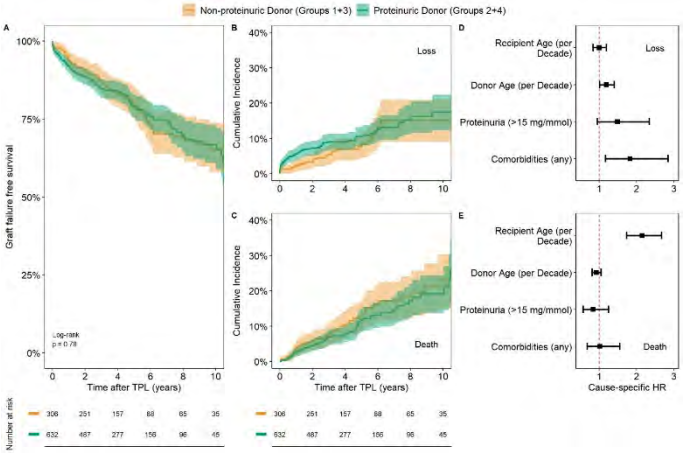
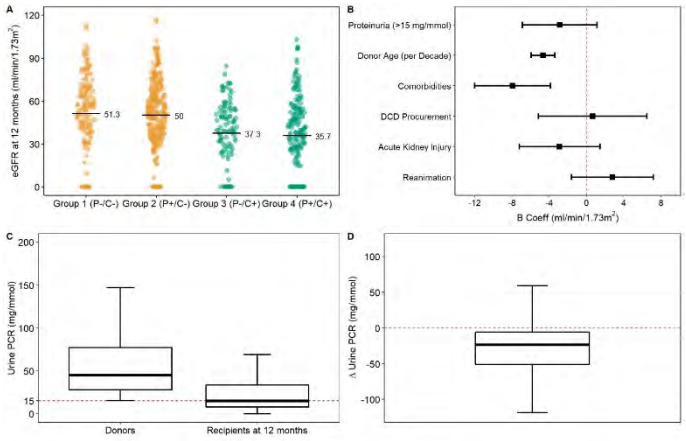
Background: Proteinuria is frequent in patients with nephropathies and associated with progressive kidney disease and risk for end stage kidney disease. In this nationwide cohort study, we evaluated the prevalence of pathological urine findings in deceased donors candidates and measured the impact on outcome after kidney transplantation.

Methods: Data of the Swiss Organ Allocation System and the Swiss Transplant Cohort Study were analyzed. They comprised 1725 donor candidates and 1516 kidney recipients transplanted between 2008 and 2019. We correlated urine findings with donor characteristics and quantified the impact of proteinuria on outcome and allograft function at 12 months.

Results: Proteinuria above 15 mg/mmol occurs in 74% of deceased donor candidates and is associated with reanimation, acute kidney injury and lag time between ICU admission and urine sampling. Proteinuria is not associated with donor age or reported donor comorbidities, including hypertension, diabetes mellitus and vascular disease. Donor proteinuria is not associated with patient or allograft survival, nor is it predictive of allograft function at 12 months. In 79.7% of recipients transplanted from a proteinuric donor, proteinuria declines or vanishes within first 12 months after transplantation. Urine findings influence allocation decisions in 4.5% of non-immunological organ declines and are the leading cause for decline in 0.2% of cases.







Conclusions: We report a high prevalence of pathological urine findings in donor candidates and find no evidence of a deleterious impact of proteinuria on graft function and/or survival. Low-level proteinuria should not be considered a limiting contraindication for kidney allocation in deceased donor transplantation.

*YSN paper

OC 25

Treatment of acidosis in hemodialysis patients is biased by the type of vascular access*

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Background: Metabolic acidosis represents one of the major complications of chronic kidney disease. Although target blood bicarbonate levels have not been formally established for hemodialysis patients, predialysis levels are commonly measured from the arterial blood line and dialysate bicarbonate concentration is adjusted accordingly. Depending on the type of vascular access (AV fistula (AVF) or graft (AVG) vs. catheter), bicarbonate concentrations are measured in arterial vs. central venous blood. We aimed to investigate whether the site of sampling (AVF/AVG vs. catheter) influences bicarbonate levels and may lead to systemic bias in the management of acidosis.

Methods: We have simultaneously sampled blood from the AVF/AVG and catheter for bicarbonate measurement in patients who temporarily had both types of vascular access. We retrospectively compared routine predialysis blood bicarbonate levels and dialysate bicarbonate concentrations in chronic hemodialysis patients with catheter vs. AVF/AVG. Interim results from an ongoing study are presented here.

Results: Bicarbonate levels were significantly higher in central venous blood (catheter) compared to simultaneously drawn arterial blood (AVF/AVG) (22.3±2.8 vs. 20.6±2.4, $p < 0.001$, $n = 16$). In the second part of the study, patients with a dialysis catheter ($n = 24$) had similar predialysis blood bicarbonate levels compared to patients with an AVF/AVG ($n = 33$) (21.7± 1.9 vs. 21.3±2.1, $p = 0.45$), while they were prescribed a lower dialysate bicarbonate concentration (31.5±2.4 vs. 32.8±2.5, $p = 0.056$).

Conclusions: Bicarbonate levels are higher in blood drawn from a catheter compared to blood drawn from an AVF/AVG. If dialysate bicarbonate concentration is adjusted to target the same predialysis blood bicarbonate levels in patients with a catheter as in those with an AVF/AVG, metabolic acidosis is systematically undertreated in the former. Further study is needed to determine whether this could contribute to the worse outcome of patients with catheters. Different bicarbonate target levels should probably be used depending on the type of vascular access.

*YSN paper

POSTER PRESENTATIONS – BASIC SCIENCE / GENETICS / EXPERIMENTAL NEPHROLOGY & NCCR KIDNEY.CH

P 1

Role of monogenetic genes in nephrolithiasis*

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Background: Kidney stone disease (nephrolithiasis) is a disease with increasing prevalence, high morbidity and high economic burden. Besides non-genetic risk factors for kidney stone development (e.g. metabolic syndrome, a diet high in salt and protein) genetic predisposition to kidney stone disease is an important, often-neglected aspect in diagnosis and treatment of nephrolithiasis. Previous data from small scale studies in selected subpopulations of kidney stone formers suggest a monogenetic cause of kidney stone disease in 10-15% of the population. However, large scale studies using next generation sequencing techniques have not been performed thus far.

Methods: We analyzed the prevalence of monogenetic stone disease (explained by mutation in 1 of 33 known kidney stone genes) by use of whole exome sequencing (WES) data in a cohort (the Bern kidney stone registry) of 841 well-characterized kidney stone formers >18 years of age. Analysis of whole exome sequencing data was done by a standardized approach for variant prioritization using the variant classification criteria of the American College of Medical Genetics and Genomics (ACMG).

Results: We detected 82 likely causative mutations in 20 of 33 analyzed genes, leading to a molecular diagnosis in 9.7 % of all cases; 30% of the detected mutations were novel. Around 60 % of the mutations were in autosomal dominant monogenetic genes, fitting with previous data showing more frequent recessive causes of nephrolithiasis in children, but more dominant causes in adults.

Conclusions: Monogenetic forms of nephrolithiasis are less frequent than previously published in a large, non-selected kidney stone former cohort. This is likely due to reduced referral bias, the Bern Kidney Stone Registry mostly consisting of regular first or second stone formers. However, knowledge of the molecular cause of nephrolithiasis may still facilitate personalized medicine and have implications for therapy for the individual patient and/or his family.

*YSN paper

P 2

Peroxisomes are dispensable for normal renal function*

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Background: Peroxisomes are single membrane-bound cellular organelles identified in the kidney in 1954. Peroxisomes are ubiquitously present in eucaryotic cells with highest abundance in renal proximal tubule cells and hepatocytes. The variety of metabolic and antioxidant functions in which peroxisomes are involved is highlighted by human mutations in *PEX* genes which encode peroxins proteins required for proper peroxisomal biogenesis. Hence, the complete loss of peroxisomes causes a devastating multiorgan failure called Zellweger syndrome which includes renal impairment. However, the (patho)physiological role of peroxisomes in the kidney remains unknown.

Methods: Here we addressed the role of peroxisomes in renal function in male and female adult or infant mice with conditional ablation of Pex5-driven peroxisomal biogenesis in the renal tubule (cKO mice).

Results: Functional and histological analyses of infant and adult cKO mice did not reveal any overt kidney phenotype. However, male cKO mice (cKOm) exhibited substantial reduction in kidney weight to body weight ratio. Stereological analysis of electronic microscopy results showed a complete absence of peroxisomes accompanied by an increase of the number and volume of mitochondria in proximal tubule cells of cKOm mice. Integrated deep transcriptome-sequencing and metabolome analyses on the kidney revealed profound reprogramming of a great number of metabolic pathways, including biosynthesis of different classes of lipids such as plasmalogens and sphingomyelins (two major classes of membrane lipids) and the metabolism of glutathione. Although this analysis suggested compensated oxidative stress, four weeks of high fat feeding challenging the ability of proximal tubule cells to metabolize lipids did not induce significant renal impairments in cKOm mice.

Conclusions: We demonstrate that renal tubular peroxisomes are dispensable for normal renal function. This indicates a large flexibility of proximal tubule cells both in terms of lipid membrane composition and metabolic/antioxidant functions. Our data also suggest that renal impairments in Zellweger syndrome patients are of extrarenal origin.

*YSN paper

P 3

Role of the phosphate transport facilitator XPR1 in bone homeostasis and phosphate-dependent FGF23 secretion- NCCR Kidney.CH*

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Background: Evidence point at Xenotropic and Polytropic retrovirus Receptor 1 (XPR1) as a protein involved in the cellular phosphate export pathway and phosphate homeostasis: systemic constitutive deletion of *Xpr1* in mice is lethal and kidney-specific deletion of *Xpr1* induces hypophosphatemic rickets with hypercalciuria. XPR1 is expressed in the bone, but its function remains elusive. We hypothesized that XPR1 is crucial for bone homeostasis and is involved in the sensing mechanism of phosphate in the bone.

Methods: We established an inducible whole body *Xpr1* KO mouse model. The mice were placed in metabolic cages for urine and blood analysis, followed by femur uCT and histomorphometry. The *Fgf23* mRNA and protein (cterminal and intact FGF23) levels were assessed from tibia and femur incubated *ex vivo* for 24h with increasing phosphate concentrations. Primary osteoblast cells were isolated from control and *Xpr1* mouse calvaria.

Results: Conditional whole body *Xpr1*KO mice are constantly decreasing their body weight upon *Xpr1* deletion, and develop profound hypophosphatemia, compared to their control littermates. Histomorphometry analysis and uCT on femurs of *Xpr1* KO mice show high trabecular bone density, despite low bone formation rate and low number of osteoclasts. Increased intact FGF23 secretion by tibia and femur was observed in control mice in response to increased phosphate concentration in the media. By contrast, the bone samples from *Xpr1*KO mice are resistant to phosphate induced FGF23 secretion. No changes were observed for the c-terminal FGF23 in response to increased phosphate concentration, for both the control and *Xpr1* KO mice.

Osteoblasts were successfully prepared from control and *Xpr1* KO mouse calvarie and *Xpr1* expression was inactivated by tamoxifen treatment.

Conclusions: XPR1 is essential for phosphate homeostasis and FGF23 secretion upon phosphate exposure. Osteoblasts will now be used to further study phosphate dependent FGF23 secretion.

*YSN paper

P 4

Post-transcriptional regulation of TWEAK and its consequences on the kidney allograft outcome*

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Background: Calcineurin Inhibitor Toxicity (CNT) occurs due to long-term treatment with Cyclosporine A and Tacrolimus after kidney transplantation. Common characteristics for CNT are tubular atrophy, interstitial fibrosis and arteriohyalinosis (ah/aah). The pro-inflammatory cytokine TWEAK is involved in the pathogenesis of CNT and TWEAK deficiency protects from CNT. The 3'UTR of many cytokines ensured rapid decay. Cytokines, such as TNF, IFNɣ and IL6 are post-transcriptionally regulated by AU-rich elements (ARE) within the 3'UTR.

Methods: We employed an *in silico* screen of the 3'UTR of TWEAK for potential AREs and validated their relevance in TWEAK regulation *in vitro* and *in vivo*. Specifically, we generated constitutive active Luciferase-plasmid constructs under the control of genetic variants of TWEAK's 3'UTR. Furthermore, we generated a transgenic mouse deficient for AREs in TWEAK's 3'UTR and analyzed cytokine, organ infiltration and growth retardation in heterozygote and homozygote animals compared to wildtype littermates.

Results: We identified AREs within the 3'UTR of the human TWEAK, which are highly conserved among mammalian species. Indeed, luciferase reporter assays revealed that TWEAK mRNA is rapidly degraded like TNF. Meanwhile, disruption of the AREs completely abrogated rapid RNA decay *in vitro*. To show the biological relevance of these AREs, we established a mouse line by CRISPR/Cas9, deficient in the AREs in the 3'UTR of TWEAK. These transgenic mice revealed increased levels of TWEAK, IL6R and Granzyme B in plasma and increased mRNA expression of TWEAK, TNF and IL6 in peripheral blood at 8 weeks of age.

Conclusions: In summary, we identify AREs as important sequences for the regulation of TWEAK *in vitro* and *in vivo*. Deletion of a non-coding sequence of TWEAK is sufficient to induce a spontaneous inflammatory phenotype in mice. Further experiments will focus on the molecular mechanism of TWEAK mRNA decay and the specific phenotypes in spontaneous and induced inflammation models *in vivo*.

*YSN paper

P 5

Chronic hypoxia reduces the expression of the anti-aging proteins Klotho and Sirt6 in mice and humans

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Background: Chronic fetal hypoxia impacts proper renal organogenesis and increases the risk for chronic kidney diseases (CKD) in adults. Furthermore, highland residents of various ethnicities exhibit a significant correlation between high altitude and incidence of renal diseases. However, still not much is known about how long-term hypoxia is implicated in the onset and progression of CKD. Here, we show that reduced expression levels of anti-aging proteins plays an important role in this process.

Methods: Gravid mice were exposed to chronic hypoxic conditions (10 % oxygen) for 7 days. The immediate consequences of fetal hypoxia on renal development were studied using a proteomics approach, ELISA, and PCRs. Its long-term consequences on physiology were assessed in adult offspring at 8 and 15 months. The study was complemented with an analysis of healthy human volunteers sojourning 4 consecutive weeks at the Jungfraujoch.

Results: Of the 436 proteins significantly differentially regulated in chronic fetal hypoxia 15 belonged to the GO term "Aging" including the anti-aging proteins klotho and Sirt6. Both proteins were not only reduced in the fetal renal tissue, but also in circulation, and importantly still so in aged hypoxic offspring. Physiologically, renal function was reduced in hypoxic offspring with concomitant induction of fibrotic markers in the kidney. The chronic hypoxia-mediated reduction of anti-aging proteins was preserved between mice and humans, as serum klotho and SIRT6 levels were also significantly downregulated in humans after a long-term stay at high altitude.

Conclusions: Taken together, we uncovered that reduced levels of the anti-aging proteins klotho and Sirt6 contribute to renal functional decline in mice exposed to chronic hypoxia in utero. This phenotype is associated with a characteristic biomarker profile in tissue and serum samples, exploitable for detecting and targeting accelerated aging in chronic hypoxic human diseases.

P 6

Osteoblast-specific deletion of Memo1 in mice severely impairs the expression of FGF23 (NCCR-Kidney.CH project)*

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Background: Memo deletion in mice caused a bone disease with diminished osteoblast and osteoclast biomarkers in serum (Moor et al., JBMR Plus 2018), resembling the alterations occuring in adynamic bone disease in humans with renal failure, as well as those found in klotho-deficient mice (Kawaguchi et al., J Clin Invest 1999). In addition, FGFR signaling is impaired in Memo-deficient osteoblasts (Moor et al., JBMR Plus 2018). We previously detected lower *Fgf23* expression in cultured Memo-deficient osteoblasts, as the expression of FGF23 by bone cells requires autocrine or paracrine FGFR/Klotho signaling (Kaludjerovic et al., FASEB J 2017). Here, we demonstrate that *Memo1* in osteoblasts is required for *Fgf23* expression in murine bone.

Methods: Exon 2 of the *Memo1* gene was deleted in the osteoblast-osteocyte lineage in Memo fl/fl mice using a Cre recombinase under the Col1a1 promotor to obtain osteoblast-specific knockout (obKO) mice. Memo obKO and Crenegative littermate control mice were genotyped by tail genomic DNA. Organs were studied by micro-computed tomography, by qPCR and Western blot.

Results: Memo obKO were viable without changes in gross anatomy. Weight at weaning age was transiently impaired in male but not in female Memo obKO compared to littermate controls. *Memo1* expression was blunted in the femur of Memo obKO, whereas it remained comparable to controls in kidney and liver tissues. Micro-CT revealed no differences between genotypes in trabecular or cortical bone of vertebrae, femur and tibia. *Fgf23* gene expression by qPCR was undetectable in the femur of Memo obKO mice. Western blotting revealed a decrease of FGF23 protein in females and a tendency to lower expression in males of the Memo obKO genotype.

Conclusions: These findings demonstrate a role of Memo in the osteoblast-osteocyte lineage in contributing to the normal expression of FGF23. These data expand previous findings of FGFR-Klotho dependent regulation of FGF23 expression by the bone.

*YSN paper

P 7

Deleting the TGF-b receptor impairs proximal tubule metabolism and response to chronic injury*

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Background: the proximal tubule (pt) is the most metabolic and pivotal segment in the pathogenesis of chronic kidney disease (ckd). excessive tgf-b signaling and mitochondria dysfunction are two features of ckd progression; how tgf-b intrinsically affects pt mitochondria is unknown. recent studies reported beneficial role of intact tgf-b signaling in chronically injured pt; we hypothesized that tgf-b signaling is important to maintain pt mitochondrial integrity and metabolism.

Methods: to test this hypothesis, mice lacking the tgf-b receptor 2 (tgfbr2) in the pt (ggt-cre;tgfbr2fl/fl) and their floxed (tgfbr2fl/fl) littermates were injured using aristolochic acid model of ckd, and mitochondria integrity and renal injuries were analyzed.

Results: as expected, deletion of tgfbr2 in the proximal tubule worsened cortical tubular injury and fibrosis. Electron and multiphoton microscopy analysis respectively showed disrupted mitochondria structure and energization in injured knockout mice as compared to floxed wild types. pt cells lacking Tgfbr2 have increased ROS production, decreased ATP and increased lactate production, suggesting mitochondrial dysfunction and metabolic rewiring in the absence of tgfbr2. transcriptomic analysis performed on pt cells confirmed mitochondria as the most affected cellular component in the absence of tgfbr2. analysis of mitochondria homeostatic factors revealed increased pgc1a (biogenesis) whereas pink1 (quality control) was decreased in pt cells lacking tgfbr2. further analysis of mitophagy using mito-qc mice revealed decreased mitophagy in knockout mice. Moreover, mitochondrial electron transport chain (etc subunits (complex I, II and IV) were impaired and polg, a mt-genome polymerase, was decreased in the absence of Tgfbr2. Mitoq, a mitochondria specific antioxidant, decreased ROS in pt cells lacking Tgfbr2 and improves etc protein level in injured ko mice.

Conclusions: these data support a crucial role of intact tgf-b signaling to maintain pt mitochondrial integrity and adaptive response to chronic injury by regulating etc subunits expression, mitochondrial biogenesis and mitophagy.

*YSN paper

P 8

Single cell profiling in COVID-19 associated acute kidney injury reveals patterns of tubule injury and repair in human*

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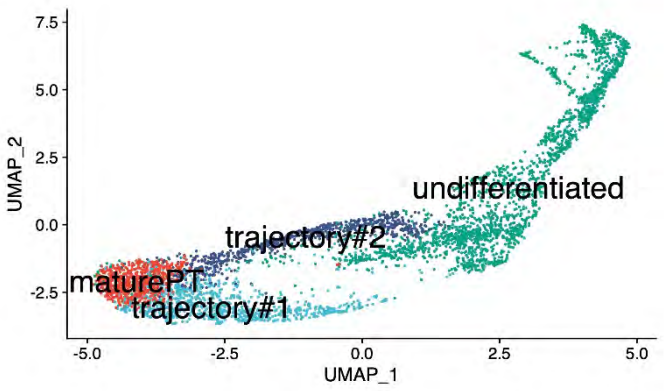
Background: Acute Kidney Injury (AKI) affects up to one in two critically ill patients. The cellular mechanisms of kidney tubule repair after acute kidney injury are poorly characterized in humans.

Methods: We recruited 5 patients admitted to the Geneva University Hospital's Intensive Care Unit for severe COVID19 and experiencing AKI. For each of them, a kidney biopsy was performed before the planned withdrawal of resuscitation measures. We further applied single-cell RNA sequencing to analyze the kidney in the first days after acute injury.

Results: After data processing and quality control, we obtained 20,165 single-cell transcriptomes. The most prominent finding in the snRNAseq analyses was in the proximal tubule (PT) compartment. We defined two cell populations corresponding to mature and undifferentiated PT cells, connected by two cell state transitions (Figure 1). Undifferentiated PT cells display an injured pattern characterized by metabolic impairment, reduction of the tubule transport function, and expression of injury markers confirmed in immunochemistry. We found that tubule repair follows two converging patterns involving the plasticity of mature tubule cells and the expansion and differentiation of progenitor-like cells. Tubule repair by cell plasticity displayed substantial similarities among mice and men and determined the transient expansion of undifferentiated tubule cells with altered functional and metabolic properties. Progenitor-like cells marked by PROM1 proliferated in response to injury and followed a differentiation process characterized by the sequential activation of the WNT, NOTCH, and HIPPO signaling pathways.



Conclusions: Here we generated the first map of PT injury and repair in humans. Taken together, our analyses reveal cell states transitions and fundamental cellular hierarchies underlying kidney injury and repair in patients.

*YSN paper

P 9

Use of deep-learning to calculate glomerular number, size and density in regular histopathology biopsies show no differences between women and men*

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Background: Many studies suggest that women are less likely to develop chronic kidney disease (CKD) and progress less rapidly to end-stage kidney disease than men, but whether histological differences explain this observation remains unclear. We propose a new artificial intelligence-based method to assess glomerular density (GD) and size and applied it to postmortem samples of healthy individuals. We hypothesized that women may have a higher GD and area than men which may contribute to their relative nephroprotection.

Methods: Autopsies performed by the university Center of Legal Medicine of Geneva between 2009-2015 were included if the subjects were aged ≥18 years and had no known kidney disease. A large biopsy was taken from each kidney, hematoxylin&Eosin stained and scanned. Hereafter, a new deep-learning based algorithm (HALO 3.1 software (Indica Labs)) analyzed the samples. The algorithm differentiated between cortex and medulla, and measured glomeruli count, density and size (see Figures 1 and 2).

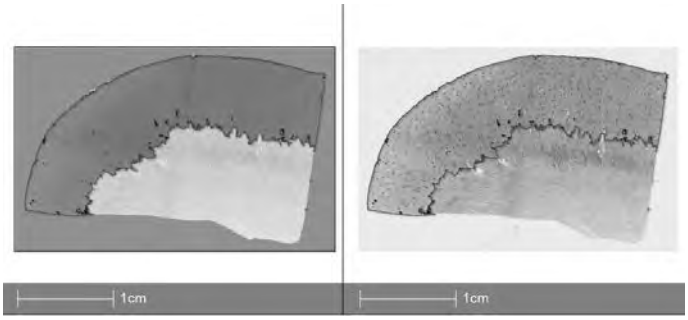

Figure 1: cortex medulla differenciation by halo

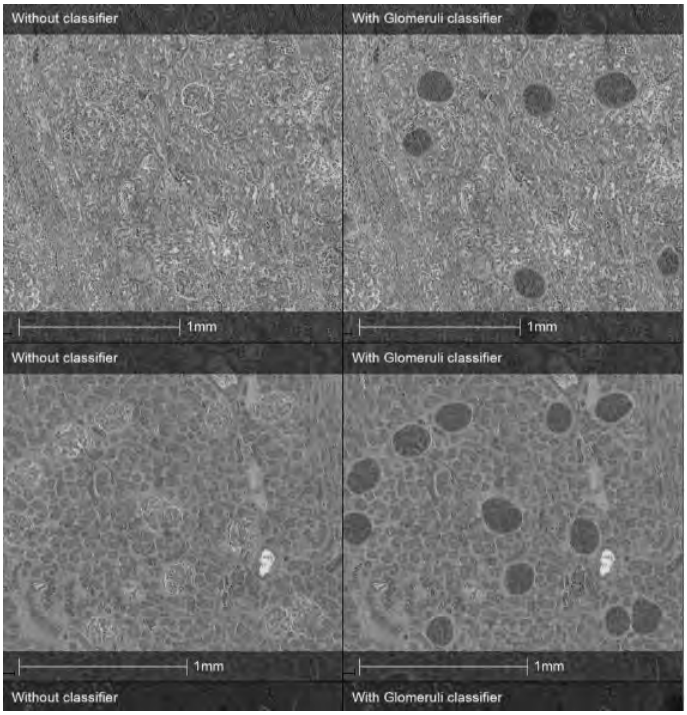

Figure 2: Glomeruli counting by halo

Results: Out of 1166 forensic autopsies, 86 met all inclusion criteria (54 men). Mean±SD age was 43.5 ±14.6 y, women were slightly older (49.0±12.0 vs 40.2 ±15.2 years, p <0.0062); 786±277 glomeruli were analyzed per participant. There was no significant difference in GD between men and women (2.18 ± 0.49 vs 2.29± 0.57 glomeruli/mm^2, p = 0.71). Glomerular area and diameter also did not differ. GD correlated inversely with kidney weight (r = -0.36, p 0.0007), glomerular area (r = -0.59 p = 0.0000) and age (in women, r = -0.48 p = 0.005). Glomerular area increased with age (r = 0.35 p = 0.0008).

Conclusions: In this study, there were no sex-differences in glomerular density or area. Considering that female kidneys are smaller, this strongly suggests that the relative nephroprotection of women is not due to structural or histological differences. The use of artificial intelligence can be of great help in analyzing renal biopsies, and provide supplementary histological information.

*YSN paper

P 10

Dietary consumption in the Swiss Kidney Stone Cohort – NCCR Kidney.CH*

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Background: Kidney stones are a frequent condition, with a prevalence around 5-10% in Europe. Previous studies showed associations between kidney stones and diet. Thus, studying kidney stone formers' diet is of key importance to establish efficient dietary measures for the prevention and management of kidney stones.

Methods: The Swiss Kidney Stone Cohort (SKSC) is a multicentric cohort of stone formers. Participants were seen at baseline, 3 months, 1 year and once a year during 3 years. A control group of non-stone formers was recruited in the general adult population. Repeated consecutive 24-h dietary recalls and 24-h urines were collected. We used two consecutive 24-h dietary recalls at baseline to describe the diet in the stone and non-stone former groups. For each participant, we used the average consumption of 19 food groups from the two recalls as response variables in two-part models that estimate separately the kidney stone status influence on the probability of consumption (logistic regression) and on the amount reported by consumers (linear regression). The covariables in the models were kidney stone status, age, sex, BMI, linguistic region and education level.

Results: The characteristics of the 458 participants with two 24-h dietary recalls at baseline are summarized in Table 1. The sex-specific mean consumed amounts for each food group were similar between the two groups, except for vegetables and alcoholic beverages (Table 2). In the two-part model (Table 3), the kidney stone status was significantly associated with the probability of consuming nuts and seeds, cakes and biscuits as well as alcoholic beverages. Among consumers, kidney stone formers reported smaller amounts of vegetables and alcoholic beverages than non-formers.

Conclusions: Overall, the diets of kidney stone formers and non-formers are similar. We observed associations of kidney stone status with vegetables and alcoholic beverages consumption. This data helps guiding food recommendations in stone formers in Switzerland.

*YSN paper

Table 1. Characteristics of the participants with two 24-h dietary recalls at baseline

		SKSC	Non-kidney stone formers
Participants with two 24-h dietary recalls at baseline		**N=261**	**N=197**
Women, n (%)		93 (36%)	90 (46%)
German speaking part of CH, n (%)		148 (57%)	109 (55%)
Age (years), mean [min,max]	All	47.2 [19,79]	43.4 [20,81]
	Men	48.2 [20,79]	45.7 [22,81]
	Women	45.6 [19,73]	40.6 [20,62]
BMI (kg/m^2), mean (SD)	All	26.5 (4.7)	25.2 (4.4)
	Men	26.7 (4.5)	26 (3.8)
	Women	26.2 (5.2)	24.2 (4.9)
Total caloric intake (kcal/24h)	All	2015	2065
	Men	2203	2274
	Women	1674	1817

Table 2. Food consumption values for the SKSC and non-stone formers groups, by gender

	SKSC		Non-kidney stone formers	
	Mean consumption (SD), g		Mean consumption (SD), g	
	Men	Women	Men	Women
Potatoes	45(62)	45(59)	49(72)	39(61)
Vegetables	138(107)	154(108)	188(196)	214(146)
Legumes (pulses)	4(20)	4(16)	9(28)	3(14)
Fruits	148(146)	139(118)	133(137)	168(162)
Nuts and seeds	6(13)	5(13)	10(19)	10(16)
Dairy products	241(194)	195(183)	263(199)	228(182)
Cereals	261(153)	175(99)	255(127)	182(92)
Meat	119(93)	78(70)	115(89)	81(72)
Fish and seafood	34(57)	26(45)	26(43)	29(38)
Eggs	19(31)	15(22)	23(34)	20(30)
Oils and fat	19(16)	21(20)	22(20)	20(16)
Sugar, chocolate and sweets	36(42)	32(39)	38(43)	31(33)
Cakes and biscuits	49(79)	32(53)	41(59)	29(49)
Spices and sauces	39(42)	33(35)	34(34)	30(31)
Soups	39(100)	44(94)	33(90)	50(110)
Dietetic and sports food	5(31)	0(2)	10(58)	3(12)
Savory snacks	11(30)	14(32)	12(32)	10(25)
Non-alcoholic beverages (ml)	2269(854)	2008(689)	2125(844)	2133(927)
Alcoholic beverages (ml)	152(242)	43(104)	277(412)	116(164)

Table 3. Influence of the kidney stone status (kidney stone formers coded as 1 and non-formers as 0) on the probability of consumption (logistic regression) and differences in the mean dietary consumption between kidney stone formers and non-formers, among consumers (linear regression with log-transformed dependent variable)

		Logistic regression (step 1)			Linear regression (step 2)		
	Number of consumers (%)	**OR**	**95% CI**	**p-value**	**Coeff[a]**	**95% CI**	**p-value**
Potatoes	217 (47.4)	1.082	0.704;1.663	0.718	-0.038	-0.249;0.172	0.721
Vegetables	436 (95.2)	NA	NA	NA	-0.183	-0.366;-0.001	0.048
Legumes (pulses)	46 (10)	NA	NA	NA	NA	NA	NA
Fruits	354 (77.3)	0.976	0.569;1.668	0.929	0.086	-0.115;0.287	0.401
Nuts and seeds	158 (34.5)	0.532	0.337;0.836	0.006	-0.293	-0.750;0.165	0.208
Dairy products	446 (97.4)	NA	NA	NA	-0.062	-0.250;0.127	0.520
Cereals	455 (99.3)	NA	NA	NA	0.033	-0.087;0.152	0.592
Meat	405 (88.4)	0.512	0.248;1.024	0.063	-0.071	-0.256;0.114	0.451
Fish and seafood	187 (40.8)	0.854	0.548;1.332	0.485	0.302	0.036;0.568	0.026
Eggs	225 (49.1)	0.776	0.505;1.192	0.248	0.077	-0.196;0.349	0.580
Oils and fat	430 (93.9)	NA	NA	NA	-0.058	-0.243;0.127	0.537
Sugar, chocolate and sweets	391 (85.4)	1.126	0.604;2.089	0.707	-0.104	-0.332;0.124	0.370
Cakes and biscuits	251 (54.8)	1.930	1.236;3.042	0.004	0.124	-0.128;0.375	0.333
Spices and sauces	442 (96.5)	NA	NA	NA	0.233	-0.082;0.549	0.146
Soups	116 (25.3)	0.988	0.614;1.595	0.962	0.261	-0.399;0.922	0.434
Dietetic and sports food	48 (10.5)	NA	NA	NA	NA	NA	NA
Savory snacks	115 (25.1)	0.878	0.537;1.435	0.602	0.109	-0.306;0.523	0.604
Non-alcoholic beverages	458 (100)	NA	NA	NA	0.053	-0.028;0.133	0.201
Alcoholic beverages	218 (47.6)	0.322	0.202;0.507	<0.001	-0.415	-0.742;-0.088	0.013

*NA: less than 50 participants in the consumers or non-consumers groups
[a] the dependent variable (mean consumption) has been log-transformed

POSTER PRESENTATIONS – TRANSPLANTATION

P 11

Impact of different urinary tract infection phenotypes within the first year post-transplant on renal allograft outcomes

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Background: Urinary tract infection (UTI) is the most frequent infection after renal transplantation, and the highest incidence is observed within the first year post-transplant. The objective of this study was to evaluate the impact of different UTI phenotypes within the first year after renal transplantation on allograft function, as well as allograft and patient survival.

Methods: We analyzed 2368 renal transplantations performed between Mai 2008 and December 2017, which were captured in the Swiss Transplant Cohort Study. Patients were categorized into four groups based on their compiled UTI events observed within the first year after transplantation: (a) no colonization or UTI, (b) colonizations only, (c) occasional UTI with 1-2 episodes, (d) recurrent UTI with ≥3 episodes.

Results: In total, 2363 infection episodes were detected in 2368 recipients. 1404 recipients had no colonization or UTI (59%), 353 had colonizations only (15%), 456 had occasional UTI (19%), and recurrent UTI were recorded 155 patients (7%). Patients with recurrent UTI had a 7-10ml/min lower eGFR at one-year post-transplant compared to the other groups (44ml/min vs 54, 53 and 51ml/min; p <0.001). Recurrent UTI had no impact on patient survival, but was independently associated with a reduced death-censored allograft survival (HR 2.11, 95% CI 1.30-3.41, p = 0.002) in the whole cohort, as well as for both sexes. Additionally, occasional UTI had a negativ impact on death-censored allograft survival only in male subjects. The one-year incidence of urosepsis was equal in females and males (4.4% vs 4.7%; p = 0.71), and not associated with a lower death-censored allograft survival.

Conclusions: Occasional and recurrent UTI in men as well as recurrent UTI in women within the first year after transplantation is an independent and clinically relevant risk factor for impaired allograft function and reduced deathcensored allograft survival. Better treatment strategies to prevent especially recurrent UTI are urgently needed.

P 12

Aftercare by external nephrologists suggests excellent outcomes regarding gfr decline and proteinuria, whereas aftercare by the transplant center ensures prompt biopsy-confirmed diagnoses of allograft dysfunction*

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Background: Despite substantial medical progress, median kidney allograft survival remains stable at 13 to 15 years. However, whether and to what extent the transplant center's follow-up of kidney transplant recipients (KTRs) influences long-term outcomes, compared to external aftercare, is still unclear.

Methods: We analyzed 586 KTRs from 2009 to 2019, showing kidney allograft survival of at least 24 months and not developing rejection within the first year post-transplant. All KTRs underwent aftercare in the transplant center for at least 12 months. After that, KTRs were either followed three-monthly in the transplant center (n = 224) or three-monthly by external nephrologists, thus only yearly in our center (n = 362). We analyzed kidney allograft outcomes regarding allograft survival, kidney function, GFR decline, proteinuria, de novo DSA, and rejection.

Results: No differences in pre- and post-transplant characteristics were observed at 12 months post-transplant. Particularly, baseline GFR and proteinuria were comparable at 12 months post-transplant. Interestingly, GFR decline was -0.9ml/min/year among KTRs followed in the transplant center compared to -0.3ml/min/year among KTRs followed by external nephrologists (p = 0.043). In addition, proteinuria was lower among KTRs followed by external nephrologists over a 5-year period (p <0.05). While no differences were observed for the development of de novo DSA (p = 0.704), KTRs followed in the transplant center were more likely to undergo indication biopsies to evaluate any cause of kidney allograft dysfunction (p <0.001).

Conclusions: Our findings suggest that the quality of medical follow-up is independent of the caregiver. The observed better progression of renal function with external follow-up suggests more individualized care due to greater familiarity between patient and physician. For patients with complications, care by the transplant center is crucial, as prompt biopsies may lead to immediate treatment adjustment and prevent more severe courses.

*YSN paper

P 13

Gait speed as single fried frailty phenotype item predictive for length of stay but not readmission in kidney transplantation: a secondary data analysis of a multicenter, prospective cohort study*

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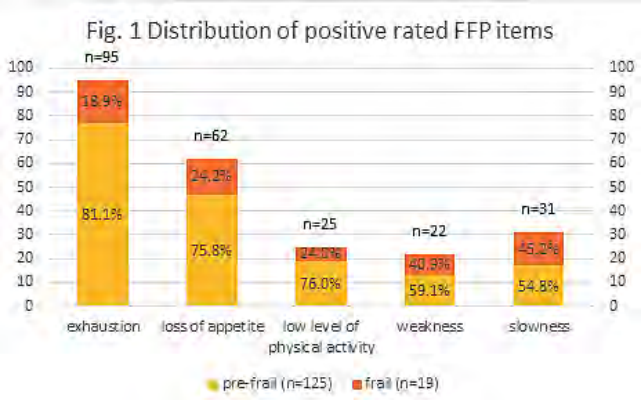
Background: Physical frailty has been found to be a strong indicator for negative outcomes after kidney transplantation (KTx). The 5 item Fried Frailty Phenotype (FFP) assesses physical frailty, yet the predictive power (PP) of its single items remains unclear. We aim to assess the PP of the FFP on length of hospital stay (LOS) and readmission following KTx.

Methods: We performed a secondary data analysis including 230 adult kidney transplant patients (age 53.8 ±13.4 years; 37.1% female; 24.3% preemptive KTx) from the GERAS study (Exploring frailty and mild cognitive impairment in adult kidney transplant recipients to enhance risk prediction for biochemical, psychosocial, and health cost outcomes), nested within the Swiss Transplant Cohort Study (STCS) using a prospective study design. Frailty was assessed pre-KTx with the FFP. LOS (days) and hospital readmission (six months post-KTx) were captured using data from the STCS. The FFP (Table 1) consists of three subjective measures (unintentional weight loss, exhaustion, level of physical activity) and two objective measures (weakness and slowness). Kendall's τc correlation was performed to analyze item to item correlations. PP for

the two outcome variables was assessed using univariate and multivariate analyses.

Results: 41.3% of participants reported exhaustion (highest prevalence), while 9.6% reported weakness (lowest prevalence). Although weakness and slowness were less prevalent, often these participants were frail (Figure 1).



Both, univariate (τc = 0.224, p <0.001) and multivariate (β 0.299, p <0.001) analyses showed that slowness was predictive of longer LOS. Each second slower on the 5-meter distance, increased LOS by 9%. Alternatively, patients walking faster than 0.83 m/s were four-times more likely to leave the hospital at day 13 or earlier. None of the FFP items predicted readmission.

Item	Question/Measurement	Answer Options/Cut-off	Score
Loss of appetite	"Have you, in the last three months, been eating more/less than usual?"	less	1
		unchanged	0
		more	
Exhaustion	"In the last week, did you feel on at least three days, that everything you did was an effort?"	yes	1
		no	0
	"In the last week, did you feel on at least three days, that you could not get going?"	yes	1
		no	0
Low level of physical activity	"How often do you engage in activities that require a low or moderate level of energy, such as gardening, cleaning the car or going for a walk?"	more than once a week	0
		once a week	
		1-3x a month	1
		hardly ever, or never	
Weakness	Grip strength in kilograms measured by a hand-held dynamometer (Jamar Hydraulic Hand Dynamometer, Patterson Medical), mean values of three consecutive tests of maximum grip strength of each hand (24)	mean value above sex- and age adjusted normative value - 2SD (25)	0
		mean value equal or below sex- and age adjusted normative value -2SD (25)	1
Slowness	Average time in seconds of three consecutive measurements to complete a 5m walk at the patient's habitual pace	average = 6 seconds	1
		average < 6 seconds	0

Version	Coefficients				Model Summary		
	Predictor	Unstandardized Coefficients B (95% CI)	Stand. Coeff. Beta	p-value	R Square	Adj. R Square	S.E. of the Estimate
dichotomous	(Constant)	2.226 (1.997-2.454)	n/a	<0.001	0.134	0.122	0.423
	Slowness [no/yes]	0.392 (0.228-0.555)	0.299	<0.001			
	donor type [living/deceased]	-0.161 (-0.276 to -0.046)	-0.175	0.006			
	age	0.005 (0.001-0.009)	0.144	0.025			
ordinal/ continuous	(Constant)	1.856 (1.580-2.132)	n/a	<0.001	0.133	0.117	0.424
	exhaustion1	0.127 (0.001-0.253)	0.125	0.049			
	Slowness continuous	0.086 (0.043-0.129)	0.258	<0.001			
	donor type [living/deceased]	-0.159 (-0.275 to -0.042)	-0.173	0.008			
	age	0.004 (0.000-0.009)	0.131	0.043			

Dependent Variable: Ln Length of Hospital stay [days]

Conclusions: Pre-KTx walking speed predicted increased LOS after KTx. and might be easier to implement in routine clinical practice. Yet further validation of our findings would be valuable.

*YSN paper

P 14

Estimating the expected serum creatinine range may identify kidney transplant recipients with allograft dysfunction*

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Background: Many clinicians struggle to assess the expected kidney allograft function. While falling creatinine levels usually rule out allograft dysfunction, stable creatinine levels may represent a state of allograft dysfunction requiering histopathologic evaluation.

Methods: Al-Sehli et al. created a formula predicting the expected creatinine range, considering recipient and donor criteria and the adaptability of a single kidney. This formula was applied to 250 living donor (LD) and 390 deceased donor (DD) kidney transplant recipients (KTRs) from 2009 to 2019. KTRs were classified as falling below, within, or above the expected range.

Results: 222 LD KTRs (88.8%) and 292 DD KTRs (74.87%) fell below or within the expected range, while 28 LD (11.2%) and 98 DD (25.13%) KTRs exceeded it (p <0.001). KTRs exceeding the expected range had a lower recipient to donor body weight ratio (p <0.001) and more likely received a DCD kidney allograft (p = 0.0025). Post-transplant complications like DGF, vascular or urological complications, TCMR/ABMR, CMV, EBV, or BKV infection didn't explain the classification of KTRs above the expected range (p >0.05). Lowest observed serum creatinine of DD KTRs falling below or within the expected range was 93 µmol/l (median, range 24-202µmol/l) and 104µmol/l (46-236µmol/l) for DD KTRs falling above the expected range (p <0.05). Interestingly, the number of DD KTRs with baseline proteinuria >200mg/mmol*10 was higher among KTRs exceeding the expected range (19.6% vs. 9.00%; p = 0.0095). GFR decline was lowest among DD KTRs falling below the expected range (0.6ml/min/year vs. 0.9ml/min/year).

Conclusions: The greater number of DD KTRs exceeding the expected range may be explained by more ischemia-reperfusion injury and susceptibility to immune-related injury compared to LD KTRs. The observed higher baseline proteinuria and faster GFR decline in a subgroup of DD KTRs exceeding the expected range suggests an underlying pathology. If the expected range isn't reached, an indication biopsy may clarify if this classification is meaningful.

*YSN paper

P 15

hla-derived epitope mismatching may prove useful as a predictive biomarker among kidney transplant recipients with rejection: an analysis of indication and follow-up biopsies*

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Background: Indication biopsies due to a deterioration of kidney allograft function often require follow-up biopsies to assess treatment response or lack of improvement. Immune-mediated injury, namely borderline rejection, T-cell mediated rejection (TCMR), or antibody-mediated rejection (ABMR), results from preformed or de novo alloreactivity due to donor and recipient HLA mismatches. The impact of HLA mismatches on alloreactivity is determined by the total HLA-epitope load that can be calculated using the Predicted Indirectly Recognizable HLA Epitopes (PIRCHE) algorithm.

Methods: We analyzed 123 kidney transplant recipients (KTRs) from 2009-2019 who underwent a first indication biopsy and a follow-up biopsy performed within a median of 3 months. We divided the KTRs into three groups according to the first biopsy: (1) No rejection/borderline (n = 68); (2) TCMR (n = 21); (3) ABMR (n = 34). KTRs with ABMR were subdivided into three groups according to the microvascular inflammation score (MVI). The HLA-derived epitope-mismatches were calculated using the PIRCHE algorithm.

Results: Group 1 (no rejection/borderline): KTRs with higher total PIRCHE scores were more likely to develop TCMR in the follow-up biopsy (p = 0.024). Interestingly, these differences were significant for

both, HLA-class 1 (p = 0.015), and HLA-class 2 (p = 0.013). No differences were observed for those KTRs developing ABMR in the follow-up biopsy. Group 2 (TCMR): KTRs with ongoing TCMR in the follow-up biopsy were more likely to show higher total PIRCHE scores (median 101.50 vs 74.00). Group 3 (ABMR): KTRs with higher total PIRCHE scores were more likely to show an increase of the MVI score in the follow-up biopsy. This difference was more pronounced for the HLA-class II (median 70.00 vs. 31.76; p = 0.086).

Conclusions: PIRCHE scores may prove useful as a biomarker to predict the histopathological changes of immune-related injury from a first indication biopsy to a follow-up biopsy. This immunological risk stratification may contribute to individualized treatment strategies.

*YSN paper

P 16

Short- and long-term impact of neutropenia within the first year after kidney transplantation

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Background: Neutropenia is a very common, but poorly explored problem after renal transplantation. The aim of this retrospective single-center study was to investigate short- and long-term impact of neutropenia occurring within the first year after kidney transplantation, with a special emphasis on different neutropenia grades.

Methods: We included 721 transplantations performed between 2008 and 2019. Based on the nadir neutrophil count, patients were grouped as having neutropenia grade 2 (<1.5-1.0*109/L), grade 3 (<1.0-0.5*109/L), and grade 4 (<0.5*109/L). Depending on the severity and dynamics of neutropenia, potentially offending drugs were reduced or discontinued. Steroids were added/increased as replacement for reduced/discontinued mycophenolate to prevent allograft rejection.

Results: In this unselected cohort, 225/721 patients (31%) developed at least one neutropenic episode within the first year post-transplant: grade 2 (n = 105), grade 3 (n = 65), and grade 4 (n = 55). Most neutropenia episodes were presumably drug-related (71%) and managed by reduction/discontinuation of potentially responsible drugs (mycophenolate 51%, valganciclovir 25%, trimethoprim/sulfamethoxazole 19%). Granulocyte colony-stimulating factor was only used in 2/357 neutropenia episodes (0.6%). One-year incidence of (sub)clinical rejection, one-year mortality as well as long-term patient and graft survival were not different among patient without neutropenia and neutropenia grade 2/3/4. However, the incidence of infections was about 3-times higher during neutropenia grade 3 and 4, but not increased during grade 2.

Conclusions: Neutropenia within the first year after kidney transplantation represents no increased risk for rejection and has no negative impact on long-term patient and graft survival. Adding/increasing steroids as replacement for reduced/discontinued mycophenolate might supplement management of neutropenia.

P 17

Analysis of DCD Porcine Kidney Graft Viability during Sub-Normothermic Perfusion using Magnetic Resonance Imaging and Spectroscopy*

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Background: Better preservation strategies for the storage of donation after circulatory death grafts could increase the number of kidneys available and improve patient survival. Warm (22 and 37°C) ex-vivo perfusion has emerged as a feasible strategy to recover organs, but the underlying mechanism remains elusive. Using magnetic resonance imaging spectroscopy (MRIs), we evaluated kidney viability, and adenosine triphosphate (ATP) production during sub-normothermic *ex-vivo* kidney perfusion (SNOP) versus hypothermic machine perfusion (HMP) in a porcine kidney autotransplantation model.

Methods: To mimic donation after circulatory death (DCD), kidneys from 45 kg pigs underwent 60 minutes of warm ischemia, prior to procurement. Kidneys were then perfused *ex-vivo* at 4°C with (HOMP), and without oxygen (HMP) or at 22°C (SNOP) before autotransplantation. During the *ex-vivo* perfusion, and after transplantation we assessed energy metabolites using MRIs. In addition, we performed Gadolinum (Gd) perfusion sequences. Each sample underwent histopathological analyzing and scoring. mRNA expression was analyzed on renal biopsies at various time points.

Results: Using MRI, we found that in pig kidney, total ATP content was 4 times higher during ex-vivo perfusion at subnormothermic temperature compared to cold perfusion, with or without oxygen. At 22°C, ATP levels gradually increased up to 10hrs of perfusion, then progressively declined. Similarly, AMP content was increased in SNOP perfused organs, then slowly consumed. over time. In addition, SNOP improved cortical and medullary perfusion (Gd elimination). Finally, SNOP graft had lower grade of histological damages 1hr after transplantation compared to cold perfused organs (injury score SNOP 8.8-12.2, HMP 13.5-18.8, HMOP 17.5-18.5).

Conclusions: In kidneys, SNOP improved graft viability when compared with hypothermic perfusions. These results suggest that SNOP might dampen the negative effect of warm ischemia and promote kidney metabolism such as ATP production. Future clinical studies will define the benefits of SNOP in improving kidney graft function, and patient's survival.

*YSN paper

P 18

Age at time of kidney transplantation as a predictor for mortality, graft loss and self-rated health status: a competing risks survival analysis of the Swiss Transplant Cohort Study*

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Background: The numbers of older patients considered eligible for and undergoing kidney transplantation are increasing. However, the effect of age at time of transplantation on health outcomes in kidney transplantation remains inconclusive. The objective of this study was to analyze the relationship between age at time of kidney transplantation with mortality, graft loss and self-rated health status in adult kidney transplant recipients.

Methods: This study used data from the Swiss Transplant Cohort Study and included prospective data of kidney transplant recipients who received a single-organ kidney transplant between 2008 and 2017. Time to

event analysis was performed using Cox' regression analysis, and -in the case of graft loss- competing risk analysis. To analyse the relationship between age and self-rated health status, a random-intercept regression model predicting recipient's repeatedly measured health status over time, was applied.

Results: 2366 kidney transplant recipients were included with an average age of 52.9 years at the time of transplantation. 8.4% of study participants experienced graft loss and 12.6% died (Table 1). Age at the time of transplantation linearly predicted mortality. It was also predictive for graft loss, though nonlinearly, showing that recipients aged between 35 and 55 years presented with the lowest risk of experiencing graft loss (Figure 1). No relationship of age with health status could be detected (Figure 2).

Table 1 Sample characteristics

Variable	Specification variable	Total sample (n = 2366)
Outcomes		
Mortality events	n(%)	298 (12.6)
Mortality events of patients without graft loss	n(%)	234 (9.9)
Graft loss events	n(%)	198 (8.4)
Time to death in months (n=298)	Mean (SD)	45.9 (33.0)
	Median (IQR)	42.9 (54.0)
	Min – max	0.1-120.4
Time to graft loss in months (n=198)	Mean (SD)	34.5 (31.6)
	Median (IQR)	28.6 (52.8)
	Min – max	0.0-118.0
Length of follow-up in months	Mean (SD)	72.0 (34.1)
	Median (IQR)	70.1 (61.2)
	Min – max	0.1-120.4
Socio-demographic recipient characteristics		
Age at transplantation	Mean (SD)	52.9 (13.6)
	Median (IQR)	55.0 (19.0)
	Min – max	18.0-82.0
Sex	Female, n(%)	848 (35.8)
Race	Caucasian, n(%)	2153 (91.7)
Marital status	Single, n(%)	378 (17.9)
	Married/living together, n(%)	1406 (66.7)
	Divorced/separated, n(%)	246 (11.7)
	Widow(er), n(%)	79 (3.7)
Psychological and behavioral recipient characteristics		
Depressive symptomatology [1]	Mean (SD) HADS score	4.5 (3.7)
	Median (IQR) HADS score	4 (4)
	Min – max	0-21
Medication non-adherence [2]	Yes, n(%)	677 (28.6)
Current smoking	Yes, n(%)	418 (19.6)
Biomedical recipient characteristics KT and donor characteristics		
Etiology of renal disease	Cause unknown, n(%)	136 (5.8)
	Congenital, n(%)	57 (2.4)
	Diabetic nephropathy, n(%)	195 (8.3)
	Glomerulonephritis, n(%)	561 (23.9)
	HIV nephropathy, n(%)	3 (0.1)
	Hereditary non PCKD, n(%)	76 (3.2)
	Interstitial nephropathy, n(%)	
	Nephrosclerosis, n(%)	79 (3.4)
	Other, n(%)	265 (11.3)
	PCKD, n(%)	283 (12.1)
	Previous GF, n(%)	454 (19.3)
	Reflux/Pyelonephritis	118 (5.0)
	None, n(%)	120 (5.1)
Type of renal replacement therapy	Peritoneal dialysis, n(%)	411 (17.4)
	Haemodialysis, n(%)	319 (13.5)
	Mean (SD)	1631 (69.1)
Years on dialysis	Median (IQR)	4.0 (5.0)
	Min – max	3.0 (41.0)
		1.0-42.0
Anti-CMV status	Seropositive, n(%)	1459 (61.9)
Cancer history	Yes, n(%)	258 (10.9)
Endocrine-metabolic comorbidity [3]	Yes, n(%)	2017 (85.3)
Cardiopulmonary comorbidity [4]	Yes, n(%)	1180 (49.9)
KT and donor characteristics		
Type of KT	Deceased-donor, n(%)	1392 (58.8)
	Living-donor, n(%)	974 (41.2)
Extended criteria donation [5]	Yes, n(%)	311 (36.0)
Total number of HLA mismatches [6]	Mean (SD)	3.8 (1.5)
	Median (IQR)	4 (2)
	Min – max	0-6
Donor age [7]	Mean (SD)	52.4 (16.1)
	Median (IQR)	55.0 (18)
	Min – max	0-88

Legend: SD, standard deviation; IQR, interquartile range; HADS, Hospital Anxiety and Depression Scale; KT, kidney transplantation; STCS, Swiss Transplant Cohort Study; HIV, human immunodeficiency virus; PCKD, polycystic kidney disease; GF, allograft failure; Anti-CMV, anti-cytomegalovirus; HLA, Human Leukocyte Antigen; 1 Each HADS depression-subscale item was answered on a 4-point Likert scale (0 = 'not at all' to 3 = 'most of the time'), the total score was calculated by summing the item scores and used as a continuous variable (range 0 – 21); 2 Medication non-adherence (yes/no) was defined as any missed doses, having missed at least one dose of medication and/or having missed two or more consecutive doses over the past 4 weeks; 3 Defined as having hypertension, hyperlipidemia, diabetes mellitus 1 or 2 according to STCS definitions; 4 Defined as having coronary heart disease, cerebral vascular disease, peripheral vascular disease, left ventricular dysfunction according to STCS definitions; 5 Defined as a KT from a donor aged ≥ 60 years or aged ≥ 50 years with at least two of the following conditions: history of hypertension, serum creatinine >1.5 mg/dl or cerebrovascular accident as cause of death; 6 min 0; max 6; 7 Continuous variable in years since birth.

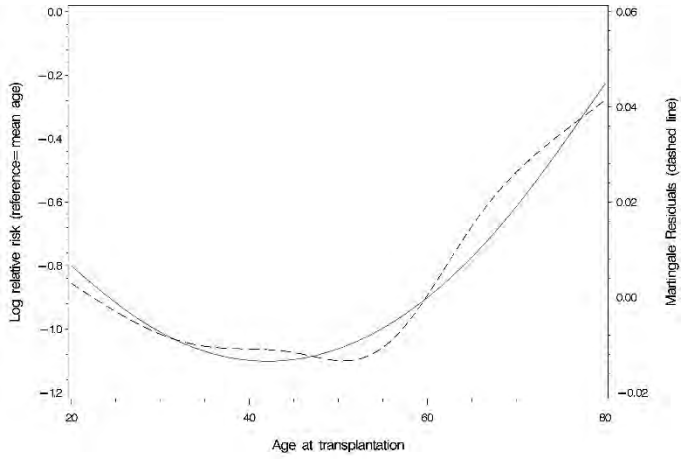

Figure 1: Nonlinear relationship between the probability of graft loss and age at transplantation

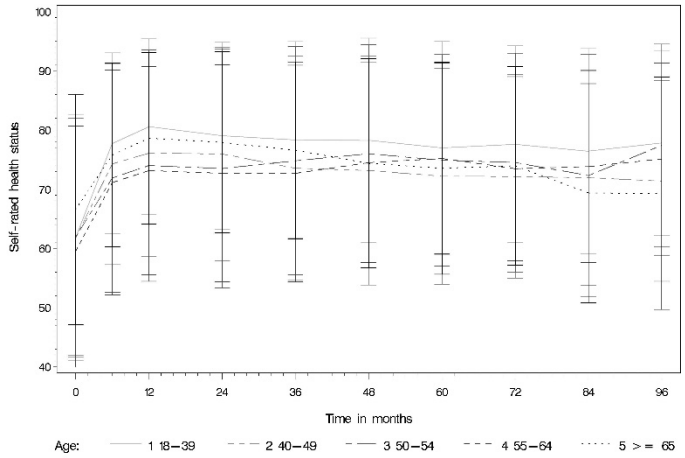

Figure 2: Self-rated health status over time

Conclusions: Higher mortality in older recipients complies with data from the general population. The non-linear relationship between age and graft loss and the higher scored self-rated health status at all follow-up time-points compared to the pre-transplant status -regardless of age- highlight that age alone might not be an accurate measure for risk prediction and clinical decision making in kidney transplantation. Exploring other independent predictors, such as frailty as an indicator for biological age should be considered.

*YSN paper

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Terminal transplant failure due to Covid-19 associated nephrotic glomerulonephritis

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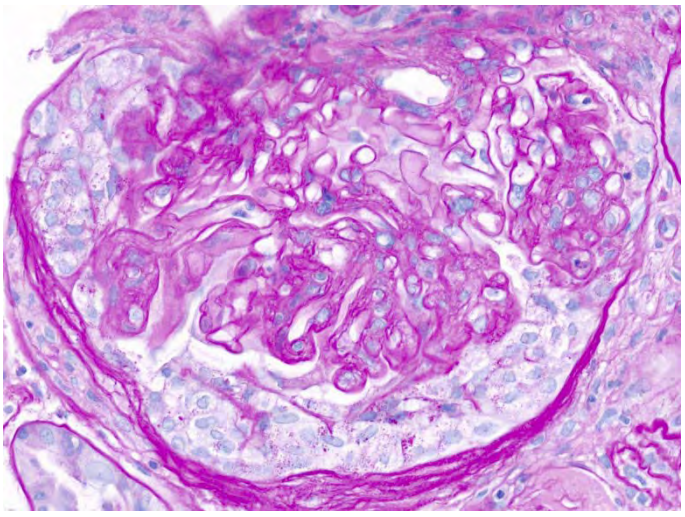
Background: Covid 19 infection associated glomerulopathy has most often been described as collapsing FSGS and occurs almost exclusively in black patients carrying APOL1 risk genotypes.

Methods: We report an acute, COVID19-associated nephrotic glomerulonephritis in a caucasian transplant recipient which led to terminal graft failure.

Results: This 67 y old white female had received a living donor kidney 31 years ago for medullary cystic disease. Her clinical course on cyclosporin/MMF had been stable with an eGFR around 20 ml/min/1.73 m² in the last years. On her 31st annual checkup, she presented with an unusually high blood pressure (171/108), but afebrile (36.9°C), with an eGFR or 21 ml/min/1.73 m², a protein/creatinine ratio (PCR) of 503 mg/mmol and normal serum albumin. Physical examination was unremarkable except for some pain from thoracic herpes zoster 2 months previously. Her husband had tested positive for Covid19 on the same morning. She developed fever (38.9 °C) and cough on the same evening and tested positive for Covid19 the next day. MMF was paused and low dose steroids were instituted. In the following weeks, full nephrotic syndrome developed (edema, PCR of 1350 mg/mmol, serum albumin ↓ to 28 g/l). eGFR decreased to 8-10 ml/min/1.73 m².

Renal biopsy on day 42 showed several instances of focal segmental sclerosis with collapsing morphology (Figure 1, consistent with "collapsing glomerulopathy"). In addition there were signs of capsular proliferation and electron dense deposits in the GBM, consistent with glomerulonephritis. Sequencing of Exon 6 of the APOL1 gene was negative for G1 and G2 risk alleles in the patient and her kidney donor.

Nephrotic syndrome never remitted, and renal function did not recover. Peritoneal dialysis was initiated 9 months after the Covid 19 infection.



Conclusions: This case documents an unusal Covid19-associated glomerulonephritis with "collapsing features" which led to the loss of a 31 years functioning living donor kidney.

POSTER PRESENTATIONS – CLINICAL NEPHROLOGY / HYPERTENSION / MINERAL / ELECTROLYTES

P 20

A small deletion with a large impact

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Background: A 49-year-old female was referred to us because of hyperphosphatemia. The patient reported progressive hardening of the skin of the lower extremities. She also mentioned repeated dental root fractures. Family history was unremarkable.

Methods: Physical examination revealed indurations of the skin of the lower extremities up to the middle of the calves. Xray showed diffuse cutaneous calcifications in the lower legs. Laboratory workup displayed an elevated serum phosphate ranging from of 1.77-2.15 mmol/l (normal value 0.87-1.45 mmol/l). Renal function was mildly impaired (eGFR 60 ml/min/1.73 m^2) without pathological albuminuria. PTH, 25-OH and 1,25-OH vitamin D were normal. FGF-23 (1.24 pg/ml) ranged just above the lower limit of detection.

Results: Genetic analysis revealed a homozygous 5800 bp deletion 2q24.3 encompassing exons 3, 4 and partially 5 of the GALNT3 gene. Deletions in this region or mutations in the GALNT3 gene are known to cause hyperphosphatemic familial tumoral calcinosis (HTC). Deletions of this small size affecting the GALNT3 gene have not been reported in the literature.

Conclusions: HTC is a rare cause of hyperphosphatemia, which should be sought when the more frequent causes have been ruled out. Therapeutic options are dietary phosphate restriction, phosphate binders and acetazolamide which increases urinary phosphate excretion. Lowering phosphate can lead to resolution of deposits.

P 21

Pooled efficacy and cardiovascular safety results of roxadustat compared with placebo/darbepoetin alfa for treatment of anaemia in patients with non–dialysis-dependent (NDD) chronic kidney disease (CKD)

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Background: Further evaluation of efficacy and cardiovascular safety for roxadustat in non–dialysis-dependent (NDD) chronic kidney disease (CKD) is needed.

Methods: Results from three phase 3, double-blind studies in stage 3-5 NDD-CKD (roxadustat vs placebo; ALPS, ANDES, OLYMPUS) were pooled and compared with results of an open-label study (roxadustat vs darbepoetin alfa [DA]; DOLOMITES). The primary efficacy endpoint was haemoglobin response. The secondary efficacy endpoint was haemoglobin change from baseline (CFB) to Weeks 28-36 using least squares mean difference (LSMD) without rescue therapy. Major adverse cardiovascular event (MACE; comprising death, myocardial infarction, and stroke) and MACE+ (MACE plus hospitalisation with heart failure or unstable angina) were adjudicated and compared between roxadustat vs placebo or DA using a Cox proportional hazards model.

Results: Overall, 4886 patients were included (placebo-controlled: 2386 roxadustat, 1884 placebo; DA-controlled: 323 roxadustat, 293 DA). Roxadustat was superior to placebo for haemoglobin response without rescue therapy (80.2% vs 8.7%; difference of proportion [DOP], 71.50%; 95% confidence interval [CI], 69.40-73.51) and noninferior to DA (89.5% vs 78.0%; DOP, 11.51%; 95% CI, 5.66-17.36). Mean haemoglobin CFB (Weeks 28-36) achieved superiority in pooled analysis vs placebo (LS mean, 1.91 vs 0.14; LSMD, 1.77; 95% CI, 1.69-1.84) and noninferiority vs DA (LS mean, 1.85 vs 1.84; LSMD, 0.02; 95% CI, -0.13 to 0.16). Risk for MACE or MACE+ was similar for roxadustat vs placebo (MACE, 480 [20.1%] vs 350 [18.6%]; hazard ratio (HR), 1.10; 95% CI, 0.96-1.27; MACE+, 578 [24.2%] vs 432 [22.9%]; HR, 1.07; 95% CI, 0.94-1.21) and vs DA (MACE, 38 [11.8%] vs 41 [14.0%]; HR, 0.81; 95% CI, 0.52-1.25; MACE+, 54 [16.7%] vs 43 [18.1%]; HR, 0.90; 95% CI, 0.61-1.32).

Conclusions: Roxadustat corrected haemoglobin more effectively than placebo and comparably to DA in patients with stage 3-5 NDD-CKD. Cardiovascular safety was comparable between roxadustat and DA and placebo.

P 22

Validation of [TIMP-2]·[IGFBP7] to Predict Acute Kidney Injury in Emergency Department Patients – a diagnostic accuracy study*

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Background: Acute kidney injury (AKI) is common and associated with increased morbidity and mortality. Unfortunately, its diagnosis is slow and often retrospective, delaying the initiation of nephroprotective measures. The US Food and Drug Administration recently approved the urinary biomarker [TIMP2]x[IGFBP7] (NephroCheck®) for the early detection of advanced AKI (advAKI) in intensive care unit patients. The ability of [TIMP2]x[IGFBP7] to detect AKI in the emergency department (ED) setting is unknown.

Methods: The *Basics in Acute Shortness of Breath Evaluation Study* prospectively enrolled patients presenting the ED with acute dyspnea. AKI was defined according to the criteria of the KDIGO clinical practice guideline. Urinary [TIMP2]x[IGFBP7] concentrations were measured using a clinical immunoassay (NephroCheck®). The diagnostic performance of [TIMP-2]x[IGFBP7] at prespecified and validated cutoff levels to predict stage 2/3 AKI (i.e. advAKI) within 24 hours of a sample collection in ED patients was the primary endpoint.

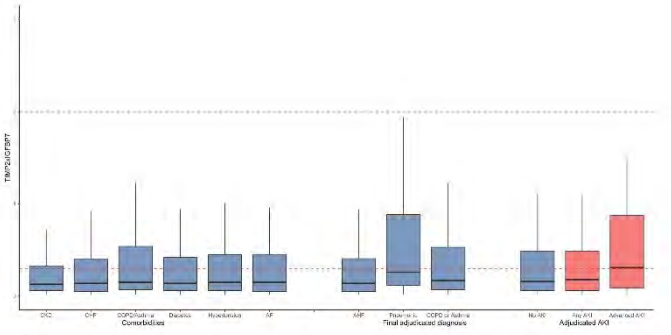

Figure 1 Box plots showing the discrimination between non-AKI conditions and AKI of different severities according to [TIMP2]•[IGFBP7] concentrations. The red line represents the prespecified and validated cutoff levels of [TIMP2]•[IGFBP7] at 0.3 and 2.0 (ng/mL)²/1000.

Results: Of 915 patients, 64(7%) patients developed advAKI. Patients with a diagnosis of advAKI had significantly higher [TIMP2]x[IGFBP7] concentrations of 0.31(ng/mL)2/1000 [0.08-0.89] compared with those without advAKI (0.16(ng/mL)2/1000 [0.06-0.49], p = 0.02). The AUC-ROC for [TIMP2]x[IGFBP7] to detect advAKI was 0.58 (95%CI 0.51-0.65). The sensitivity and specificity at the validated cutoff-levels 0.3 and 2.0(ng/mL)2/1000 were 50% (95%CI 37-63) and 65% (95%CI 61-68) as well as 11% (95%CI 3-19) and 94% (95%CI 92-96), respectively. We found lower [TIMP2]x[IGFBP7] concentrations in various comorbidities. In multivariable linear regression model, advAKI was the strongest predictor of [TIMP2]x[IGFBP7] levels (regression coefficient β = 0.61, p <0.01). However, a significant interaction (p = 0.03) was observed

between chronic kidney disease (CKD) and advAKI for the prediction of [TIMP2]x[IGFBP7].

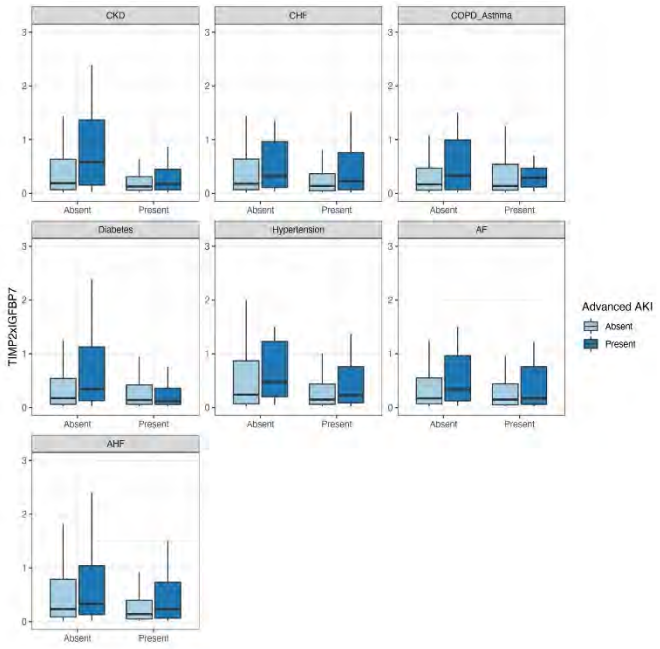

Figure 2 [TIMP2]•[IGFBP7] (A) levels across different comorbid states in patients with and without advanced AKI. AKI denotes acute kidney injury; CKD denotes chronic kidney disease; CHF denotes chronic heart failure; COPD denotes chronic obstructive pulmonary disease; AF denotes atrial fibrillation.

Variable	Overall n=915	No advanced AKI n=851	Advanced AKI n=64	p-Value
Demographics				
Age (median [IQR])	76 [65, 83]	76 [65, 83]	75 [67, 82]	0.711
Male (%)	539 (59)	499 (59)	40 (62)	0.599
Medical history				
Hypertension (%)	667 (73)	614 (73)	53 (83)	0.080
Diabetes (%)	239 (26)	215 (25)	24 (38)	0.038
CKD (%)	322 (35)	284 (33)	38 (59)	<0.001
Atrial fibrillation (%)	318 (35)	289 (34)	29 (45)	0.077
Chronic heart failure (%)	351 (39)	318 (38)	33 (52)	0.033
COPD/Asthma (%)	289 (32)	272 (32)	17 (27)	0.405
Preadmission medication				
Angiotensin-converting enzyme inhibitor (%)	294 (33)	265 (32)	29 (48)	0.010
Angiotensin II receptor blocker (%)	204 (23)	188 (22)	16 (26)	0.527
Aldosterone antagonist (%)	92 (10)	75 (9)	17 (28)	<0.001
Diuretic (%)	511 (57)	462 (55)	49 (80)	<0.001
Physical exam at ED				
sBP (mmHg)	136 [119, 153]	137 [120, 154]	117 [105, 144]	<0.001
HR (beats/min)	91 [75, 107]	91 [76, 107]	87 [68, 100]	0.037
Respiratory Rate (breaths/min)	22 [18, 28]	22 [18, 28]	20 [16, 26]	0.202
Temperature (°C)	37.1 [36.6, 37.6]	37.1 [36.6, 37.6]	36.9 [36.5, 37.4]	0.025
Oxygen saturation (%)	95 [92, 98]	95 [92, 98]	96 [91, 97]	0.928
Laboratory parameters at admission				
Hemoglobin (g/l)	130 [115, 143]	130 [116, 144]	117 [101, 131]	<0.001
White blood cell count (10^9/l)	8.9 [7.0, 11.7]	8.9 [7.0, 11.7]	8.9 [6.7, 12.8]	0.692
C-reactive protein(mg/l)	13.6 [4.4, 43.4]	12.9 [4.2, 41.3]	29.7 [6.7, 106.6]	0.001
NT-proBNP (ng/ml)	2250 [440, 6631]	2067 [403, 6311]	6128 [2012, 15212]	<0.001
Baseline steady state creatinine (median [IQR])	80 [63, 104]	79 [63, 101]	90 [60, 134]	0.074
Adjudicated diagnosis				
Acute heart failure (%)	558 (61)	519 (61)	39 (61)	1.000
COPD/Asthma (%)	145 (16)	139 (16)	6 (9)	0.159
Pneumonia (%)	147 (16)	133 (16)	14 (22)	0.215
Pulmonary embolism (%)	55 (6)	52 (6)	3 (5)	1.000

Table 1 Baseline characteristics of patients presenting with advanced AKI. AKI denotes acute kidney i CKD denotes chronic kidney disease; COPD denotes chronic obstructive pulmonary disease; sBP der systolic blood pressure; HR denotes heart rate; NT-BNP denotes N-terminal pro-brain natriuretic pepti Values are numbers (percentages) or median [Interquartile range]

Conclusions: The diagnostic accuracy of [TIMP2]x[IGFBP7] to predict advAKI in ED patients is moderate. Lower [TIMP2]x[IGFBP7] concentrations caused by various comorbidities appear to lower the diagnostic accuracy for AKI. Of note, [TIMP2]x[IGFBP7] concentrations in ED-AKI patients, and AKI frequency appeared to be lower than described in ICU patients.

*YSN paper

P 23

Health-related quality of life in Fabry disease: a cross-sectional international multicenter study*

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Background: Fabry disease (FD) is a rare X-linked lysosomal storage disorder caused by α-galactosidase A (α-Gal A) deficiency. The progressive accumulation of globotriaosylceramide results in life-threatening complications, including renal, cardiac, and cerebrovascular diseases. In order to improve health care of FD-patients, knowledge of its predictors is important. The aim of our study was to evaluate health-related quality of life (HrQol) in FD and to identify its independent determinants by exploring a wide range of demographic, social and clinical parameters.

Methods: In this cross-sectional multicenter study, 124 adult patients with FD were recruited at three specialized European centers in Germany and Switzerland. Demographics, social status and clinical parameters as well as data on HrQol (EQ5D, EQVAS) and depression were collected by means of self-reporting questionnaires. HrQol and its predictors were evaluated by univariate and multivariate regression analyses.

Table. Independent determinants of HrQol in multiple regression analysis

	EQ5D Index			EQ VAS		
	B	95% CI	p-value	B	95% CI	p-value
Constant	1.17	0.93; 1.22	0.0	109.31	93.11; 121.34	0.0
Classic phenotype	-0.14	-0.22; -0.04	<0.01	-12.51	-21.12; -5.92	<0.01
Kidney disease	-0.06	-0.22; -0.03	0.03	-6.79	-14.12; -2.77	0.04
Heart involvement	-0.17	-0.29; -0.05	<0.01	-20.03	-28.50; -11.08	<0.01
Stroke/TIA	-0.07	-0.17; -0.04	0.03	-4.91	-7.01; -1.05	0.04
Burning limb pain	-0.14	-0.27; -0.08	0.04	-7.95	-17.23; -2.89	0.03
Depression (BDI)	-0.04	-0.18; -0.02	<0.01	-0.89	-2.01; -0.53	<0.01
Agalsidase α	0.04	0.01; 0.12	0.04	3.92	0.51; 7.27	0.04
Agalsidase β	0.11	0.04; 0.29	0.02	15.88	5.69; 28.03	0.01
Adjusted R^2*	0.531			0.458		

* Total adjusted R^2 for each model

Abbreviations: HrQol, health-related quality of life; B, regression coefficient; BDI, Beck Depression Inventory, TIA, transient ischemic attack

Results: Study population consisted of 72 female and 52 male FD patients (median age 48yrs) of whom 87.9% (N = 109) were on enzyme replacement therapy (ERT) (68.8% [N = 75] were on agalsidase α and 31.2% [N = 34] on agalsidase β). Univariate analysis revealed various factors reducing HrQol, such as age >40 years, classic phenotype, organ involvement (kidney and heart disease, stroke/*transient ischemic attack*, gastrointestinal disturbances), depression, and burning limb pain. However, only the following factors were identified as independent predictors of decreased HrQol: classic phenotype, kidney and heart disease, stroke/TIA, depression, and burning limb pain (Table). ERT was an independent determinant of increased HrQol.

Conclusions: Modifiable factors, such as burning limb pain and depression identified as independent predictors of HrQoldeterioration should be addressed in programs aiming to improve HrQol in FD. A multidisciplinary approach is essential in FD-patients since diverse organ involvement prominently compromises HrQol in affected patients. Our findings that the classic phenotype is a strong predictor of HrQol worsening.

*YSN paper

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Renal biopsy findings in patients with isomorphic microscopic hematuria and low-grade proteinuria – Should we extend the indications for renal biopsy?*

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Background: The diagnostic value for renal biopsy in patients with isomorphic hematuria (IMH) and low-grade proteinuria (LGP) is often questioned. We investigated the outcomes of renal biopsies with IMH and LGP.

Methods: We included 213 renal biopsies analyzed between 2010 and 2021 at the Institute of Pathology at the University Hospital Basel, which fulfilled the following criteria: (1) absence of kidney failure, (2) absence of reported dysmorphic microscopic hematuria, and (3) proteinuria ≤ 1 g per day.

Results: In renal biopsies of patients with IMH and LGP, 21% were diagnosed with proliferative and necrotizing glomerulonephritis (Figure 1), with ANCA-associated vasculitis representing half of the clinical diagnoses (Figure 2).

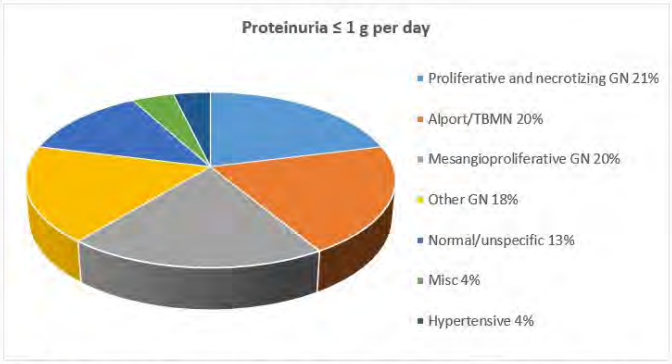

Figure 1: Histological diagnoses in renal biopsies of patients with isomorphic hematuria and proteinuria ≤ 1 g per day. Total number of biopsies: 213. GN: glomerulonephritis, TBMN: thin basement membrane nephropathy.

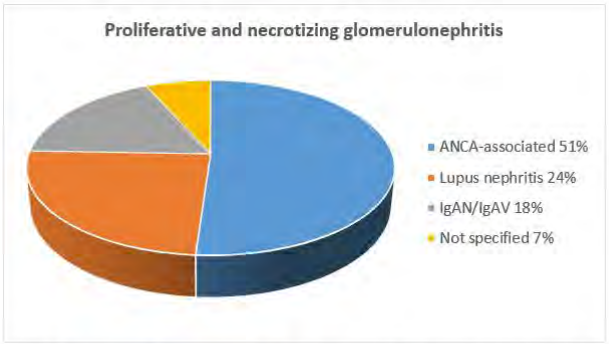

Figure 2: Diagnosis of renal biopsies with proliferative and necrotizing glomerulonephritis. Total number of biopsies: 45. IgAN: IgA nephropathy, IgAV IgA-associated vasculitis.

20% of the biopsies corresponded to Alport syndrome or thin basement membrane nephropathy (TBMN), another 20% to mesangioproliferative glomerulonephritis including IgA nephropathy, and 13% had normal or unspecific histology. Hypertensive nephropathy was only found in 4% of the biopsies. 114 of the patients had a proteinuria ≤ 0.5 g per day. In this population, Alport syndrome and TBMN were the most common histological diagnosis (29%). Proliferative and necrotizing glomerulonephritis was found in 23%, 50% thereof corresponding to ANCA-associated vasculitis (Figure 3).

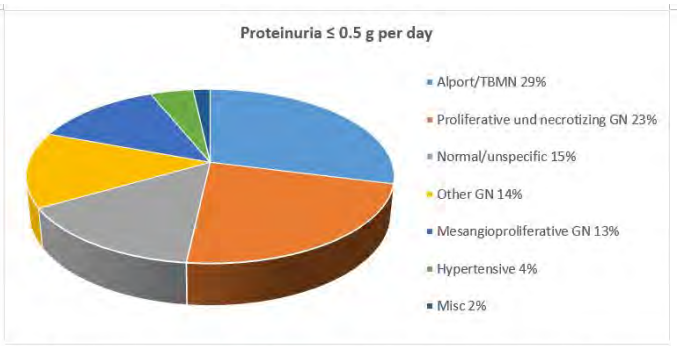

Figure 3: Histological diagnoses in renal biopsies of patients with isomorphic hematuria and proteinuria ≤ 0.5 g per day. Total number of biopsies: 114. GN: glomerulonephritis, TBMN: thin basement membrane nephropathy.

Conclusions: Surprisingly, proliferative and necrotizing glomerulonephritis with potential therapeutic consequences was a common finding in renal biopsy of patients with IMH and LGP. Clinical pretesting might have led to a selection bias in our population. Nevertheless, a more generous indication for kidney biopsy should be considered.

*YSN paper

P 25

Accuracy of flash glucose measurement in hemodialysis patients with and without diabetes mellitus*

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Background: Management of diabetes mellitus is difficult in hemodialysis (HD) patients due to altered insulin metabolism, interference of dialysis schedules with food intake, dietary restrictions and unreliability of HbA1c. Flash glucose monitoring (FGM) may provide an attractive option for glucose monitoring in these patients and offers a means to monitor glucose levels in non-diabetic HD patients with suspected hypoglycemia. Therefore, we aimed to validate FGM in diabetic and non-diabetic HD patients.

Methods: We measured interstitial blood glucose (BG) using Freestyle Libre® FGM devices in 15 HD patients (8 diabetic, 7 non-diabetic) during 14 days. Simultaneously, Patients performed self-monitoring of BG (SMBG) four times daily, using capillary glucose monitoring devices. Timely paired measurements were compared using mean difference to quantitate systematic error, and mean absolute difference (MAD) and mean absolute relative difference (MARD) to quantitate random error.

Results: In a total of 720 paired measurements, mean FGM values were significantly lower than SMBG (6.12 ± 2.52 vs. 7.15 ± 2.39 mmol/l, p = 1.3 E-86). The systematic error was significantly larger in non-diabetic vs. diabetic patients (-1.17 vs. -0.82 mmol/l), patients with vs. without fluid removal during HD (-1.07 vs. -0.82 mmol/l), with high (≥7mmol/l) vs. normal (<7mmol/l) BG (-1.16 vs. -0.84 mmol/l) and during dialysis vs. non-dialysis days (-1.09 vs. -0.90 mmol/l). Overall, MARD was 17.4% and MAD 1.20 mmol/l. Adding a correction term of +1.0 mmol/l for the systematic error to all FGM measurements improved MARD and MAD to 11.9% and 0.82 mmol/l, respectively.

Conclusions: FGM systematically underestimates BG levels in HD patients. The systematic error depended on diabetes status, BG level, dialysis schedule and fluid removal during dialysis, but these influences were relatively small compared to the overall systematic error of the entire cohort. After a correction of +1 mmol/l, FGM measurements quite accurately reflect BG levels.

*YSN paper

P 26

Variability and Reproducibility of urinary electrolytes and free water excretion on repeated 24h urinary collections in Young Healthy Human*

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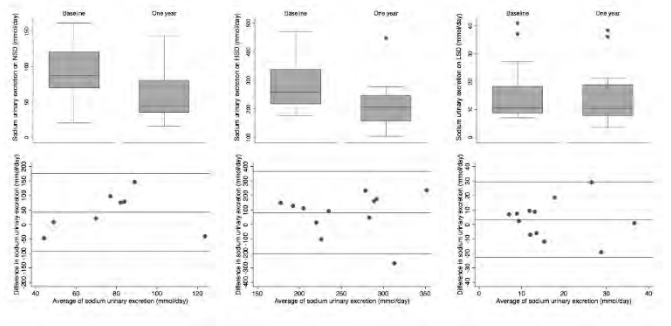
Background: There is salt controversy in health hazard and reliability of intake estimation. Recent data showed long-term instability in salt balance in astronauts simulating flight to Mars. However, there is a need to assess properly sodium intake in a free environment. The aim of this study was to establish variability and reproducibility of urine sodium, chloride, volume, urea, osmolarity and potassium excretion.

Methods: Sixteen volunteers were randomly allocated to normal (6gr NaCl/24h), high (15gr NaCl/24h) and low (3gr NaCl/24h) sodium diet for 7 days with 24-hour urine collection.

Results: Our results showed that subjects were on sodium balance from day 4 to 7 with no more diet effect on all parameters. Once in balance, it seems that sodium diet significantly impacts urine sodium, chloride, urea, osmolarity, potassium excretion ($p < 0.001$) and volume ($p = 0.010$). The same protocol was repeated one year after on 12 subjects.

At 1 year interval, urine sodium and parameters excretion were reproducible at day 6 independently of the sodium intake.



	Effect of sodium diet from day 1 to day 6	Effect modification over time of sodium diet from day 1 to day 6[a]	Effect of sodium diet from day 4 to day 6	Effect modification over time of sodium diet from day 4 to day 6[a]
Sodium	**Yes (p<0.001)**	**Yes (p<0.001)**	**Yes (p<0.001)**	No (p=0.163)
Chloride	No (p=0.085)	**Yes (p<0.001)**	**Yes (p<0.001)**	No (p=0.380)
Volume	**Yes (p<0.001)**	**Yes (p=0.024)**	**Yes (p=0.010)**	No (p=0.071)
Urée	No (p=0.750)	Non (p=0.113)	**Yes (p<0.001)**	No (p=0.401)
Osmolarity	**Yes (p=0.005)**	**Yes (p<0.001)**	**Yes (p<0.001)**	No (p=0.057)
Potassium	No (p=0.055)	Non (p=0.333)	**Yes (p<0.001)**	No (p=0.225)

Conclusions: Our data suggest that 24hour urine collection is reliable and reproducible if diet is unchanged for at least 3 days.

*YSN paper

P 27

A phase 2 study to evaluate the efficacy and safety of pegcetacoplan in the treatment of patients with posttransplant recurrence of C3G or IC-MPGN

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Background: Complement 3 glomerulopathy (C3G) and immune complex membranoproliferative glomerulonephritis (ICMPGN) are rare but devastating kidney diseases characterized by excessive production and glomerular deposition of C3 breakdown products. C3G/IC-MPGN have no approved therapies, and 50% of patients develop recurrence of disease and graft loss after transplant. Pegcetacoplan, an investigational C3 and C3b inhibitor, has the potential to address the underlying pathophysiology of C3G and IC-MPGN. This is a phase 2, open-label, randomized, controlled study of the efficacy and safety of pegcetacoplan in renal transplant recipients with recurrence of C3G or IC-MPGN (ClinicalTrials.gov identifier: NCT04572854).

Methods: Twelve patients aged ≥18 years with posttransplant recurrence of C3G or IC-MPGN, proteinuria ≥1 g/d, and estimated glomerular filtration rate (eGFR) ≥30 mL/min/1.73 m^2 will be recruited. The diagnosis of C3G or ICMPGN will be confirmed by a renal allograft biopsy. Exclusion criteria include secondary C3G or IC-MPGN (eg, due to malignancy, infection, or graft rejection). Patients will be randomized 3:1 to receive either subcutaneous injection of pegcetacoplan (1080 mg/20 mL, twice weekly) or no drug intervention for 12 weeks (in addition to standard care for both groups). Thereafter, all patients will receive pegcetacoplan until week 52. All patients will undergo renal allograft biopsy during screening and at weeks 12 and 52. The primary endpoint is the proportion of patients with reduction in C3c staining on renal biopsy after 12 weeks of treatment. Secondary endpoints include reduction in C3c staining after 52 weeks of treatment, reduction in proteinuria, and stabilization or improvement in eGFR. Safety outcomes, including treatment-related adverse events and discontinuations, will be monitored throughout the study.

Results: This study will assess the potential for pegcetacoplan to address the underlying disease pathophysiology of C3G/IC-MPGN in patients with posttransplant disease recurrence.

Conclusions: This is a study design abstract.

P 28

Endocrine Disorders in Patients with Fabry disease: Insights from a reference centre prospective study*

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Background: Fabry Disease (FD) is a rare X-linked storage disease characterized by a- galactosidase A deficiency and diffuse organ accumulation of glycosphingolipids. Enzyme replacement and chaperone therapies are only partially effective. It remains unclear if FD-related endocrine disorders contribute to the observed morbidity. *The aim of the study was to* investigate the function of the endocrine system in patients with FD.

Methods: We conducted an observational prospective study from 2017 to 2020 including 77 patients with genetically confirmed FD (27 men, 20/27 Classic, 7/26 Late Onset phenotype, 50 women, 41/50 and 9/50 respectively), who are systematically followed by our reference center.

Results: During winter and summer season, many patients had a VitD shortage despite supplementation (Table 1), (Figure 1). Three new cases (3.9%) of subclinical, two (2.6%) of manifest and six (7.8%) of known hypothyroidism were identified. Of note, men had significantly higher renin levels than women [61.4 (26.1- 219.6) vs.25.4 (10.9-48.0) mU/L, $p = 0.003$]. There were no major abnormalities in adrenal, growth and sex-hormone axes. Patients of Classic phenotype had significantly higher High-Density Lipoprotein Cholesterol (HDL-C) levels ($p = 0.002$) and in men those levels were positively correlated with globotriaosylsphingosin (Lyso-Gb3) values (Table 2). 10/77 (13%) of the patients were underweight.

Conclusions: VitD supplementation should be considered for all patients with FD. Thyroid screening should be routinely performed. Malnutrition should be prevented or treated, particularly in Classic phenotype patients. Overall, our data suggest that FD specialists should actively seek and diagnose endocrine disorders in their patients.

*YSN paper

Table 1: Vitamin D and Phosphorus/ Calcium values including substitution information. Continuous variables are presented as median and interquartile range, if more than two values were available; Kruksal-Wallis test was performed for the comparison of the groups; p<0.05 was considered statistically significant; VitD, Cholecalciferol; 25(OH)VitD, 25-hydroxy-VitaminD.

		Men (n=27)		Women (n=50)		Normal values	P
	Phenotype	Classic (n=20)	Late Onset (n=7)	Classic (n=41)	Late Onset (n=9)		
Mineral Metabolism Axis	25 (OH)VitD (µg/L)	17 [14.15-26.15]	28 [21.65-31.8]	23.2 [17.9-30.8]	18.6 [16.8-27]	>20	0.062
	Patients who require VitD treatment n, %	16 (80)	3 (42.9)	30 (73.2)	6 (66.7)		
	Patients who do not require VitD treatment n, %	4 (20)	4 (57.1)	11 (26.8)	3 (33.3)		
	VitD supplementation dosage (IU/d)	1000 [1000-1200]	1000 [854.14-1250]	1000 [1000-1000]	-		0.479
	Phosphorus (mmol/L)	0.91 [0.76-0.97]	0.93 [0.88-0.97]	1.02 [0.91-1.1]	0.86 [0.79-0.96]	0.87- 1.45	**0.003**
	Hypophosphatemia n, %	6(30)	1(14.3)	1(2.4)	3(33.3)	<0.80 mmol/L	
	Calcium total (mmol/L)	2.3 [2.27-2.33]	2.4 [2.36-2.43]	2.3 [2.23-2.36]	2.29 [2.24-2.34]	2.19- 2.54	0.054
	Calcium Substitution n, %	3(15)	1(14.3)	3(7.3)	0(0)		

Patients who require VitD treatment: undersupplementation or without supplementation but with low VitD levels.

Patients who do not require VitD supplementation: with normal VitD levels without supplementation.

Figure 1. 25-hydroxy-Vitamin D levels categorized as deficient, insufficient or sufficient in patients with FD under supplementation treatment or not, divided according to season.

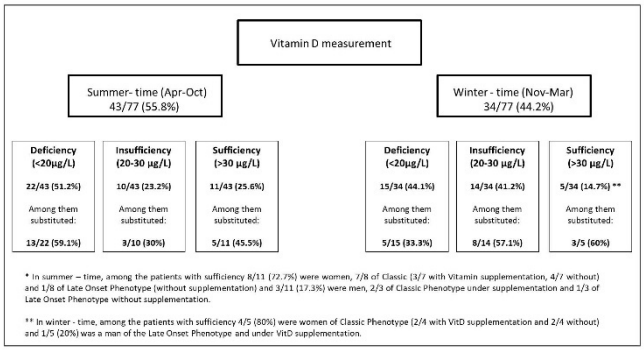

Table 2: Body Mass Index and Lipid Parameters of patients with FD. Continuous variables are presented as median and interquartile range, if more than two values were available; Kruksal-Wallis test was performed for the comparison of the groups; p<0.05 was considered statistically significant; BMI, Body Mass Index; TC, Total Cholesterol; HDL-C, High-Density Lipoprotein Cholesterol; non-HDL-C, non-High-Density Lipoprotein Cholesterol; LDL-C, Low-Density Lipoprotein Cholesterol, TG, Triglycerides; n: number.

		Men (n=27)		Women (n=50)		Normal values	P
	Phenotype	Classic (n=20)	Late Onset (n=7)	Classic (n=41)	Late Onset (n=9)		
BMI status	BMI (kg/m²)	23.2 [20.6-25.1]	24.4 [21.9-26.6]	23.6 [20.8-26.5]	23.5 [22.1-27.6]	20-25	0.713
	<20 n, (%)	4 (20)	0 (0)	4 (9.75)	2 (22.2)		
	20-25 n, (%)	11 (55)	4 (57.1)	22 (53.65)	4 (44.4)		
	25-30 n, (%)	5 (25)	3 (42.9)	10 (24.4)	1 (11.1)		
	>30 n, (%)	0 (0)	0 (0)	5 (12.2)	2 (22.2)		
Lipid Status	TC (mmol/L)	4.7 [3.75-5.05]	3.8 [3.65-4.35]	4.5 [4.1-5.1]	4 [3.8-4.4]	<5.0	0.106
	High TC n, %	4 (20)	1 (14.3)	5 (12.2)	0 (0)		
	HDL-C (mmol/L)	1.5 [1.28-2.01]	1.07 [0.92-1.17]	1.6 [1.41-1.8]	1.31 [1.09-1.6]	>1.0	**0.002**
	Non-HDL-C (mmol/L)	2.8 [2.15-3.5]	2.7 [2.5-3.2]	2.8 [2.5-3.4]	2.8 [2.4-3.1]	<3.9	0.829
	LDL-C (mmol/L)	2.5 [1.7-2.95]	2.1 [1.9-2.6]	2.3 [1.9-3]	2.1 [1.8-2.6]	<3.0	0.734
	High LDL-C n, %	4 (20)	0 (0)	7 (17.1)	1 (11.1)		
	TG (mmol/L)	1.21 [0.7-1.44]	1.48 [1.28-1.73]	1.19 [0.75-1.45]	0.79 [0.72-0.85]	<2.0	0.086
	High TG n, %	2 (10)	1 (14.3)	5 (12.2)	1 (11.1)		

P 29

Difference between office blood pressure and day ambulatory blood pressure at a given level: can it be predicted?*

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Background: Blood pressure (BP) measurement is one most common medical act performed during outpatient clinics.For a given patient, BP can vary dramatically depending if it is taken at the office (OBP),or during a 24 hour ambulatory blood pressure monitoring (ABPM).The vast majority of studies that have compared OBP and ABPM used the Bland and Altman (BAM) method. However, BAM is possibly introducing a statistical bias as it supposes that the bias is constant across BPlevels, which is not the case.The goal of our study was to assess the difference between OBP and ABPM at every level of systolic BP (SBP)by comparing BP measurements using the Bias plot method.

Methods: This was a retrospective study including participants, who underwent an ABPM between 1/01/2019 and 31/12/2020. All measurements were done using the validated DIASYS3 ABPM device. Daytime BP taken between 7 AM to 10 PM were used for analysis.The two first measures taken in the presence of the nurse defined OBP. The subsequent ambulatory values defined ABPM values.

Results: 647 ABPM were analyzed (Table 1). The difference between systolic OBP and systolic ABPM ranged from +10 to -10 mmHg for BP value between 100 to 200 mmHg(differential bias: 33.01;proportional bias: 0.78 mmHg) (Figure 1).

Variable	N=647
Age (years)	53 ,4 +-14 (45-66)
% Female	47%
Mean Systolic ABPM (mmHg)	150 +- 18 (138-151)
Mean systolic OBP (mmHg)	149 +- 20 (136-161)
Hypertensive patient (%)	83%
Mean BMI	27 +- 4.2 (23-30)

Table 1) demographic data of patients

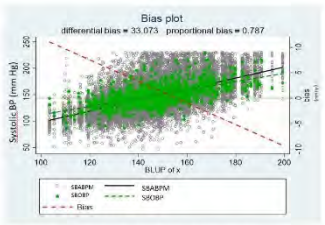

Figure 1) Bias plot between systolic baseline office blood(SBOBP) pressure and systolic 24h ambulatory blood pressure (SBABPM).
For Patients with a mean SBABPM Below 150 mm Hg the difference between SBOP and SBABPM was positive (withe coat effect) and for patients with a mean SABPM SBP higher than 150 mm Hg, the difference was negative (masked effect).

The difference between systolic OBP and systolic ABPM for normotensive patients ranged from +12 mm Hg to +4 mm Hg for values between 105 to 135 mm Hg (differential bias:38.8; proportional bias:0.74) .(Figure 2a). In hypertensive patients, the difference ranged from+6 to-9mmHg for value between 135 to200 mmHg (differential bias: 31.3; proportional bias:0.8).(Figure 2b)

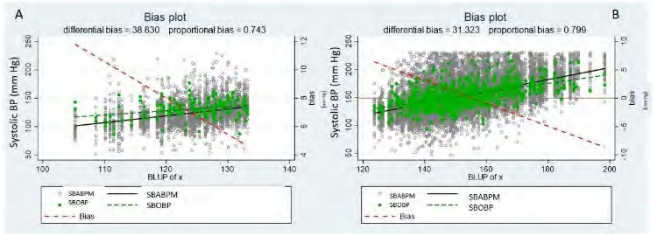

Figure 2) Bias plot between systolic baseline office blood(SBOBP) pressure and systolic 24h ambulatory blood pressure (SBABPM) A for normotensive patients, B for hypertensive patients

Conclusions: Our study shows that difference OBP and ABPM is not uniform across BP values and depends on mean of ABPM BP.As ABPM value are increases, the difference gets smaller and can be calculated using the bias plot. This could serve in anticipating ABPM results from OBP values.

*YSN paper

P 30

Variability of 24-hour urinary sodium and volume excretion in young healthy male subjects based on consecutive urine collections: impact on categorization of salt intake*

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Background: To assess individuals' sodium intake, single 24h urine collections as well as formulas based on urinary sodium concentration are criticized for their possible bias leading to misclassifications of sodium intake. Today, three non-consecutive 24h urine collections are recommended to estimate sodium intake at the individual level.

Methods: We assessed the variability of urinary sodium and volume excretion measured during 3 consecutive 24h urine collections on three levels of sodium intake. Using a cross-over design, 16 volunteers were randomly allocated to a normal (6 g NaCl/24h), high (15 g NaCl/24h) and low (3 g NaCl/24h) sodium diet. High and normal sodium diets were obtained adding sodium tablets to the low sodium diet.

Results: The mean (± SD) urinary Na+ excretion of the last 3 days was respectively 253 ± 46, 75 ± 27 and 18 ± 6.4 mmoles/24h on the high, normal and low sodium diets. There was no difference in 24h urinary volume between the 3 diets. On low sodium diet, all urine collections were <50 mmoles/day confirming the low sodium classification. On high salt, 24h sodium excretion was >170 mmoles in all but 4 collections and no subject could be misclassified as low or normal salt eaters. On normal salt diet, 25% of subjects could have been misclassified as low salt eaters based on 3 collections and 41.6% based on two collections.

Conclusions: Thus, on high and low sodium, a single urine collection may be sufficient to categorize an individual's current sodium intake correctly. On a normal salt intake, the risk of misclassification is higher and repeated nonconsecutive urine collections may be preferable.

*YSN paper

P 31

Introducing entrustable professional activities in swiss nephrology training

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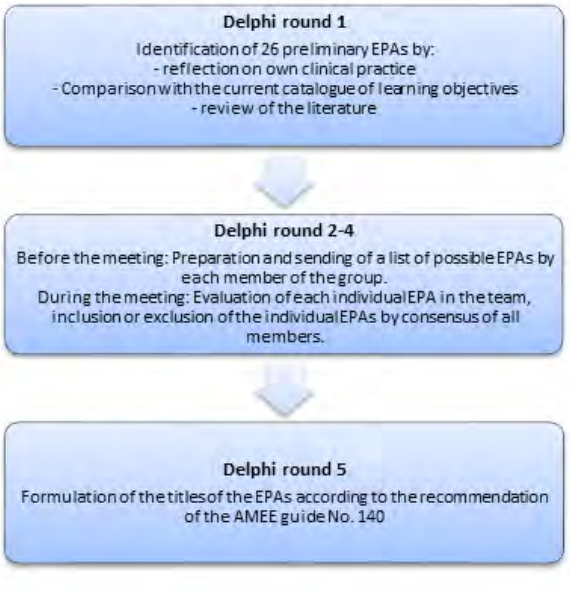
Background: Competency-based medical education has found its way into pastgraduate education and is recommended by the SIWF. Nevertheless, testing competences like the CanMEDs-roles is difficult, which has led to the appearance of entrustable professional activities (EPAs). An EPA is a unit of professional practice that constitute what clinicians do as daily work (1). The Delphi method is recommended to build EPAs, in order to achieve consensus and content validation. The aim of this study is to determine whether a final Delphi round involving the whole nephrology community is useful after a dedicated group has reached consensus on EPAs in nephrology.

Methods: A working group was formed that included five nephrologists from five different nephrology training centres in Switzerland (Aarau, Bern, Lausanne, Lucerne, Lugano). Two EPA experts from SIWF advised the group. A Delphi method was used to identify EPAs in nephrology and to reach consensus among the group members.

Results: From October 2020 to April 2021, in a total of 7 meetings and 5 Delphi rounds, 41 EPAs in nephrology were identified (table 1).

Each member of the working group prepared a list of possible EPAs and sent it to all members before each Delphi round. During the meeting, each EPA was either included or deleted by consensus from each member of the working group. For the last Delphi round, the 41 EPAs were integrated into a survey that will be sent to all nephrologists and nephrology trainees in Switzerland. In this survey, each individual EPA is rated on a 7-point Likert scale in terms of its importance in nephrology education and consistency in clinical practice (figure 1).

General Nephrology
1. Manage an outpatient referred for a kidney disease 1.1. Manage a patient with elevated creatinine? 1.2. Manage a patient with hematuria? 1.3. Manage a patient with proteinuria?
2. Assess and manage a patient with CKD 4/5 (including conservative care, facilitating patient' transition to an ESRD treatment modality)?
3. Perform renal replacement therapy counselling?
4. Assess and manage a patient with diabetic nephropathy?
5. Assess and manage a patient with glomerulonephritis? 5.1. Assess and manage a patient with membranous glomerulopathy? 5.2. Assess and manage a patient with minimal change disease/ FSGS? 5.3. Assess and manage a patient with lupus nephritis? 5.4. Assess and manage a patient with IgA nephropathy? 5.5. Assess and manage a patient with vasculitis?
6. Manage a patient receiving immune-modulating therapy
7. Assess and manage for a patient with genetic disease?
8. Assess and manage a patient with polycystic kidney disease?
9. Assess and treat a patient with difficult-to-control or suspected secondary hypertension?
10. Assess and provide a management plan for a patient with repeated nephrolithiasis?
11. Manage palliative care in ESRD patient?
12. Manage a patient with AKI and provide an initial management plan
13. Identify and manage a patient with rapid progressive glomerulonephritis?
14. Manage a CKD patient with acute pulmonary edema?
15. Manage a patient with a hypertensive emergency?
16. Manage a patient with an electrolyte disturbance? 16.1. Manage a patient with hyperkalemia? 16.2. Manage a patient with hypokalemia? 16.3. Manage a patient with hypernatremia? 16.4. Manage a patient with hyponatremia? 16.5. Assess and provide an initial investigation and management plan for patient with acidosis 16.6. Assess and provide an initial investigation and management plan for patient with alcalosis?
17. Manage a pregnant patient with proteinuria and/ or hypertension?
Hemodialysis
18. Manage a patient on chronic hemodialysis? 18.1. Manage cardiovascular problems during HD (including blood pressure problems, cramps and volemia)? 18.2. Manage a monthly chronic HD visit (including anemia, CKD MBD, evaluation HD adequacy, medication adherence, polymedication, manage social problems of a HD patient)?
19. Manage a patient with vascular access problems?
20. Manage palliative care in a HD patient?
21. Manage a patient with hypotension after hemodialysis?
22. Order prescriptions for a patient needing acute/urgent/first RRT (HD/CRRT)?
23. Manage a patient with acute dialysis access dysfunction (including fistula occlusion, infection)?
24. Manage a dialysis patient with pulmonary edema?
Peritoneal dialysis
25. Order initial prescriptions for peritoneal-dialysis?
26. Perform a regular PD follow up visit (including evaluate PD adequacy)?
27. Manage a PD patient with (suspected) exit-site or PD-catheter infection?



Conclusions: 7 Experts reached consensus on 41 EPAs in nephrology. Analysis of the score of each EPA will help determine if a last Delphi round involving a large stakeholder community is useful.

P 32

COVID-19 infection in Fabry disease : a systematic cohort study*

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Background: One of the lessons learnt during the Corona-virus-19 disease (COVID-19) pandemic is that vulnerable populations must be identified early to prevent increased mortality. Fabry disease (FD) is a rare X-linked lysosomal storage disorder leading to chronic kidney disease (CKD), cardiomyopathy, pneumopathy and premature strokes. We aimed to systematically analyse the COVID-19 disease course in our FD cohort.

Methods: During pandemic (02.2020-09.2021) we have regularly followed 100 genetically confirmed FD patients. In 61/100, titers of serum antibodies against SARS-CoV-2 were measured in samples drown between 03.20 and 03.21. SARSCoV-2 diagnosis was performed by PCR test. The symptoms and duration of COVID-19 were reported by the patients during the routine clinical visits or via telephone.

Results: 13/61 (21.3%) (classic FD: 4/14 men and 6/31 women, late-onset FD: 3/8 men and 0/8 women) FD patients were diagnosed with SARS-CoV-2 infection. 3/13 (23.1%) were asymptomatic (2/3 women of classic but uncomplicated FD, 1/3 man with late-onset FD, LVH, stroke and CKD-Stl) and 1/13 (7.7%) patient reported only arthralgias (man, late-onset FD with LVH). Fabry pain crisis reported 38.5% of the patients. 5/13 (38.5%) suffered from mild COVID-19 (2/5 men with classic uncomplicated FD, 3/5 women of classic phenotype). 2/13 (15.4%) patients experienced moderate COVID-19 manifestations (man of classic phenotype and women of classic phenotype, both without FD-related end-organ damage), with the female patient reporting long-COVID signs. 2/13 patients (15.4%), male one classic and one late-onset phenotype, both kidney transplant recipients with LVH, were hospitalized with severe COVID-19 but only oxygen therapy was needed.

Conclusions: During SARS-CoV-2 pandemic, no FD patient died or required ICU. Only two males, kidney recipients, needed hospitalisation. We suggest that FD is not, by itself, a risk factor for severe COVID-19 and the risk is driven, as in general population, from the end-target organ diseases, such as the progressed CKD or kidney transplantation.

YSN paper

P 33

Tubulointerstitial nephritis and uveitis syndrome: a systematic review*

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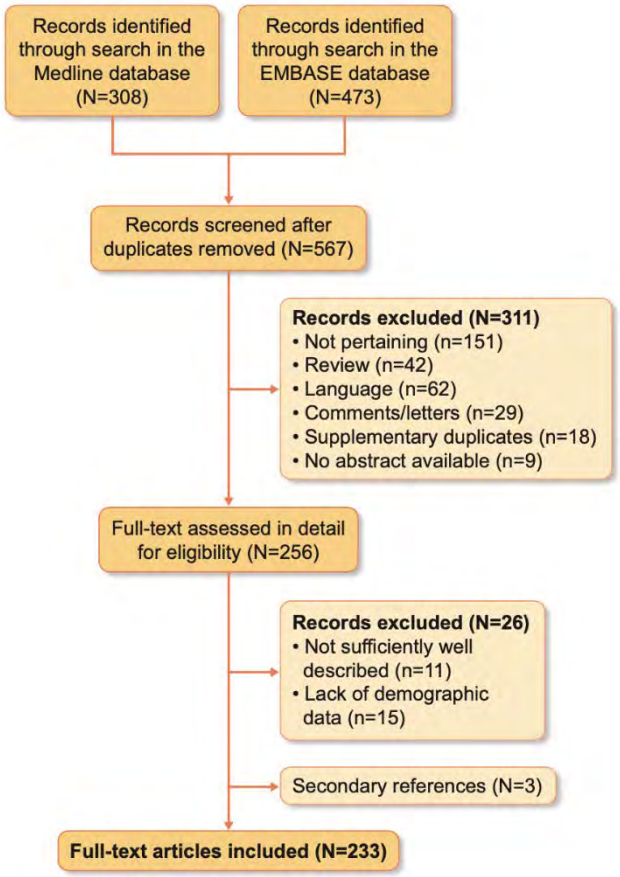
Background: Tubulointerstitial nephritis and uveitis (TINU) syndrome is defined as the occurrence of tubulointerstitial nephritis (TIN) and uveitis in the absence of other systemic diseases. TINU is a multisystemic autoimmune disorder that may occur in response to various environmental triggers. The most comprehensive review on this condition was published in 2001.

Methods: We conducted a systematic review of the literature for cases of TINU syndrome. MEDLINE and Embase databases were screened. Full-length articles or letters published from inception up to March 2020 and reporting cases with both TIN and uveitis were selected. We investigated differences between males and females and paediatric and adult cases. Multiple logistic regression was performed to identify potential risk factors for chronic kidney disease (CKD) development.



Results: A total of 233 articles reporting 592 TINU cases were retained for the analysis. The median age of the included subjects was 17 years (interquartile range 13–46) with a female pre- dominance (65%). Uveitis most frequently (52%) followed renal disease and was mostly anterior (65%) and bilateral (88%). Children tended to have more ocular relapses, while they were slightly less likely than adults to suffer from acute kidney injury and to develop CKD. Sex comparisons revealed that female were older than males at the age of diagnosis. Adult age as well as posterior or panuveitis were associated with an increased risk of developing CKD.

Conclusions: TINU affects both children and adults, with some differences between these two categories. Adult age and the presence of a posterior uveitis or panuveitis appear to be associated with the development of CKD.

*YSN paper

Characteristics	*N*	Values
Gender (male:female), *n* (%)	592	208 (35):384 (65)
Age (years), median (IQR)	592	17 (13–46)
Trigger(s) for TINU[a], *n* (%)	352	
None		223 (63)
Drugs		72 (21)
Infection		22 (6)
Toxic agent		23 (7)
More than one possible trigger		12 (3)
Uveitis, *n* (%)	592	
Anterior		382 (65)
Posterior		13 (2.2)
Intermediate		29 (4.9)
Panuveitis		62 (10)
Not specified		106 (18)
Uveitis (unilateral:bilateral), *n* (%)	500	60 (12):440 (88)
Uveitis onset, *n* (%)	480	
Before renal involvement		90 (19)
Concurrent renal involvement		142 (29)
After renal involvement		248 (52)
Acute renal failure, *n* (%)	421	392 (93)
Urinary abnormalities, *n* (%)		
Proteinuria	402	349(93)
Leucocituria	250	210 (59)
Microscopic haematuria	201	138 (84)
Glycosuria	280	229 (82)
Hypergammaglobulinaemia, *n* (%)	204	112 (55)
Autoantibodies[b], *n* (%)	314	46 (15)
Renal biopsy, *n* (%)		
Consistent with tubulointerstitial nephritis	485	485 (100)
Length of follow-up	413	
Months, median (IQR)		18 (10–28)
Ocular relapse(s), *n* (%)		207 (50)
Renal relapse(s), *n* (%)		54 (15)
CKD, *n* (%)		102 (25)

Demographic clinical and labor data

P 34

Phase 3, randomized, multicenter study to evaluate the efficacy and safety of pegcetacoplan in treatment of C3G or IC-MPGN

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Background: Complement 3 glomerulopathy (C3G) and immune complex membranoproliferative glomerulonephritis (ICMPGN) are rare diseases characterized by excessive deposition of C3 breakdown products in renal glomeruli leading to proteinuria and progressive renal disease. Pegcetacoplan is a targeted C3 investigational therapy for diseases related to complement overactivation. This is a phase 3, randomized, placebo-controlled, double-blind, multicenter study of the efficacy and safety of pegcetacoplan in individuals with C3G or IC-MPGN.

Methods: Approximately 90 patients (age, ≥12 years; weight, 20-100 kg) diagnosed with C3G or IC-MPGN, either as primary disease or posttransplant disease recurrence, will be recruited. Inclusion criteria include 2+ staining for C3c, global glomerulosclerosis <50%, urine protein-to-creatinine ratio (uPCR) ≥1000 mg/g, and estimated glomerular filtration rate (eGFR) >30 mL/min/1.73 m^2. Exclusion criteria include previous pegcetacoplan exposure, C3G/ICMPGN secondary to other conditions, and significant infection/malignancy. Patients will be randomized 1:1 to receive subcutaneous infusions of pegcetacoplan (1080 mg/20 mL) or matching volume of placebo twice weekly for 26 weeks (in addition to standard care). Thereafter, in the open-label period, all participants will receive pegcetacoplan twice weekly for another 26 weeks. Assessments include first-morning uPCR every 4 weeks and renal biopsies at baseline/screening and week 26. The primary endpoint is proportion of participants with reduction in uPCR ≥50% relative to baseline at week 26. Secondary endpoints include change in eGFR relative to baseline at weeks 26 and 52, proportion of participants with decreased C3c staining from baseline at week 26, and change in C3G histologic index activity score from baseline at week 26. Safety outcomes will also be monitored throughout the study. Participants may enter a subsequent long-term extension study or an 8-week follow-up period.

Results: This phase 3 study will assess efficacy and safety of pegcetacoplan in individuals with C3G or IC-MPGN.

Conclusions: This is a study design abstract.

P 35

Recurrent kidney stones behind a rare genetic disease: A case report of a Beckwith-Wiedemann Syndrome

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Background: Beckwith-Wiedemann syndrome (BWS) is a rare genetic condition on chromosome 11 affecting 1:13500 births. The disease is characterized by macrosomia and abnormal overgrowth of various organs. Particularly affected are the tongue (macroglossia) and the abdomen (omphalocele). Kidney abnormalities such as nephromegalia and simple or medullary cysts have also been described. However, nephrocalcinosis, with or without nephrolithiasis, is less frequent. Therefore, the association of recurrent kidney stones with BWS might not be straight forward.

Methods: Case Report

We report a case of a 51 year-old Caucasian woman who attended our outpatient clinic because of persistent bilateral loin pain. The patient, known for a BWS, has a 30 yrs H/O frequent bilateral kidney stones, complicated by urinary tract infections. She underwent many urological interventions (ureteroscopy and extracorporeal shock wave lithotripsy). Unfortunately, stone analyses were never performed.

Results: Clinical examination revealed a normotensive overweight patient (BP 130/82 mmHg, BMI 37.8 Kg/m^2). Initial laboratory data confirmed a normal renal function (PCreatinine 52 mmol/l, eGFR 107ml/min/1.73 m^2). There was no metabolic acidosis and calcium, phosphate and PTHi were normal. Spot Urine pH was consistently between 5-5.5. The 24hr-urine collection revealed a calcium excretion of 2.3 mmol/day (N: 2.5-8.0), a citrate excretion of 4.98 mmol/day (N: 1.0-6.5) and a low sodium excretion, consistent with a salt consumption of 3.2g/day. Kidney ultrasound showed normal kidneys size with multiple bilateral non-obstructive stones (max 1.5 cm). A genetic counseling confirmed the correlation between abnormalities of 11p15.5 chromosome found in BWS and the medullary-sponge kidney with nephrolithiasis. A therapeutic regime with Potassium Effervettes was initiated.

Conclusions: Recurrent kidney stones should not be underestimated and the presence of an underlying metabolic and/or a genetic disorder should always be considered and further investigated. In patients with known BWS and renal abnormalities nephrological work-up and genetic counseling are mandatory.

P 36

Adrenal pheochromocytoma, a rare cause of arterial hypertension in a patient with autosomal dominant polycystic kidney disease

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Background: Patients with ADPKD frequently present arterial hypertension even prior to significant loss of renal function, a clinical situation that alters the detection of secondary rare causes of hypertension. Diagnosis of pheochromocytoma in renal failure poses also a diagnostic dilemma due to lack of reliability of conventional urinary measurements of catecholamine excess. Plasma concentrations of free metanephrines are relatively independent of renal function. Very few cases are described in the literature and its recognition is challenging.

Methods: A 48-year-old woman with ADPKD in the pre-terminal renal failure stage, candidate for preemptive kidney transplantation, presented sudden hypertension crises up to 220/135 mmHg with cardiac palpitations. A pheochromocytoma was suspected.

Results: The determination of free plasma and urinary metanephrines showed an increased level of free plasma metanephrine (3xN), of free plasma normetanephrine (2xN) and a slightly elevated level of free plasma methoxytyramine. The urine assays confirmed the mixed and excessive secretion of metanephrines and normetanephrines.

An abdominal MRI confirmed the presence of a 29 mm right adrenal mass of radiological appearance compatible with a pheochromocytoma without suspect radiological criteria (Fig 1). This adrenal lesion was already present 2 years ago (Fig 2) but not diagnosed due to the size of the multiple renal cysts and the presence of many hemorrhagic cysts (Fig 3). A DOTATATE-PET / C confirmed a single right adrenal lesion. A bi-nephrectomy with a right adrenalectomy was successfully performed under alpha and beta blockade.

Conclusions: In conclusion, pheochromocytoma is a rare cause of hypertension in ADPKD; the determination of plasma and urine concentrations of free metanephrines is suitable for the diagnosis of pheochromocytoma among patients with renal failure rather than catecholamine or total metanephrine. Careful preoperative planning and surgical technique are essential to a favorable outcome.

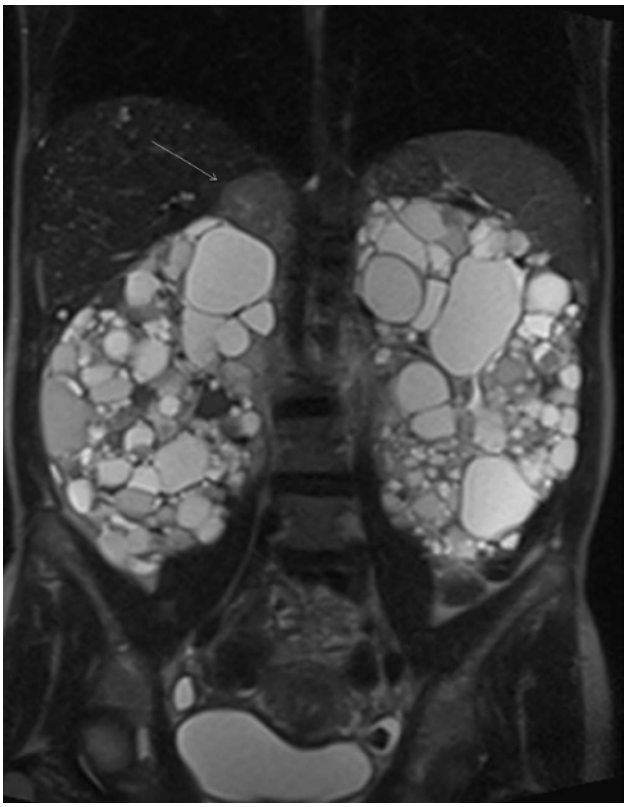

Fig 1

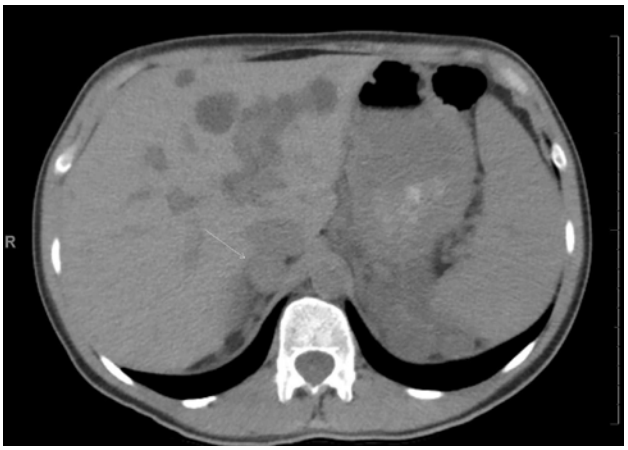

Fig 2

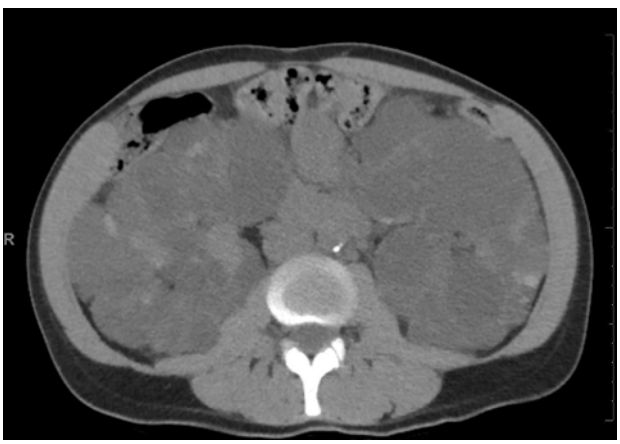

Fig 3

P 37

Estimating Baseline Serum Creatinine for the Diagnosis and Classification of Acute Kidney Injury

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Background: The 2012 KDIGO Clinical Practice Guideline for Acute Kidney Injury defines and classifies AKI from changes to serum creatinine. When baseline creatinine is missing, the guideline recommends to back calculate it from an assumed MDRD-GFR of 75ml/min/1.73 m^2. We describe an alternative method.

Methods: From the NHANES 2015-2018 cohort we calculated the distribution of serum creatinine values for the adult US population as a whole, and for gender, age and weight subgroups.

We then assessed bias, precision and accuracy of the derived mean values to predict baseline creatinine in an external validation cohort (NHANES 2011-14). Results were compared to the performance of back calculated MDRD values.

Results: Absolute differences between back calculated MDRD and true creatinine values in the validation cohort show a mean bias of 7.2 umol/l and an interquartile precision range of 0 to +20 umol/l. Accuracy is rather low, with P15 values at 43% and P30 at 73%.

In contrast, using our gender-based population mean creatinine values eliminates bias (0 umol/l) and improves precision (IQR -6 to 11.6 umol/l) and accuracy (P15 57%, P30 85%). Adding age and weight categories leads to a minor further increase in accuracy with no improvements in bias and precision.

Conclusions: We describe population mean baseline creatinine values for assessing acute kidney injury. Compared with the current standard approach our method is much easier to apply and eliminates bias, shows more precision, and improves accuracy.

P 38

Successful conservative management in two pediatric cases of xanthogranulomatous pyelonephritis

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Background: Xanthogranulomatous pyelonephritis (XPN) is a chronic pyelonephritis due to massive destruction of renal tissue by lipid-laden macrophages. Association with pelvic obstruction, calculi or tumor are often reported. XPN is usually treated with partial or full nephrectomy.

Methods: We report two cases of successful conservative management.

Results: A 13-year-old boy was admitted with fever, flank pain, weight loss and sweating. Investigations by computed tomography (CT) and magnetic resonance imaging (MRI) showed hypovascularized mass (6 cm) in lower pole of left kidney with necrotic extension to perinephric fat (stage 2). Blood tests revealed inflammatory syndrome and normal kidney function. Kidney biopsy was performed, leading to diagnosis of XPN without malignancy. Urine culture and tissue samples were sterile. Intravenous ceftriaxone was applied for 2 weeks with relay by 2-weeks of oral ciprofloxacin. Control MRI at month 1 showed 50% regression of renal mass, and at month 4, a residual mass of 1.5 cm.

A 17-year-old adolescent presented ten-days history of fever, flank pain, fatigability, sweating with rapid weight loss. Laboratory tests showed high white blood cell count and CRP value. Urine and blood cultures were sterile. Abdominal CT and MRI revealed a multi-loculated cystic mass (6x7 cm) in the left kidney, with infiltration of perinephric fat, extending to lower pole of the spleen (stage 3). The XPN was diagnosed given the typical presentation. Patient was treated with piperacillin-tazobactam for 11 days, relayed by 2-month oral ciprofloxacin. Ultrasound and MRI control at month 2 of treatment showed an almost complete mass regression.

Conclusions: XPN should be considered as unusual differential diagnosis of renal mass. We applied conservative treatment in our patients, with successful clinical and radiological results, including normal kidney function on iodine 123Hippuran renal scan. Although surgical management is applied in the most of cases, conservative treatment may be effective even in stages 2 or 3.

P 39

Minimal change disease (MCD) after Moderna COVID-19 vaccination*

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Background: Post vaccination minimal change disease with nephrotic syndrome and acute kidney injury has been reported after influenza and Pfizer-BioNTech vaccine. Further research is needed to prove a correlation.

Methods: Clinical case, renal biopsy, dialysis

Results: We present a case of a 65 years old patient, who developed minimal change disease 8 days following first injection with Moderna COVID-19 vaccine. In his medical history the patient has collagenous colitis and was on treatment with budenofalk. He presented with full blown nephrotic syndrome and developed dialysis dependent acute kidney injury for two weeks. Renal biopsy showed minimal change disease with 90% loss of podocyte processes in electron microscopy. Two weeks of dialysis and immunosupressive therapy over three months after the event lead to recovery of renal function to baseline. The patient received the second COVID-19 vaccination without developing complications or relapse.

Conclusions: We present one of the first patients with minimal change disease after Moderna COVID-19 vaccine. There was an association between the timing of the vaccination and clinical manifestation of nephrotic syndrome. A definite causal relation still needs to be elucidated. A possible pathomechanism would be, that mRNA vaccines initiate T-cell mediated injury. However further studies are needed to find the immunological mechanism of action after COVID-19 vaccination. Out of many millions of mRNA vaccines administered so far, to our knowledge, 7 cases of de novo minimal change disease have been described as well as up to 17 other glomerular diseases de novo and relapsing after COVID-19 vaccination.

*YSN paper

Figure1: Time axis events

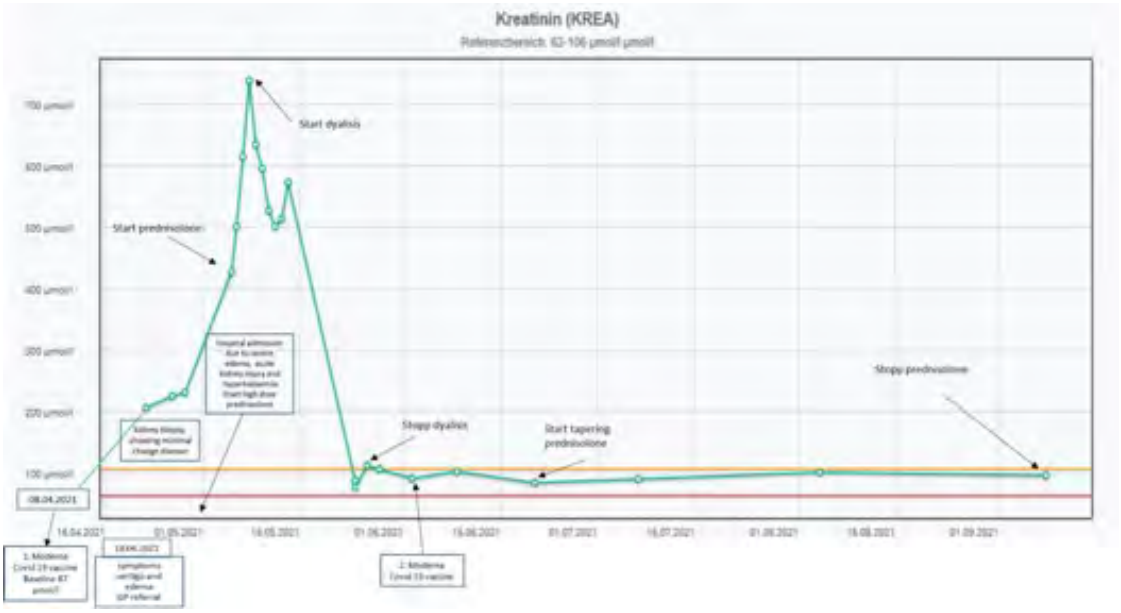

Figure 2: Time axis kidney function and events

P 40

Chronic kidney disease after domino liver transplantation using organs from donors with hereditary transthyretin amyloidosis: a case-report

Curzio Solca 1, Luca Bernardi 2, Vanina Gurtner - De La Fuente 3, Thomas Menter 4, Giulia Magini 5

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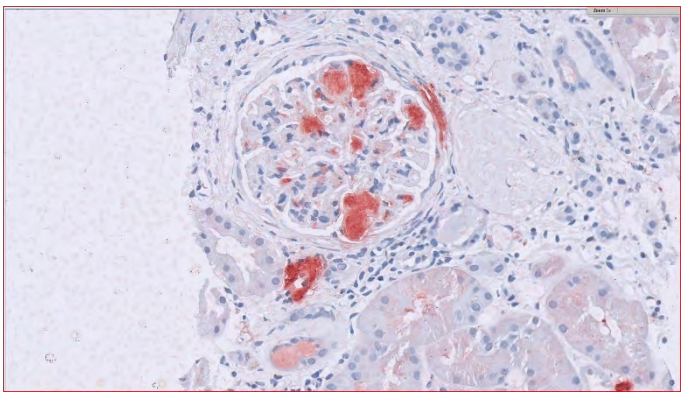
Background: Hereditary transthyretin amyloidosis (ATTRv) is an autosomal dominant disease characterized by deposition of amyloid fibrils in cardiac tissue, peripheral nerve system and/or kidney depending on the genotype*1*. The clinical manifestations of the Val50Met mutation can occur as early as 20-40 years of age. This early onset ATTRv causes peripheral sensory-motor and autonomic neuropathy with walking imbalance as well as kidney involvement*1-4*. Except of the usual antiproteinuric medications and liver transplantation there are no disease-specific treatment for renal involvement*1*. Domino liver transplantation (DLT) consists of transplanting an explanted ATTRv liver into a selected non-ATTRv patient. Given the organ shortage, the use of these liver is appealing because it was thoughts the disease requires at least 20 years to develop symptoms in the affected individuals*5*.

Methods: -

Results: We report a case of a 70 years old man receiving DLT using a ATTRv (Val50Met) liver following a hepatitis C induced cirrhosis. The medical history was characterized by an untreated arterial hypertension and a metronidazole induced sensory-motor polyneuropathy. Ten years after liver transplantation laboratory data showed a decline of eGFR-EPI to 42 ml/min/1.73 m^2 and an albuminuria of 105 mg/mmol creatinine. The kidney biopsy revealed glomerulal, interstitial and vascular amyloid deposits immunohistologically classified as ATTR amyloid (Figure 1).



The electroneurography of the lower limbs showed a severe sensory-motor axonal polyneuropathy. No cardiomyopathy was identified. An antiproteinuric therapy with a sartan was immediately started and blood pressure was normalized.

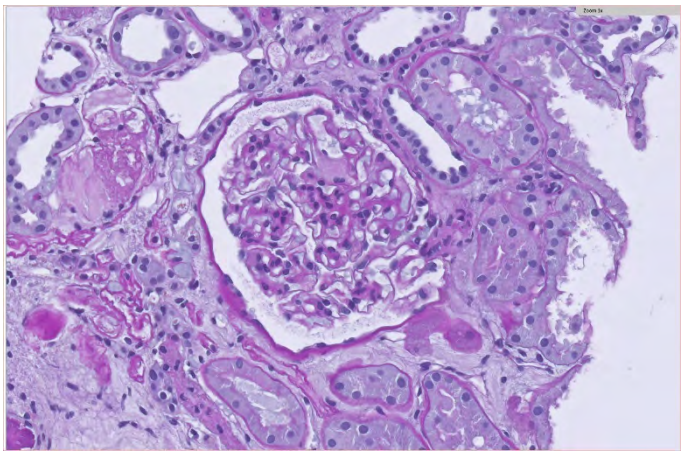


Figure 2: PAS

Conclusions: DLT patients receiving an ATTRv liver may display clinical manifestation of ATTRv 10-15 earlier than ATTRv native patients. Recipient selection is essential; candidates with pre-existing neuropathy, nephropathy or long life expectancy are at risk of ATTRv complications. Therefore annual clinical monitoring of renal function, proteinuria, albuminuria, cardiological and neurological status should be recommended.

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Safety data of percutaneous kidney biopsies: a ten-year single center cohort study

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Background: Percutaneous kidney biopsy is routinely performed in the evaluation of kidney disease and care after kidney transplant. We reviewed all biopsy procedures over the last 10 years as a quality item.

Methods: Retrospective analysis of prospectively collected data in all percutaneous kidney biopsies performed in our institution. Outpatients are monitored for 5 hours after the procedure and an ultrasound (US) is performed before discharge. Inpatients are examined only if symptomatic. A 16G single-use automatic biopsy device (Argon Medical Devices Tru-Core™ II) is used with real-time ultrasound guidance. Pain is assessed systematically using the VAS Scale. Results are given in percentage, standard deviation of the mean (SD) or standard error of the median (SE).

Results: A total of 1030 biopsies was collected between January 2010 and June 2011, of which 580 in transplanted kidneys (TK). In native kidneys (NK) 3.19 (SD 0.8) punctures were performed to gain 2.44 (SD 0.57) cylinders, in TK 2.42 punctures (SD 0.63) for 2.07 cylinders (SD 0.27). In the control US hematoma were more frequent after native (8.9%) than after transplant (2.9%) biopsies, whereas AV fistula were more frequent in TK (10%) than in NK (3.1%). Hospitalisation occurred in 1.3% (NK) and 1.2% (TK). After NK biopsies endovascular 0.4% or operative 0.7% procedures were required, none after TK biopsies. Blood transfusion was needed in 0.7% (NK) and 0.2% (TK). Patients' pain perception was similar: VAS during biopsy 2.07 (SE 1.61) for NK vs 2.01 (SE 1.52) for TK, VAS after biopsy 0.48 (SE 0.75) for NK vs 0.63 (SE 0.94) for TK.

Conclusions: Percutaneous real-time US-guided biopsy of native and transplanted kidneys with a G16 needle provides a good tissue yield at a very low complication rate with less than 1% requiring an invasive measure. Pain is perceived mostly during the biopsy and is of mild intensity.

P 42

cANCA-glomerulonephritis secondary to bartonella henselea endocarditis (cat scratch disease)

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Background: Kidney disease as an extracardiac manifestation of infective endocarditis is relatively common with hematuria, parenchymal infarction and glomerulonephritis seen in up to 40-50% of patients. The histopathology shows significant variability in patients with infective endocarditis and is associated with a number of pathogenic organisms.

Methods: Clinical case, renal biopsy, serology, PCR testing.

Results: We present a case of a Swiss farmer with blood culture negative endocarditis caused by *Bartonella henselea* associated with glomerulonephritis with the nessecity of acute kidney replacement therapy. Serial blood cultures were negative, however PR3-ANCA was positive mimicking vasculitis. Kidney biopsy showed immune-complex glomerulonephritis. The serology was positive for *Bartonella henselae* with cross-reactivity to *Coxiella burnetii*. Diagnosis of *Bartonella henselae* endocarditis was confirmed by PCR ("polymerase chain reaction") in a

sample of the operated aortic valve. After operative and antibiotic treatment of the endocarditis kidney function recovered and dialysis treatment could be stopped.

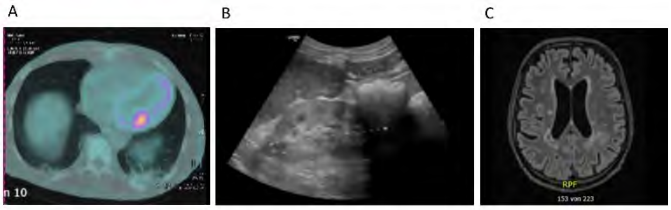

Figure 1: *Bartonella henselea* Endocarditis associated glomerulonephritis in a bioprosthetic aortic valve with a) PET-CT FDG Heart, b) septic embolism to spleen and c) cerebral stroke.

Conclusions: Culture- negative endocarditis poses a diagnostic challenge. Identification of the aetiologic cause is crucial since treatment differs in agent and duration. In patients with a history of valve disease with an unclear infection it is essential to consider endocarditis early in the course of disease. A high index of suspicion should guide broad sampling including PCR and serologic testing. Cross-reactivity of *bartonella sp.* "cat scratch disease" and *coxiella burnetii* "Q fever " is known. *Bartonella henselea* endocarditis can lead to immune-mediated glomerulonephritis. ANCA-positivity can mimick vasculitis in immune-mediated glomerulonephritis.

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Failure to Thrive in Infants – Nephrologists to the Rescue*

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Background: Kidney diseases are possible causes of failure to thrive in infancy. Sometimes this is caused by a congenital renal tubulopathy. A systematic understanding of renal pathophysiology is essential for timely diagnosis and treatment.

Methods: We describe three infants with failure to thrive, who were referred to nephrology for further investigation after initial evaluations by their pediatrician who had failed to elucidate the cause. All three children were 4 to 6 months old and underwent the same diagnostic approach, including blood and urine samples, and an abdominal ultrasound. All children were breastfed and had been introduced to solid foods. Birth and past medical histories were unremarkable. Caloric intake was adequate. Infections were excluded.

Results: Child 1 was clinically dehydrated. Laboratory results revealed metabolic alkalosis (HCO3 29.8 mmol/L, pH 7.56), hyperkalemia (5.9mmol/L) and hyponatremia (121 mmol/L), suggesting Pseudo-Bartter syndrome. Further investigations revealed a pathological sweat test, confirming a cystic fibrosis. Child 2 had lost 1 kg in a month (16% of body weight) and was clinically dehydrated. Diagnostics revealed hyperkalemia (7.0 mmol/L), hyponatremia (121 mmol/L) and hypercalcemia (2.79 mmol/L). Renin- and aldosteronelevels were highly elevated, mimicking pseudo-hypoaldosteronism. Urine showed leukocyturia and bacteriuria consistent with a urinary tract infection (predisposing risk factor being unilateral megaureter seen on ultrasound).

Child 3 presented with neurodevelopmental delay and sensorineural hearing loss. Further investigations revealed metabolic acidosis (HCO3 17.1 mmol/L), hypokalemia (2.7 mmol/L), hypercalcemia (3.09 mmol/L) and hypercalciuria (Ca/Krea 2.50 mol/molKrea). Nephrocalcinosis was evident on sonography. A distal renal tubular acidosis was diagnosed.

All three children were treated according to best standard of care and their condition improved.

Conclusions: These cases illustrate that different diseases, associated with renal involvement and electrolytes disturbances, can lead to failure to thrive during childhood. Heightened awareness of the underlying pathophysiology and differential diagnoses, as well as correct interpretation of the diagnostic findings facilitates rapid diagnosis and treatment.

*YSN paper

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IgG4-Related kidney (IgG4-RKD) disease: a systemic disease with many faces

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Background: IgG4-RKD incorporates various renal lesions associated with IgG4-disease, a systemic disorder with multiple clinical features characterized by tissue infiltration with lymphoplasmacytic rich in IgG4-secreting plasma cells resulting in fibrosis of multiple organs.

Methods: We report on the broad renal histopathological spectrum, course and outcome of 4 cases with IgG4-RKD diseases.

Results: Case 1: A 78y old male patient presented with nephrotic range proteinuria (21 g/l), polyclonal hypergammaglobulinemia, and chronic lymphadenopathy. Renal biopsy showed dense lymphoplasmacytic tubulointerstitial nephritis with an increased number of IgG4-positive plasma cells and storiform fibrosis. Renal failure requiring hemodialysis occurred due to steroid-refractory IgG4 disease and rituximab therapy was initiated.

Case 2: A 64y old male patient with hyponatremia, eosinophilia, lymphadenopathy, ground-glass lung opacities presented with nephrotic proteinuria. Hypergammaglobulinemia with elevated serum IgG4 level, exceeding 5 g/l (normal <2 g/l) was evident. Renal biopsy showed IgG4-RKD, the major renal parenchymal lesion was membranous glomerulonephritis. Endoxan and steroids lead to a rapid improvement of proteinuria and hypocomplementemia.

Case 3: 73y old male patient with autoimmune pancreatitis, chronic sinusitis and lymphadenopathy, was referred due to nephromegaly with elevated serum IgG levels, >22 g/l) along with hypocomplementemia and proteinuria. Renal biopsy showed IgG4-RKD, the major renal parenchymal lesion was membranoproliferative glomerulonephritis. Excellent clinical and laboratory response was achieved under steroids.

Case 3: 74y old male patient with severe eosinophilia, polyclonal hypergammaglobulinemia, abnormal renal and liver biochemistry, biliary strictures, pancreatitis and chronic lymphadenopathy was referred for further workup. Due to several anticoagulants a renal biopsy was not performed. Based on the systemic manifestations, radiological and laboratory findings, a IgG4-related kidney-hepatobiliary diseases was postulated.

Conclusions: Although in the kidney, the most dominant feature associated with IgG4-RD is plasma cell-rich TIN, our case series depicts other uncommon patterns of renal involvement along with the, laboratory, histological, radiological data and response to treatment, in IgG4-RKD.

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NSAIDs, Dehydration and acute kidney failure in the young adults: An unrecognized entity?

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Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most widely used drug classes worldwide and they are considered safe and well tolerated [1, 2]. As a side effect of the therapy can occur an acute interstitial nephritis (AIN) or an acute tubular necrosis (ATN). There are no disease-specific therapies for acute tubular necrosis, whereas acute interstitial nephritis requires immunosuppressive therapy.

Methods: We describe three young patients (between 19-25 years) who developed ATN in the presence of NSAID and dehydration.

Results: Two of the three patients were admitted to the hospital with an incorrect diagnosis and received different medications and further diagnoses. After a detailed medical history, a diagnosis of ATN was made in all three patients and renal biopsy was avoided. Renal values recovered within 1-3 weeks due to fluid intake and avoidance of NSAIDs

The cornerstone of the pathogenesis of hemodynamically mediated acute kidney injury is the inhibition of Cyclooxygenase

1 (COX-1) enzymes with subsequent reduction of prostaglandin (PG) synthesis [10-3]. In cases of sustained renal vasoconstriction, such as in patients with intravascular volume depletion or chronic kidney disease, PG-mediated afferent arteriolar vasodilation plays an important role in maintaining renal blood flow and glomerular filtration rate by reducing pre glomerular resistance [3, 4]. This mechanism of the combined effect to decreased water diuresis (dehydration) and NSAIDs induced Cyclooxygenase (COX) inhibition might well be the underlying mechanism of ATN in these three patients.

Conclusions: Clinicians must be cautious when treating patients with NSAIDs, not only in older patients and patients with preexisting renal disease, but also in younger patients at risk of intravascular volume depletion. Diagnosis of ATN in the presence of NSAIDs and dehydration is difficult, but the medical history can help us to establish the diagnosis. An incorrect diagnosis may lead to unnecessary renal biopsy and unnecessary therapies

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Coronary angioplasty and stenting in acute coronary syndromes with very low contrast volume using Cordis 6F diagnostic catheters and improved cardiovascular and renal outcomes

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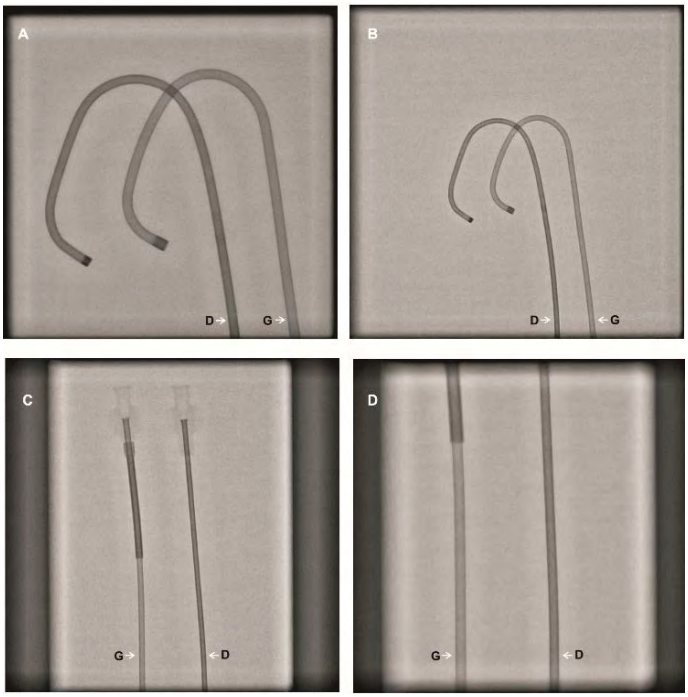
Background: To perform safely angioplasties in acute coronary syndromes with very low contrast volume using Cordis 6F diagnostic catheters, and thereby improve the cardiovascular and renal outcomes.

Methods: In 1652 patients (2138 lesions/ 2447 stents) with acute coronary syndromes, angioplasty was performed with Cordis 6F diagnostic catheters. Primary angioplasty was performed in 525 cases. In 75% of cases, iodixanol was used. A regular follow-up of the patients was performed 30 days after the procedure. All the procedures were performed through the femoral route. Tirofiban was used in 99% cases with adjusted dosages based on the creatinine values. Covid19 was positive in 23 cases by RT PCR.



Results: The mean contrast volume used per patient was 28 ml (±6 ml) including the angiogram prior to the angioplasty. 103 patients had creatinine more than 2mg/dl before the angioplasty procedures. Left main angioplasty was performed in 41 patients using single stents. 87 patients had cardiogenic shock at presentation. 77% of the cases had diabetes. IVUS was used in only two patients. Mild reversible nephropathy (CIN) was observed in six patients. Six patients were already on dialysis, and dialysis was continued thereafter. Switch-over of angioplasty to the radial route was performed in six cases. 32 deaths in total were observed in this series; 19 of these patients had cardiogenic shock (10 late presenters), and three patients expired after discharge due to possible acute stent thrombosis. Groin haematoma was seen in seven cases requiring one unit of blood transfusion. Proximal mild edge dissection in the deployed stent was seen in 3 cases. Acute in-hospital stent thrombosis was seen in 7 cases, which were managed with balloon dilatations and stents.

Conclusions: Angioplasty and stenting can be performed safely in patients with acute coronary syndromes using Cordis diagnostic catheters and a very low volume of contrast with improved clinical outcomes.

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A CASE STUDY ON MANAGEMENT OF POSTOPERATIVE CARDIORENAL SYNDROME

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Background: Postoperative complications contribute to increased mortality, length of stay and need for an increased level of care at discharge. In these complex cases, a multiple organ support therapy might be currently seen as a feasible approach. Cardiorenal syndrome (CRS) encompasses a spectrum of disorders involving both the heart and kidneys in which acute or chronic dysfunction in 1 organ may induce acute or chronic dysfunction in the other organ. We present a case of a 71-year-old female who underwent bypass surgery due to coronary artery disease (CAD). After 6 weeks she was admitted to our clinics due to severe progressing dyspnoe, fatigue and weakness. The patient underwent pleural punction, cytology of punctate revealed transudate, no malignant cells. Physyterapeutic evaluation reported: functional assessment measure level - complete asssistance is necessary, balance disorder by Berg scale accounted 0 points, sitting balance by Leahy was 1 point, Rivermade mobility index 1-3. Management approach included strict fluid balance control, 50 mg Torasemid once a day, activization, verticalization.

Methods: On primary survey, her general condition was very severe, patient was lying, passive and frail, respiratory rate was 20/min, oxygen saturation of 90% beyond oxygenotherapy; diuresis 300 ml per day, GFR 40 ml/min (by MDRD). HR was 86 bpm, irregular (atrial fibrillation), TA 90/80 mm Hg. Chest CT demonstrated bothsided hydrothorax and right sided athelectasis with infiltration.

Results: After 2 weeks general condition improved - no dyspnoe, TA 130/80 mm Hg, no need of oxygen, diuresis 1700 ml with no diuretics, GFR (by MDRD formula) 81,87 ml/min, functional assessment measure level- modified independent (requires an assistive device), balance disorder by Berg scale 10 points, sitting balance by Leahy -3, Rivermade mobility index- 4-7.

Conclusions: This case illustrates the prompt and accurate management of multiorgan damage syndrome (MODS) and frailty secondary to CRS leading to optimal patient outcome.

POSTER PRESENTATIONS – HEMODIALYSIS / PERITONEAL DIALYSIS

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Demography of the dialysis population in Switzerland in 2020

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Background: The national Swiss Dialysis Registry (srrqap) has been established originally in the year 2006. However, participation is substantial only since 2013, when data collection became mandatory by law. The primary aim of the srrqap is to provide quality control and quality improvement for dialysis therapy in Switzerland. In the present analysis, select demographic characteristics of the dialysis population in Switzerland are given.

Methods: All medical establishments in Switzerland (both public and private; N = 95) providing chronic dialysis treatment, had to provide relevant data for the year 2020. All individuals being on chronic dialytic therapy in the year 2020 were enrolled (N = 4'791). For patients alive on December 31 2020, data were gathered from this date or closest to this date. For patients who died during 2020 or were being transplanted, data refer to time of event, or to a date closest to the event.

Results: The mean and median age of dialysis patients in 2020 remained the same as in 2019 at 68.9 and 71.8 years, respectively. More than fifty percent of the patients were older than 71.8 years, and ¼ were beyond 80 years. No significant differences were found between female and male patients regarding mean age (69.2 vs. 68.8 yr, respectively). However, women have been significantly longer on dialysis compared to men (53.0 vs. 45.3 months, p = 0.000, respectively) and have a markedly lower Charlson Comorbidity Index than men (4.16 vs. 4.65, p = 0.000, respectively).

Conclusions: With a coverage of 100% for both centers and patients, the data gathered can be considered highly representative. The incidence of dialysis therapy in Switzerland with 92.5 pmp is clearly lower than in most other European countries. In 2020, 3'835 prevalent patients (444.4 pmp) were dialyzed in Switzerland. The number of dialysis patients with COPD and heart failure increased by 0.6% from 2019, reaching 16.2% and 21.8%, respectively.

Figure 1: Age trend for 2013 - 2020

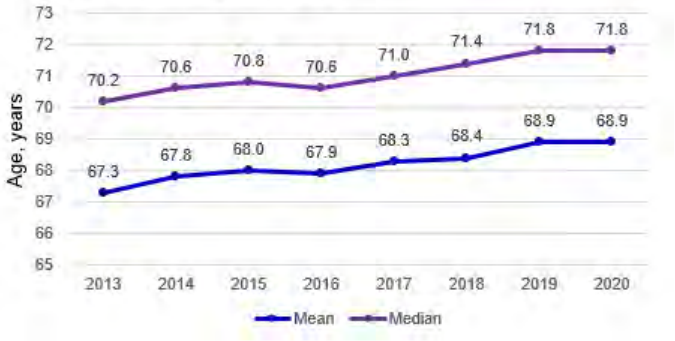

Table 1: Characteristics (given as mean and median) in dialysis patients

	All (100%)		In Centre (89.9%)		Home* (10.1%)	
	Mean	Median	Mean	Median	Mean	Median
Age, yr	68.9	71.8	69.6	72.4	63.3	66.0
Dialysis vintage, months	47.9	34.0	49.8	36.0	31.5	22.0
Comorbidities, N	3.1	3.0	3.2	3.0	2.3	2.0
Charlson Comorbidity Index	4.5	4.0	4.6	4.0	3.8	3.0
Hypertensive, %	83.1		83.2		82.3	
Sex (male), %	65.6		65.5		65.8	

Table 2: Trend of incident/prevalent count and comorbidities in dialysis patients from 2014-2020

	2014	2015	2016	2017	2018	2019	2020
Total number of patients (cumulative)	4215	4453	4502	4580	4646	4704	4791
Incidence, pmp	91.9	96.6	93.9	91.1	95.9	92.7	92.5
Prevalence, pmp	423.5	433.5	441.1	435.7	443.7	448.3	444.4
Comorbidities (mean), N	2.36	2.43	2.52	2.57	2.55	2.57	3.12
Charlson Comorbidity Index (mean)	4.44	4.42	4.49	4.51	4.49	4.48	4.48

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Hematologic factors associated with favourable long-term outcomes in paediatric patients with chronic kidney disease (CKD) on maintenance haemodialysis (HD)*

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Background: In children with CKD, anaemia is defined as haemoglobin (Hb) <11-13.0 g/dL, depending on patient's age and gender. Previous exploratory machine learning in a subpopulation of CKD-5 patients suggested an increased mortality risk with Hb <10.5 g/dL and increased red blood cell distribution width (RDW) >15%. The objective was to evaluate such associations in a traditional time-to-event analysis in a larger population.

Methods: Retrospective analysis of a cohort of patients <30 years of age who started chronic HD in childhood (< = 19 years) and received thrice-weekly HD (2004-2016) in outpatient DaVita centres. Survival at 5 years while remaining on HD was investigated by non-parametric analysis (Kaplan-Meier) stratified by terciles of mean individual Hb and RDW, respectively. A sensitivity analysis was carried out for different subpopulations (<6y/6-12y/ >12y at initiation of HD).

Results: 1493 patients were included with Hb and RDW terciles of <10.7/10.7-11.5/ >11.5 g/dL and <14.6/14.6-15.7/ >15.7%, respectively. Age at initiation of HD was <6y: n = 66, 6-12y: n = 173, >12y: n = 1254. Both Hb and RDW terciles showed strong associations with survival distributions (P <0.001 for both, log-rank test). Estimated 5-year survival [95%CI] by Hb terciles was 85.1% [81.1-89.3%] (Hb <10.7 g/dL) versus 94.9% [92.5-97.4%] (>10.7-11.5 g/dL) and 93.8% [90.8-97.0%] (>11.5 g/dL), and for RDW 98.6% [97.1-100%] (<14.6%) versus 94.1% [91.3-96.9%](14.6-15.7%) and 84.2% [80.1-88.6%] (>15.7%). Sensitivity analyses confirmed significant associations in patients >12y (P <0.001 for both Hb/RDW) and for RDW in 6-12y patients (P = 0.03 versus P = 0.14 for Hb).

Conclusions: This analysis confirmed strong associations between haematologic factors and survival in our population. Clinical utility of RDW in HD management and its physiological interpretation such as importance of specific anaemia forms, or treatment-induced RDW increase in patients requiring more intense treatment remains to be investigated, with potential impacts on existing guidelines for prescribing iron and epoetin therapy. Further studies will also include the time variation trajectories of Hb and RDW.

*YSN paper

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The frailty process in CKD patients: analysing the role of haemodialysis

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Background: Patients on haemodialysis (HD) are known to be particularly frail. This is mostly explained by factors strictly related to the replacement therapy. The aim of the study was to analyse longitudinally patients in the transitional phase from pre-dialysis to long-term dialysis. We hypothesised that patients on HD are frail not because of the replacement treatment itself, but because they are frail already in the pre-dialysis stage due to the chronic and degenerative nature of CKD.

Methods: Patients in a pre-dialysis program underwent a baseline visit in average 10 weeks before the first HD session and 4 follow-up visits

after HD start. During the period of about 2.5 years, health status, physical performance, gait quality, cognitive functioning, haematology parameters and adverse events were monitored.

Results: Between 2015 and 2018, 14 patients out of 27 recruited concluded the study (age: 72.3 ± 5.7 years, 50% male). In general, no significant changes were observed along the analysed period. Out of 45 variables, only the score of the Short Physical Performance Battery ($p < 0.01$, $F = 8.50$) and the number of comorbidities ($p = 0.01$, $F = 3.94$) showed a significant worsening.

Conclusions: Despite the low number of participants, the multifactorial analysis of the transitional phase from pre-dialysis to long-term dialysis should stimulate some considerations about the role of pre-dialysis programs in reducing complications during the transitional phase and about frailty prevention programs not only for HD but also for CKD patients in earlier stages.

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Sacubitril/Valsartan in hemodialysis patients with heart failure

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Background: Sacubitril/Valsartan (SV) reduces significantly morbidity and mortality in patients with HFrEF (PARADIGM-HF) and so it is common used in these patients, nowadays. Data about the efficacy and safety of SV in patients on hemodialysis with HFrEF is scarce, with only a few case reports and case series showing encouraging results. As patient with worsening of HFrEF and on hemodialysis do probably profit of a treatment with SV, we initiated such treatment whenever indicated.

Methods: We retrospectively analyzed NYHA classification and LVEF before and after starting SV in four patient on longterm hemodialysis therapy, as well as possible side effects.

Results: Three out of four patients showed improvement in LVEF, NYHA classification and quality of life without any serious side effects. In one patient LVEF worsened due to additional worsening of aortic valve disease. In addition, up-titration of SV in this patient was not possible due to severe hypotension. Up-titration of SV to target dose (200 - 400mg/day) in the remaining three patients was achieved.

Conclusions: In conclusion, we found that SV could safely introduced in hemodialysis patient with improvement of cardiac function and heart failure symptoms in most of these patients.

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Blood flow with three different lock solutions in the dialysis permcath™ using the Tego® connector system – an observational survey*

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Background: Well-functioning dialysis catheters are essential for an adequate hemodialysis in patients without a fistula. In all patients we use the Tego® connector system which requires just NaCl 0.9% solution to block the catheter between the dialysis treatments.

Methods: We examined 30 patients who undergo hemodialysis with a permcath™. Three different lock solutions (Citra-Lock™, NaCl 0.9% and TauroLock™-Hep500) were used each a full month in every patient. The Citra-Lock™ solution was used in the first month, May 2021. In June we used just NaCl 0.9% to block the catheter and in July TauroLock™-Hep500. In every dialysis treatment we analyzed the blood flow and how many times alteplase (Actilyse®) was necessary. In June three and in July two more patients dropped out because of newly functioning fistulas. In conclusion we used Citra-Lock™ in 30 patients, NaCl 0.9% in 27 and TauroLock™-Hep500 in 25 patients.

Results: We compared the different solutions as we analyzed the differences of blood flow between Citra-Lock™ versus NaCl 0.9% and TauroLock™-Hep500 versus NaCl 0.9% in each patient. We also examined in how many patients the treatment with Actilyse® was necessary.

Comparing NaCl with Citra-Lock the blood flow was higher with NaCl 0.9% in 14/27 patients (medium difference of blood flow was +17.3ml/min) versus with Citra-Lock™ in 13/27 patients (medium +7.2ml/min): Comparing NaCl 0.9% with TauroLock™-Hep500 the blood flow was higher with NaCl 0.9% in 14/25 patients (medium difference of blood flow was +8.9 ml/min) versus with TauroLock™-Hep500 in 11/25 patients (medium +11.7 ml/min). During the month using NaCl 0.9%, Actilyse® was necessary in 11% of all patients, using Citra-Lock™ in 17% and using TauroLock™-Hep500 in 8%.

Conclusions: Our analysis shows no significant difference in blood flow using Citra-Lock™ or TauroLock™-Hep500 compared to NaCl 0.9% as lock solution when using the Tego® connector system. We didn't examine infection rate in this short observation.

*YSN paper

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Light-chain amyloidosis treated with the novel medium cut-off Theranova dialyzer

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Background: Light-chain (AL) amyloidosis is a systemic disorder caused by extracellular deposition of pathologic, insoluble amyloid fibrils in tissue. Kidneys are the most frequently affected organs and their disfunction is a consequence of tissue disruption by amyloid deposits. The clinical presentation includes nephrotic syndrome and progressive worsening of renal function.

Methods: A 75-year-old female patient was started on HDF due to progressive worsening of renal function caused by AL amyloidosis. Her clinical state was stable, she was fit and very active. She had episodes of congestive heart failure with dyspnea and generalized weakness. This was attributed to amyloid infiltration of her cardiac muscle. Though on IHD, treatment with revlimid with dexamethasone was initiated. Hemodiafiltration was started, however, the treatment was not tolerated well (hemodynamic instability, nausea). She was therefore switched to expanded hemodialysis (HDx) with a medium cut-off Theranova 400 dialyzer. FLC as well as β2 microglobuline levels were measured regularly before and after each session.

Results: The patient started with HDx using Theranova 400 medium cut-off membrane. Her dialysis regimen consisted of 4-hours thrice weekly with dialysate flow of 500 mL/min, blood flow of 300 mL/min. Regular pre- and post- dialysis clearance monitoring of kappa and lambda free light chains as well as β2 microglobuline confirmed a consistently delivered effective removals of these molecules after each HDx session. The patient's clinical state remained stable, there were no adverse effects related to the dialyzer change noted.

	12TH FEBRUARY		19TH FEBRUARY		26TH FEBRUARY		2ND MARCH	
DATE	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER
λ FLC (mg/L)	45.07	28.6	36.81	22.5	44.31	26.67	38.21	24.72
κ FLC (mg/L)	442.16	137.13	240.84	106.6	295.12	124.97	314.91	150.83
RATIO κ / λ	9.81	4.79	6.54	4.71	6.66	4.69	8.24	6.1
β_2M (mg/L)	22.3	7.6	20.9	6.1	24.1	6.0	23.1	6.8

	23RD APRIL		4TH MAY		11TH MAY		16TH MAY	
DATE	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER
λ FLC (mg/L)	34.09	24.96	38.16	34.59	59.91	47.29	77.61	60.54
κ FLC (mg/L)	223.02	101.24	176.01	122.19	254.63	90.44	275.24	157.21
RATIO κ / λ	6.54	4.06	4.61	3.53	4.25	1.91	3.55	2.6

(editorial note: normal test results for free light chains are: kappa 3.3 to 19.4 mg/L and lambda 5.71 to 26.3 mg/L, ratio of kappa/lambda: 0.26 to 1.65)

Conclusions: Expanded hemodialysis with a novel medium cut-off Theranova filter may be considered as another possibility for the treatment of light chain amyloidosis. Due to the membrane's pore size and distribution as well as achieved substantial internal filtration, the removal of a wide spectrum of uremic toxins, including both types of free light chains, is extremely effective.

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Extreme uremic pruritus and xerosis cutis in a dialysis patient improved after switching to expanded hemodialysis with a medium cut-off Theranova membrane

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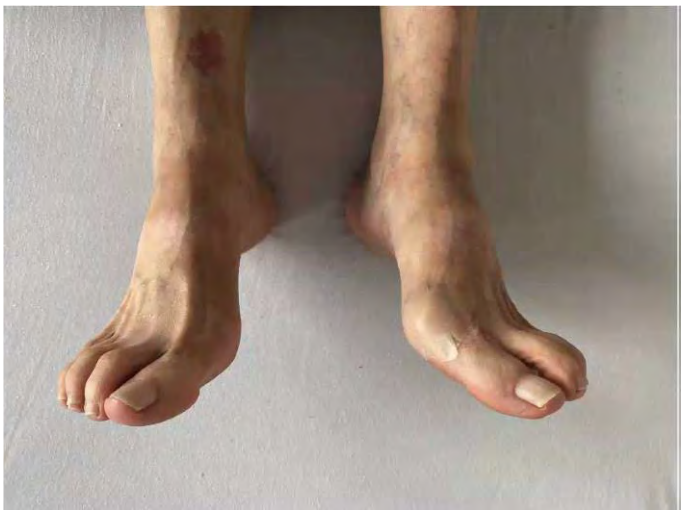
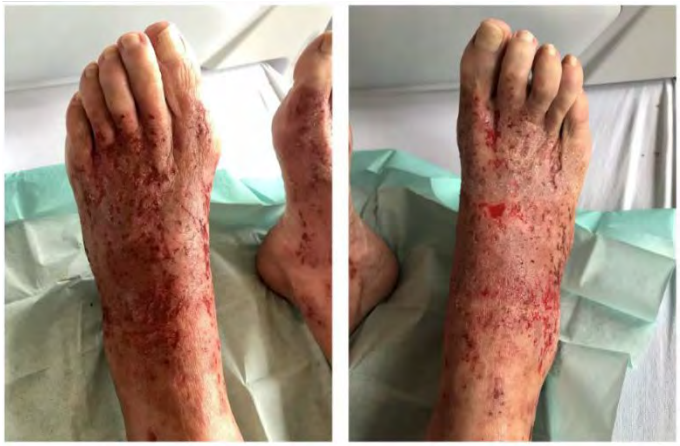
Background: Dialysis patients suffer from a wide range of unpleasant symptoms. Pruritus often leads to anxiety, depression, restless sleep, a markedly decreased quality of life and has been associated with increased hospitalizations and mortality.

Methods: A 78-year-old female with a past medical history of ADPKD was put on dialysis due to ESRD. Her clinical state was stable, RRF was 6-8 ml/min with a urine output of approximately 1800 mL/day She also suffered from xerosis cutis, pruritus and secondary skin changes. Various topical and systemic treatments were tried, however failed to provide relief. Once online hemodiafiltration with a FX 100 filter was started thrice weekly, it was hoped that pruritus would improve. However, this was unfortunately not the case as symptoms even worsened (Figure 1).



QOL drastically declined and depressive symptoms escalated, leading to moderate depression, treated with mirtazapine. Itching caused the patient to scratch the skin on her legs and feet very intensively. This led to a change of filter and mode of dialysis from HDF to expanded hemodialysis (HDx) with a Theranova 400 medium cut-off dialyzer.

Results: The patient started with HDx. Prescribed HDx consisted of 4-hours treatments, dialysate flow of 500 mL/min, blood flow of 300 mL/min. Regular monitoring of small molecular clearance confirmed a consistently delivered Kt/V of >1.3. The patient began feeling relief after 6 weeks of HDx therapy. In the next months skin changes began to heal. She started sleeping through the night, general well-being and energy levels improved significantly. Furthermore, after approximately 1-year, physical evidence of skin irritation completely resolved (Figure 2).



There were no changes in blood pressure, no edema or other adverse effects noted.

Conclusions: MCO membranes facilitate removal of large uremic toxins as well as tissue sodium due to a combination of increased convection and larger membrane pore size, often resulting in symptom improvement.

AUTHOR INDEX (FIRST AUTHORS)

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Editing company:
EMH Swiss Medical Publishers Ltd.
Swiss Medical Weekly
Farnsburgerstrasse 8
CH-4132 Muttenz, Switzerland

ISSN online supplement: 2504-1622