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INTERLAKEN (SWITZERLAND), DECEMBER 5–6, 2019

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ORAL COMMUNICATIONS – BASIC SCIENCE / GENETICS / EXPERIMENTAL NEPHROLOGY

OC 1

A Single Nucleotide Polymorphism of TWEAK predicts Arterio- and Arteriolohyalinosis and Allograft Survival in Kidney Transplantation

Ms. Andrea Karolin[1], Ms. Divya Thottan[1], Ms. Julia Zinsli[1], Dr. Stefan Rudolff[1], Dr. Michael Koller[2], Prof. Uyen Huynh-Do[1], Dr. Vanessa Banz[3], Prof. Berney Thierry[4], Prof. Thomas Müller[5], Prof. Manuel Pascual[6], Dr. Patrizia Amico[7], Dr. Isabelle Binet[8], Dr. Daniel Sidler[1]

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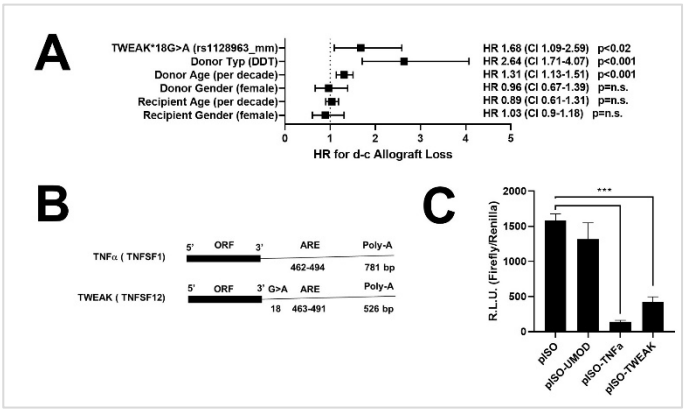
Background
We have recently demonstrated that the TNF superfamily member TWEAK is critical for the pathogenesis of Calcineurin Inhibitor Toxicity (CNT) in vitro and in vivo. CNT is a frequent side effect of calcineurin inhibitor treatment and responsible for long-term allograft deterioration and non-immunological graft loss in kidney transplantation. Although not pathognomonic for the disease, arterio- and arteriolohyalinosis (ah/aah) is characteristic for advanced CNT. So far, factors that predict CNT are elusive.

Methods
We analysed GWAS data from 1484 patients from the Swiss Transplant Cohort Study (STCS) and performed in vitro Experiments utilizing luciferase reporter assays under the control of various 3'UTR segments of TNFa, TWEAK and unrelated genes.

Results
Here, here identified a Single Nucleotide Polymorphism (SNP) within the 3'UTR of TWEAK [rs1128963 (*18G >A)] as an independent predictor for ah/aah lesions (HR 1.37, CI: 1.04-1.81, p <0.05) and for death-censored allograft loss (HR 1.69, CI: 1.68-2.59, p <0.02) [Figure A].
The 3'UTR of genes is important for post-transcriptional regulation and mRNA stability. Within the TWEAK 3'UTR, we identify an AU-rich sequence element (ARE) with potential regulatory activity. [Figure B] Similar regulation via ARE was demonstrated and extensively studied for other pro-inflammatory genes, including TNFa. Using luciferase reporter assays, we demonstrate that the 3'UTR of TWEAK critically represses reporter activity in vitro and thereby likely has important regulatory activity. [Figure C]



Conclusions
In summary, we demonstrate that a common SNP within the 3'UTR of TWEAK independently predicts ah/aahlesions and death-censored allograft loss. The 3'UTR of TWEAK may critically influences mRNA stability and thereby regulate TWEAK expression. Current experiments focus on the precise activity of the 3'UTR in general, and the G18G >A SNP in particular on TWEAK regulation in vitro and ex vivo.

OC 2

Coupling between ENaC γ-subunit and claudin-8 modulates paracellular permeability to Na+ and Cl- in renal collecting duct

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Background
Water and solute transport across epithelia can occur via the transcellular or paracellular pathways. Tight junctions play a key role in mediating paracellular ion reabsorption in the kidney. In the renal collecting duct (CD), a typical absorptive tight epithelium, coupling between transcellular Na+ reabsorption and paracellular permeability may prevent the backleak of reabsorbed solutes and promote the paracellular reabsorption of Cl-. We hypothesized that transcellular Na+ transport controls tight junction composition and paracellular permeability to Na+ and Cl- via the modulation of claudin-8 expression.

Methods
- Cell culture and electrical measurements.
- Measurement of dilution potentials (Ussing chamber).
- Conditional kidney tubule specific ENaC subunit knockout mice.

Results
In cultured CD principal cells, the overexpression and the silencing of ENaC γ-subunit were associated with parallel and specific changes in claudin-8 abundance. Increased claudin-8 abundance was associated with decreased paracellular permeability to Na+ and increased paracellular permeability to Cl- while decreased claudin-8 abundance was associated with opposite effects. These functional effects on paracellular ion permeabilities were reproduced by claudin-8 overexpression and silencing. Conditional kidney tubule-specific ENaC γ-subunit knockout mice displayed decreased claudin-8 expression, confirming the cell culture experiments. Importantly, claudin-8 abundance was not altered in ENaC α-subunit or β-subunit kidney tubule-specific knockout mice.

Conclusions
Together, our data reveal the specific coupling between ENaC γ-subunit and claudin-8 expression. This relationship between transcellular transport and paracellular permeability may play an important role in preventing the back-leak of reabsorbed solutes and water to the tubular lumen as well as coupling paracellular Cl-and transcellular Na+ reabsorption.

OC 3

A comprehensive single-cell map connects vascular heterogeneity to renal physiology

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Background
Endothelial cells are critically involved in renal physiology. Single cell transcriptomics highlighted an unexpected level of vascular heterogeneity across and within organs.

Methods
To map renal vascular heterogeneity, adult mouse kidneys were dissected into 3 zones, corresponding to the renal cortex, the outer medulla, the inner medulla, and each zone was profiled by single-cell RNA sequencing (scRNAseq) (https://doi.org/10.1101/673335). To identify each vascular compartment, we integrated established markers of ndothelial cell identity with new markers validated by enhanced RNA in situ hybridization (RNAscope) and with the anatomical information derived from the separation in zones. The physiological relevance of selected new findings was investigated by functional experiments in transgenic mice.

Results
We obtained the first comprehensive single-cell characterization of renal endothelial cells (figure 1). We found 4 main vascular compartments, corresponding to glomerular endothelial cells, cortical endothelium, vasa recta and interbundle plexus of the outer medulla. Each compartment was characterized by specific markers (validated by RNAscope and immunostaining) and displayed a multidimensional heterogeneity determined by the arterio-venous zonation, the anatomical organization and the specific functions of the vascular compartment. Among the several findings potentially revealing new mechanism of renal physiology, we further characterized the role of Aplnr in the interbundle plexus. The expression of its ligand Apela in the surrounding tubular structures suggested an unappreciated role for Apela/Aplnr in renal physiology. Functional experiments in specifically designed transgenic mice confirmed a mild defect in renal osmoregulation in the absence of Apela or Aplnr.

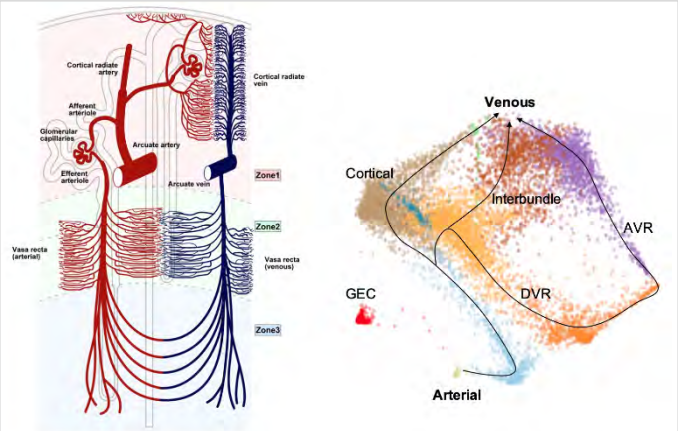

Figure 1 Left panel: schematic anatomical representation of the renal vasculature. *Right panel:* scRNAseq data obtained from renal endothelial cells of the adult mouse. The Similarity Weighted Nonnegative Embedding (SWNE) plot highlights the separation of the renal endothelium in 4 main vascular compartments, as indicated by the arrows: glomerular endothelial cells (GEC), cortical endothelium, vasa recta (DVR: descending vasa recta, AVR: ascending vasa recta), interbundle plexus. The colors indicate the different cell clusters, defined by the single cell transcriptional profile.

Conclusions
We generated a map of the renal vasculature with an unprecedented level of resolution. Single-cell analysis defines novel approaches to understand complex interactions between renal tubules and specific microvascular compartments.

OC 4

Impaired renal gluconeogenesis is a major determinant of acute kidney injury associated mortality

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Background
Acute Kidney Injury (AKI) is associated with adverse outcome and mortality independently of the cause of renal damage. The kidney contributes to up 40% of glucose production by gluconeogenesis during fasting and stress conditions. Whether kidney gluconeogenesis is impaired during AKI and how this influences systemic metabolism remains unknown.d

Methods
We analysed data from renal venous catheterism in 101 undergoing elective cardiac surgery, of whom 17 developped AKI. We further analyzed RNAseq data from kidney biopsies performed at 4 different times points in 43 patients with a kidney allograft . In mice, we use a model of ischemia reperfusion analyzed by bulk RNAseq and by single cell transcriptomics. Finally, we restrospectively analyzed serum glucose and lactate levels in a cohort of 24273 patients admitted to tintensive care unit, with and without AKI.

Results
Renal glucose production and lactate clearance are impaired during human AKI using renal arterio-venous flux obtained by renal vein catheterization. Using single cell transcriptomics in mice and RNA sequencing in human biopsies from kidney allograft patients, we show that glycolytic and gluconeogenetic pathways are respectively up and downregulated during human and experimental AKI in the proximal tubule , explaining the metabolic alterations observed. We further demonstrate that impaired renal gluconeogenesis and lactate clearance following AKI are major determinants of systemic glucose and lactate levels in critically ill patients and in patients imediatly after a kidney allograft, independently of other coufounding factors. Most importantly, altered glucose metabolism in AKI emerged as a major determinant of AKI-associated mortality. Thiamine supplementation restored renal glucose metabolism in vitro and substantially reduced AKI-associated mortality in intensive care patients.

Conclusions
This study highlights an unappreciated systemic role of renal glucose and lactate metabolism in stress conditions, delineates general mechanisms explaining AKI-associated mortality and introduces a potential therapeutic intervention for a condition with limited therapeutic options.

OC5

Time-course of sodium transport along the nephron in nephrotic syndrome: the role of potassium (NCCR project)

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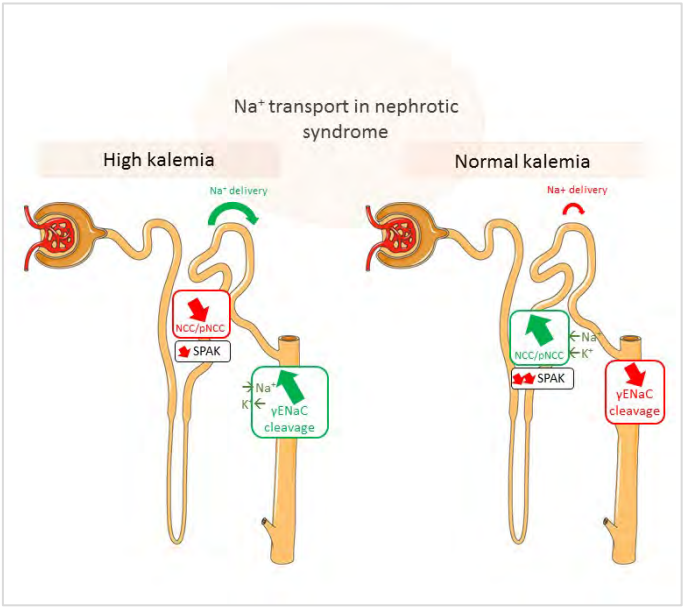
Background
The location along the nephron and the mechanisms of sodium retention in nephrotic syndrome (NS) might be determined by hemodynamics, the rate of proteinuria and GFR.

Methods
We used transgenic POD-ATTAC mice, which display an inducible podocyte-specific apoptosis, to study the mechanisms of sodium retention at different time points (days 2, 3 and 5) after the induction of NS.



Results
At day 2 after NS induction, biological parameters indicated hypovolemia. Increased abundance of NHE3 and phosphorylated NCC suggested that sodium retention mainly occurred in proximal and distal tubules. At day 3 after NS induction, sodium retention was shifted from proximal and distal tubules to the collecting system as suggested by a normalization of NHE3 abundance, a decrease in phosphorylated NCC and an increase in the cleaved form of γ-ENaC. This shift was associated with hyperkalemia resulting from low kaliuresis likely owing to decreased

GFR. Increased cleavage of γ-ENaC persisted at day 5 when hypovolemia was resolved and steady state attained. Sodium retention and γ-ENaC cleavage were independent of increased plasma levels of aldosterone. Feeding nephrotic mice with a low potassium diet prevented hyperkalemia and the shift of sodium retention from the distal tubules to the collecting system. This was suggested by persisting increased phosphorylated NCC, and decreased γ-ENaC cleavage compared with hyperkalemic nephrotic mice at day 3. Phosphorylation of NCC at day 3 in nephrotic POD-ATTAC fed with low potassium mice was independent of SPAK.

Conclusions
These results show that sodium retention in NS displays several successive phases probably relying on local rather than systemic factors. Kalemia and dietary potassium seem to play an important role in the mechanism of sodium retention in nephrotic mice.

OC 6

Regulation of NAD+ biosynthesis pathway in chronic kidney disease

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Background
Chronic kidney disease (CKD) is a major medical burden. Recent studies have highlighted the role of mitochondrial metabolism in CKD pathophysiology. The importance of NAD+ cofactor has been established in acute kidney injury (AKI) but few is known in CKD.

Methods
We analyzed the expression of genes involved in NAD+biosynthesis in 217 biopsies from the European renal cDNA bank Kröner-Fresenius and in post-transplant kidney biopsies. In animals, we used the transgenic PODATTAC mouse model of inducible CKD and unilateral urinary obstruction (UUO) mouse model of kidney fibrosis for CKD. We used ischemia-reperfusion injury (IRI) for AKI model. Tissue NAD+ content was measured by mass spectrometry, renal function by sinistrin clearance. We supplemented the food with 800 mg/kg/day of Nicotinamide Riboside (NR) from one week before CKD or AKI induction until sacrifice.

Results
In humans, NAD+ biosynthesis was impaired in the tubular compartment proportionally to CKD stage and independently of primary renal disease (fig.1). In transplanted patients with AKI, the pathway was also regulated. In POD-ATTAC and UUO mouse models, similar regulations were observed. NAD+ content was decreased in kidney cortex, implying that the observed regulation results in decreased NAD+ synthesis in the tubular compartment. We then used NR supplementation to rescue renal lesions in POD-ATTAC, UUO and IRI models. The treatment could prevent the rise in urea induced by IRI. In CKD models, NR could partially restore kidney NAD+ content. However, renal function as assessed by creatinine and sinistrin clearances was not rescued, nor were histological lesions of fibrosis. Pro-inflammatory, pro-fibrotic and metabolic pathways were not restored either.

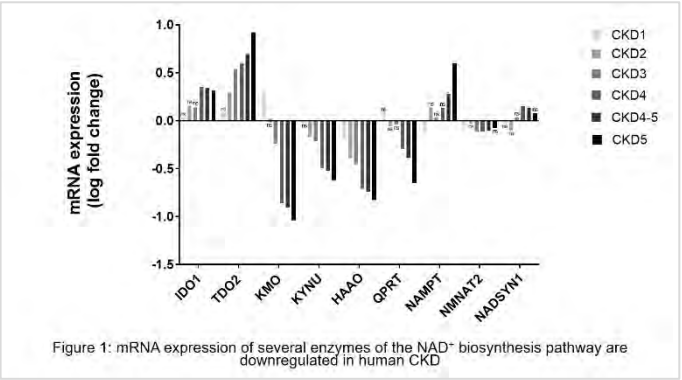

Figure 1: mRNA expression of several enzymes of the NAD^+ biosynthesis pathway are downregulated in human CKD

Conclusions
Our study shows that NAD+ synthesis is altered during AKI and for the first time in CKD in mouse and humans, resulting in low kidney NAD+ levels. NR supplementation is effective in preventing AKI, but not CKD evolution and fibrogenesis in chronic models.

ORAL COMMUNICATIONS – TRANSPLANTATION

OC 7

Impact of kidney transplantation on sleep apnea severity: a prospective controlled polysomnographic study

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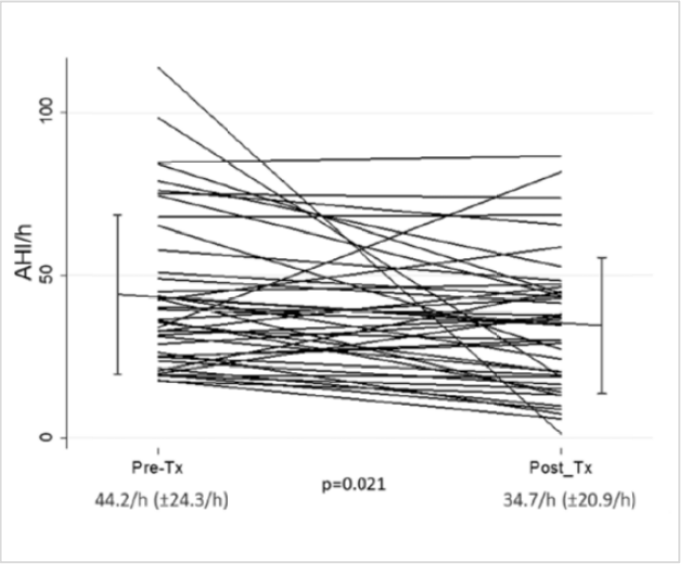
Background
Sleep apnea (SA) is prevalent in patients with end-stage kidney disease (ESKD). Previous studies identified fluid overload as an implicated pathogenic mechanism. Kidney transplantation (Tx) has been shown to restore kidney function and hydration status, but its effect on SA remains unclear. In this prospective study, we hypothesized that improvement of kidney function and hydration status after kidney Tx may result in an improvement of SA severity.

Methods
A total of 196 patients on kidney transplant waiting list were screened for SA using home nocturnal polysomnography (PSG) to measure the Apnea-Hypopnea Index (AHI) and underwent bioimpedance to assess body composition. Polysomnography and bioimpedance were repeated 6 months after kidney Tx. Patients still on the waiting list after 6 months underwent same investigations as a control group.



Results
Of 88 participants (44.9%) with SA (AHI ≥15/h) at baseline, 42 patients were reassessed 6 months post-Tx. There was a significant, although partial, post-Tx improvement in SA severity as measured by the AHI

(from 44.2±24.3/h to 34.7±20.9/h, p = 0.02) (Figure 1). There was a concomitant reduction in body water (from 54.9% to 51.6%, = 0.003), suggesting a causal implication of fluid overload. A post-Tx increase in body fat mass (from 26% to 30%, p = 0.003) may have blunted the beneficial impact of kidney Tx on SA. These parameters remained unchanged in the control group (27 patients).

Conclusions
SA is a frequent condition in ESKD patients. Kidney Tx is associated with a reduction of fluid overload but an increase in fat mass, yielding only a partial improvement in SA severity. These results suggest that SA should be systematically assessed before and after kidney Tx Acknowledgements: This study was supported by the Swiss Kidney Foundation, the Pulmonary League of Canton Vaud (Ligue Pulmonaire Vaudoise) and the Organ Transplant Foundation of Lausanne.

OC 8

Development of a point-of-care application for chemokine CXCL10 quantification after kidney transplantation

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Background
Developing tailored immunosuppressive regimens requires sensitive, non-invasive tools for serial monitoring of subclinical rejection prior to injury, as well as to follow the response to anti-rejection treatment. After kidney transplantation, urinary chemokine CXCL10 is a promising biomarker for early signs of inflammation (i.e. subclinical rejection). Several sensitive tests to quantify CXCL10 exist. However, they are not feasible for a point-of-care application for CXCL10 quantification in an outpatient setting. Therefore, the aim of this project was to develop a lateral flow immunochromatographic assay (LFIA) to measure CXCL10 in the urine compartment with typically a low concentration range.

Methods
In order to develop the LFIA test format several parameters had to be specified (i.e. nanoparticles, lining, nitrocellulose, buffers, pH, additives). Feasibility of the test method was assessed by cross-comparison of CXCL10 concentrations (range 7 pg/mL – 85pg/mL) previously determined in patient urine samples with a sensitive electrochemiluminescent immunoassay.

Results
To measure CXCL10 in such a low concentration range it is necessary to use Eu-chelate nanoparticles (fluorescence beads), which are more sensitive than the visible nanoparticles. The best results were obtained by an antibody density of 80 mg/g and a spraying concentration of 0.01%. As a running buffer, 100mM Tris buffer (pH8) containing 1.1% casein, 1% Tween 20 and 1% Isopropanol was chosen. The results show that under these conditions it is possible to measure CXCL10 concentrations as low as 5 pg/mL in running buffer. However, the results reveal an inter-assay variability >20% and low correlation with previously quantified urinary CXCL10 concentrations.

Conclusions
In conclusion, the first steps of developing a LFIA test system for CXCL10 quantification were successful. It is possible to measure CXCL10 by the LIFA test within the requested concentration range, but due to its high variation with respect to precision and reproducibility further optimization is necessary before clinical use.

OC 9

Glomerular CD68-positive cells - a new prognostic marker in renal transplant pathology

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Background
Transplant glomerulitis is a key feature of antibody-mediated rejection. Leukocytes occluding the glomerular capillaries define its morphological pattern. It is difficult to recognize and its scoring only has a fair interobserver agreement. We aimed to determine and validate a well reproducible immunohistochemical marker for glomerulitis, and looked at its prognostic value.

Methods
Receiver operator curves (ROC) using CD3, CD45, or CD68 positive cell counts in the glomeruli of kidney transplant biopsies with glomerulitis or without relevant pathology were used to determine cut-offs. Findings were independently validated, tested for interobserver agreement, and compared to other rejection patterns. The prognostic value was investigated in a cohort of patients (n = 95) transplanted in the presence of donor-specific antibodies (DSA).

Results
A cut-off >5.5 CD68 positive cells in the most affected glomerulus (CD68max) resulted in an area under the curve (AUC) of 0.966. CD68max correlated with the percentage of glomeruli with CD68 counts above the cut-off (ρ = 0.875). Three risk groups (baseline, low, high) with prognostic impact on graft survival were established using ROC comparing cases with glomerular Banff scores 0 vs. 1 (AUC = 0.891, cut-off >3.9% of glomeruli) and 1 vs. 2-3 (AUC = 0.867, cut-off >64.4%). Interobserver agreement was good and independent of the level of expertise. In the DSA positive cohort, the risk groups proved to be an early and independent prognostic marker of poor graft function.

Conclusions
Addition of a CD68 stain to the routine analysis of kidney transplant biopsies provides additional diagnostic and prognostic information.

OC 10

Outcome of Kidney Transplantation from very, very, very marginal donors

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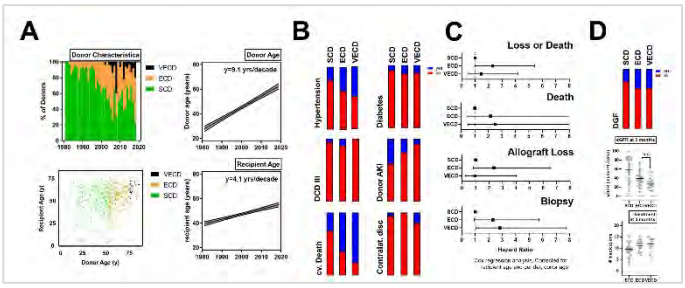
Background
Donor age is one of the most important determinants for allograft outcome in deceased donor kidney transplantation. Donor epidemiology has changed substantially in the last decades with a substantial increase of older and marginal donors.

Methods
Here, we compared donor and recipient age for deceased-donor transplantation at our institution from 01.01.1981 through 31.12.2018 (n = 1400). We further performed an age and gender matched case-control analysis of recipients from standard criteria donors (SCD, n = 38), extended criteria donors (ECD, n = 37) and very extended criteria donors (VECD, defined as donor age above 75 years, n = 25) in respect of patient and allograft outcome, allograft function and pill burden at three months.

Results
VECD had a higher prevalence of hypertension and cardiovascular death compared to SCD and ECD. Meanwhile, DCD procurement and donor AKI was rare. Contralateral kidney was discarded 16% of patients in VECD donors. Hazard for death, allograft loss or Indication Biopsy within 3 months was increased in recipients of organs from VECD compared to SCD, yet outcome was comparable to recipients from ECD kidneys. eGFR was 57, 38 and 28 ml/min/1.73 m^2 at three months post TPL.



Conclusions
In summary, for well selected donors and recipients, VECD may be a useful source to expand the kidney donor pool with satisfactory patient and allograft outcome.

OC 11

Circular RNAs in urine as biomarker of acute T cell-mediated renal allograft rejection

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Background
Circular RNAs (circRNAs) have recently been described as novel non-coding regulators of gene expression. They are detectable in the blood of patients with acute kidney injury. We tested whether circRNAs are present in urine and may serve as new predictors of outcome in renal transplant patients with acute rejection.

Methods
A global circRNA expression analysis using RNA from urine of patients with acute T cell-mediated renal allograft rejection and control transplant patients was performed. Dysregulated circRNAs were confirmed in a cohort of 62 patients with acute rejection, 10 patients after successful anti-rejection therapy, 18 control transplant patients without rejection and 13 stable transplant patients with urinary tract infection.

Results
A distinct urinary circRNA transcriptome signature identified patients with acute rejection. CircRNAs hsa_circ_0001334 and hsa_circ_0071475 were strongly altered and validated in the whole cohort. Increased hsa_circ_0001334 concentrations were specifically confirmed in patients with acute rejection and returned to base level after successful anti-rejection therapy. In addition, hsa_circ_0001334was associated with a higher decline in creatine clearance one year after transplantation.

Conclusions
CircRNAs are strongly altered in urine of patients with acute rejection. Urinary hsa_circ_0001334may serve as a novel biomarker of acute kidney rejection, identifying patients with acute rejection and predicting loss of kidney function.

OC 12

Impact of an intra-abdominal cooling device during open kidney transplantation in pigs

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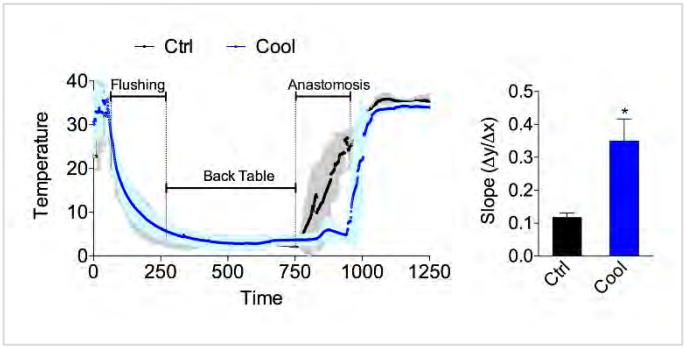
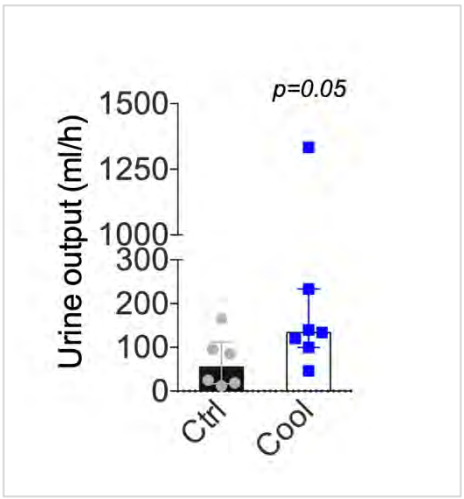
Background
Kidney transplantation using deceased donors still suffers from high post-operative dysfunction rate. During implantation into the recipient, the kidney rewarms. This second warm ischemia time, which is not monitored, is harmful especially if prolonged. We recently developed an intra-abdominal cooling device that efficiently prevents kidney rewarming during robotic transplantation, and prevent ischemia-reperfusion injuries. Here, we tested the benefits of this cooling device during open kidney transplantation in pigs.

Methods
Kidneys were procured from large pigs by open bilateral nephrectomy. Following procurement, kidneys were flushed with 4°C Institut Georges Lopez-1 preservation solution, and placed on ice. Animals then underwent double sequential autologous open renal transplantation with (n = 7) and without (n = 6) intra-abdominal cooling.

Results
Mean anastomosis time was similar between groups (43.9 ± 13 min). At reperfusion, the renal cortex temperature was lower in the group with cooling (4.3 ± 1.1°Cvs 26.5 ± 5.5°C p <0.001, Figure 1).



The cooled kidneys tended to be protected from injury, including some histopathological ischemia–reperfusion lesions. With the device, kidneys had a better immediate post-operative urine output (p = 0.05, Figure 2).



Conclusions
Our results indicate that the intra-abdominal cooling device significantly reduces second warm ischemic time during transplantation, is technically safe, and does not prolong anastomotic time.

ORAL COMMUNICATIONS – CLINICAL NEPHROLOGY / HYPERTENSION / MINERAL / ELECTROLYTES

OC 13

Doppler and contrast-enhanced ultrasound responses to a cold pressure test in healthy normotensive participants

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Background
The cold pressure test (CPT) is a classic cardiovascular stress test known to increase blood pressure and heart rate secondary to an increase in nervous sympathetic activity. Its effect on renal hemodynamics using both Doppler ultrasound (DU) and contrast-enhanced ultrasound (CEUS) has not been reported previously. We hypothesized that a CPT would induce changes in renal hemodynamics detectable by DU and CEUS. The objective was to measure the renal responses to a CPT using DU and CEUS.

Methods
This was as single center prospective study in healthy participants. Renal resistance resistive index (RRI) and acceleration time (AT) were measured 4 times during baseline conditions and 4 times during a 2 minutes CPT. The same protocol was repeated after 5 minutes pause for the measurement of the perfusion index (PI). Renal hemodynamic responses during baseline and CPT were compared with a t-test or a Wilcoxon matched-pairs signed-ranks test if variables were not normally distributed.

Results
18 healthy participants (12 women,6 men) were included. Mean age and body mass index were respectively 33.2±10.2 years and 23.7±3.4 kg/m^2. The CPT increase mean blood pressure by 12.5±2.1 mmHg, heart rate by 7.1±2.1 beats per min. The CPT decrease RRI from 0.60±0.04 to 0.57±0.05 (p = 0.02). Mean acceleration time did not change. Perfusion index increased from 2570 UI (1450;5610) to 4650UI (3127;8720), p <0.001.

Conclusions
This is the first demonstration that the CTP induces changes in renal hemodynamics expressed by lower RRI and increase PI. The CPT combined to DU and CEUS may be a valuable tool to assess the renal response to increased sympathetic drive in nephrologic or hypertensive patients.

OC 14

Diffusion MRI predicts a worse outcome in CKD and kidney allograft patients independently of eGFR

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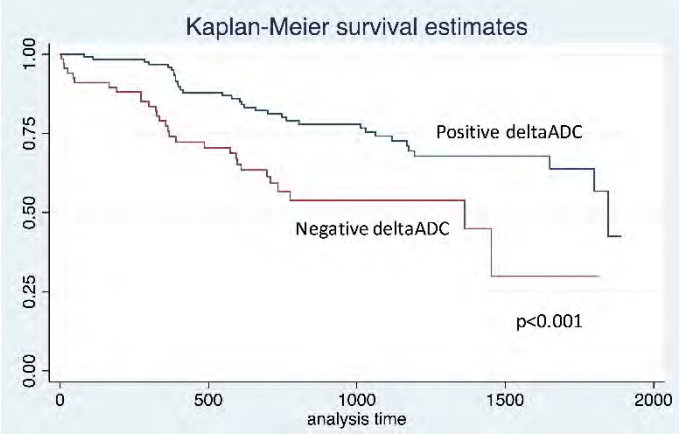
Background
Diffusion magnetic resonance imaging (MRI) is a promising non-invasive tool to evaluate kidney fibrosis. The cortico-medullary apparent diffusion coefficient difference (ΔADC) correlated to histological IF in our previous studies. The aim of this study was to assess whether ΔADC as measured with DWI-MRI is independently associated with a mixed endpoint of rapid decline of renal function, death, dialysis or MACE in native and allograft patients.

Methods
We performed a prospective study including 192 patients having undergone diffusion MRI. Patients underwent renal biopsy and diffusion-weighted imaging, within 1 week. Followup was 2.5 years in median. Event was defined as rapid decline of renal function (eGFR decline >30% ml/min/1.73m^2), death, dialysis or MACE.

Results
Patients were categorized into positive or negative ΔADC (differential between cortical and medullary ADC). Negative ΔADC occurred in 36% of patients. Patients with negative ΔADC had 2.5 more risk of rapid decline of renal function, dialysis, death or MACE (HR 2.5 95%CI: 1.5-4.1; p <0.001) compared to those with positive values. If we corrected for baseline eGFR, low ADC still predict bad renal evolution with an HR of 1.8 (95%CI: 1.09-3.3).



Conclusions
We show in this study that low ΔADC is an independent predictor of renal function decline, dialysis and death in CKD and kidney allograft patients.

OC 15

Pregnancy as a trigger for diagnosis of unknown maternal diseases: the importance of early detection

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Background
Women who developed hypertensive disorders during pregnancy are more likely to be tested postpartum for an underlying maternal disease. Though not systematically screened, in women without known risk factors, an abnormal adaptation to pregnancy could be an early sign of underlying maternal disease. The aim of this study was to determine the incidence of underlying medical disorders that had not been suspected prior to the index pregnancy.

Methods
Maternal clinical data and pregnancy outcomes of 103 consecutive women who attended the interdisciplinary NefrocentroTicino outpatient clinic were reviewed. Pregnancies were subdivided into two groups: those with known (KRF) and those with no known (NRF) risk factors for pregnancy at booking. History of hypertensive disorders in previous pregnancies, systemic diseases and/or renal diseases were classified as risk factors. The diagnosis of a maternal underlying disease was analyzed according to the gestational age in term of hypertensive disorders, renal disease and any other medical condition.

Results
In total, 103 pregnant women (age ± SD 32 ± 5 yrs) were included in the analysis. 60 pregnancies were classified as KRF (age 31.7 ± 4.9 yrs) and 43 (age 32.5 ± 5.3 yrs) as NRF. Overall underlying maternal diseases were diagnosed in 26.2% of 103 pregnancies. They included 13 hematological, 2 renal, 8 endocrine/metabolic disorders and 1 malignancy. Of 11/60 (18.3%) KRF pregnancies with underlying maternal disease, 8/11 (72.7%) were diagnosed in pregnancy and 3/11(27.3%) postpartum. In contrast of 16/43 (37.2%) NRF pregnancies, underlying maternal disorders were discovered in 6/16 (37.5%) during pregnancy and in 10/16 (62.5%) postpartum.

Conclusions
Pregnancy can be a trigger for the diagnosis of a pre-existing medical condition. Therefore, understanding and monitoring the physiological ad-

aptation to pregnancy is of primary importance. However, larger population studies are needed to determine the usefulness of an early gestation interdisciplinary approach in pregnancies with unknown risks.

OC 16

Acute and chronic effects of sodium/glucose cotransporter2 inhibition with empagliflozin on renal oxygenation in non-diabetic volunteers. A randomized, double-blind, placebo-controlled study

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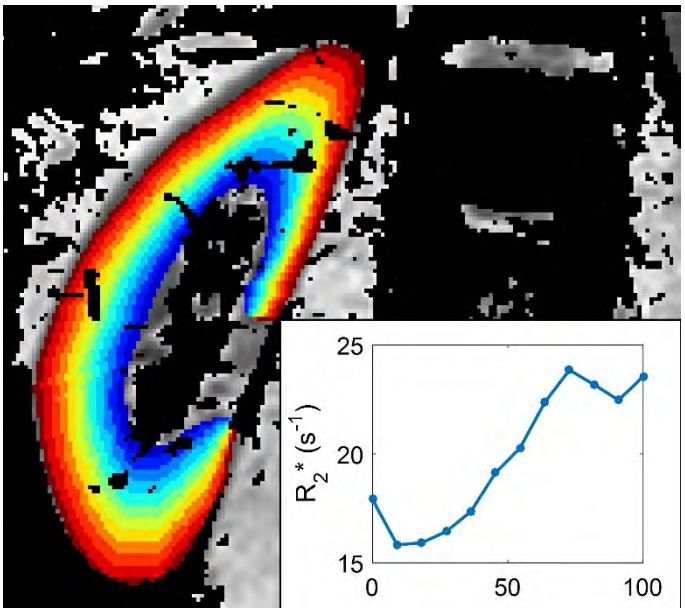
Background

The sodium/glucose cotransporter 2 (SGLT2) inhibitor empagliflozin has nephroprotective properties in high cardiovascular risk patients with type 2 diabetes. Decreased glomerular hyperfiltration is the main proposed mechanism. Whether empagliflozin has an effect on renal tissue oxygenation as an additional contributor to renal protection was explored in this healthy volunteer study.

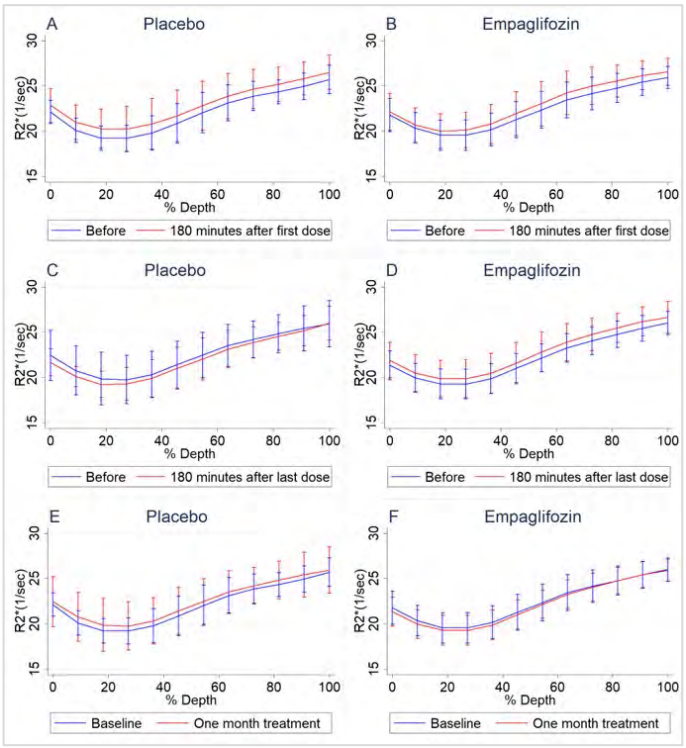
Methods

This double-blind, randomized, placebo-controlled study examined the acute and chronic effects of empagliflozin 10mg on renal oxygenation as measured by blood oxygenation-level dependent (BOLD-MRI) in 45 healthy normotensive volunteers. Clinical, blood, urine, renal ultrasound and BOLD-MRI parameters were studied at baseline and after one-month treatment. BOLD-MRI measurements were performed before and 180 minutes after empagliflozin or placebo on both occasions. MR images were analyzed using the twelve layer concentric objects (TLCO) technique, a semi-automatic procedure which divides the kidney parenchyma in 12 equal layers at increasing depth (figure 1). R2* was measured at each layer, with high R2* values corresponding to low oxygenation.



Results

Empagliflozin was associated with a rapid and sustained increase in glucosuria. Decreased proximal sodium reabsorption with empagliflozin as determined by endogenous fractional excretion of lithium was compensated after one-month therapy by the rise in plasma renin activity and aldosterone. 24h-Blood pressure decreased (from 117±9 to 112±9 mmHg, p <0.005) and hematocrit increased with empagliflozin while erythropoietin remained the same. R2* values were not altered by empagliflozin nor placebo at all times (figure 2).



Conclusions

Empagliflozin has a rapid and significant effect on tubular function with sustained glucosuria and transient natriuresis. These effects favor blood pressure reduction. No significant acute or sustained changes were found in renal cortical or medullary tissue oxygenation in our healthy subjects suggesting that changes in renal oxygenation might not be the prominent factor of renal protection with SGLT2 inhibitors. Whether this is also true in patients with type 2 diabetes needs further study.

OC 17

An algorithm for the metabolic evaluation of calcium oxalate stone formers

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Background

The metabolic evaluation of calcium oxalate stone formers guides treatment and dietary recommendations. It is indicated for all recurrent stone formers and thus, frequently performed. Its analysis is time consuming and its interpretation might be difficult and prone to error. We aimed to develop a rapid and accurate algorithm to analyze the results of the evaluation.

Methods

The algorithm consists of conditional statements and runs in STATA in approximately 3 seconds.

Input:

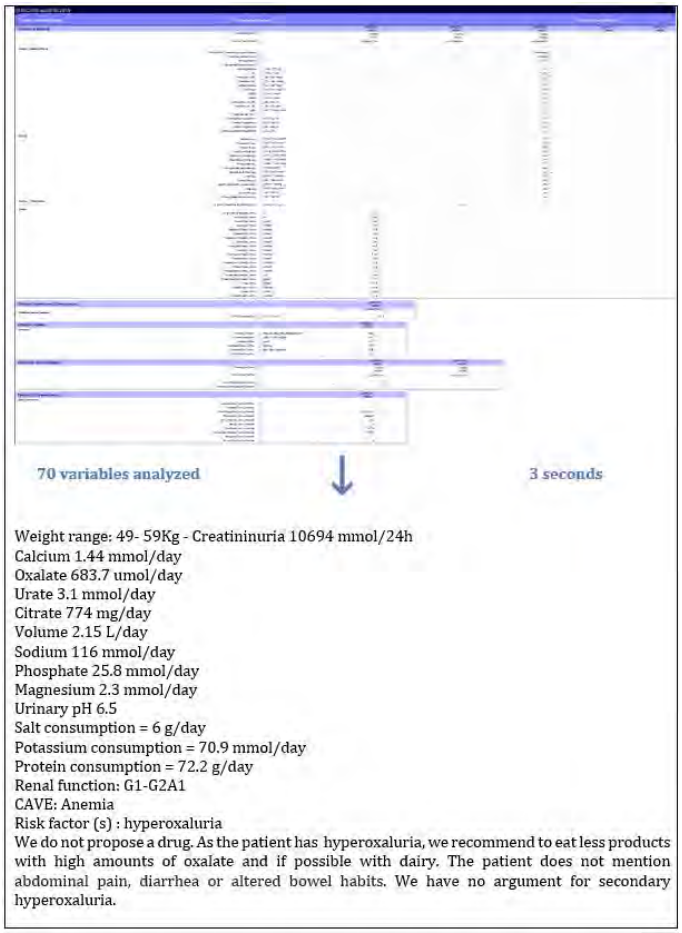
- An Excel sheet with laboratory results (venous blood gas, blood chemistry panel, electrolytes concentrations from the 24h urine collection)

Results

Output:

- The expected weight of the patient based on the 24h creatininuria
- 24-hour excretion rate of electrolytes, the estimated protein and salt consumption per 24h in grams
- Renal function in KDIGO categories
- A list of all abnormal variables (hyperparathyroidism, acidosis, hyperkalemia, …)
- Presence or absence of patterns associated with the Fanconi syndrome (phosphaturia, renal glucosuria) or incomplete distal renal tubular acidosis (hypocitraturia, urinary pH >5.5, K <3.8 mmol/L)
- A list of the risk factors for calcium-containing stones (hypercalciuria, high sodium intake, high protein intake, hyperoxaluria, hypocitraturia,

low urinary volume) • A template for the medical report with treatment propositions and dietary recommendations.



Conclusions
We developed a rapid algorithm for the interpretation of the metabolic evaluation of calcium stone formers. Its utility and its time saving capacity need to be validated in further studies. EQUIL2 or other programs for the estimation of urinary supersaturation could be added to have a complete evaluation.

OC 18

Uric acid containing stones within the Swiss Kidney Stone Cohort - NCCR Kidney.CH

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Background
The Swiss Kidney Stone Cohort (SKSC) is a unique longitudinal multicentric cohort of stone formers in Switzerland. It is accompanied by a control group matched for age and gender of population-based controls with proven absence of kidney stone on CT-scan. It aims at providing local epidemiological data on the stone former population in Switzerland and at establishing a platform for research. We now report about a specific subgroup of SKSC stone formers who passed uric acid (UA) containing stones.

Methods
On August 1, 2019, SKSC recruited 749 stone formers and 123 controls. They were all investigated with 2x24h urine collection, blood and hormonal analysis and a detailed food intake interview performed by dieticians. Urine and blood were biobanked and DNA was extracted. Patients had analysis performed at baseline, at 3 months and then annually.

Results
Stone composition analysis was available for 620 stone formers among 749 patients (83%). A total of 53 stones (8.5%) contained uric acid, including 14 of pure UA and 39 made of mixed UA and calcium salts. Among the latter, mean UA content was 62.4%, mean CaOx monohydrate content was 30.0%, mean CaOx dihydrate was 5.4% and the rest (2.2%) was ammonium urate. SKSC data also show that 4.5% of all stone formers have high fractional excretion of uric acid (FEUA >12%) and that 14.8% and 1.2% of female and male stone formers, respectively, had serum uric acid level (SUA) lower than200umol/l.

Conclusions
Stone formers recruited by SKSC and from which stone analysis is available showed lower than expected uric acid containing stones. This might indicate a recruitment bias. However, significant number of patients had high UA fractional excretion and low SUA, suggesting renal leak as being a major contributor to stone formation. Further analysis (including genetic) will help resolving these issues.

ORAL COMMUNICATIONS – HEMODIALYSIS / PERITONEAL DIALYSIS

OC19

Monthly measurement of high-sensitivity cardiac troponins T (hs-cTnT) and creatine kinase (CK and CK-MB) in asymptomatic chronic haemodialysis patients: a one-year study

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Background
Chronic haemodialysis (HD) patients suffer an excessive cardiovascular burden, in regards to the general population. Recent cardiological guidelines recommend dosing the hs-cTnT for the diagnostic workup of acute coronary syndromes (ACS) and, at present time, most hospitals in Switzerland measure this biomarker. However preliminary data have shown that hs-cTnT are already higher than normal in many HD patients without evidence of ACS. The aim of this study was therefore to measure the monthly levels and evaluate the fluctuations of hs-cTnT in comparison with creatine kinase (CK and the CK-MB) levels in asymptomatic HD patients.

Methods
44 asymptomatic chronic HD patients (mean age 67±14 years, 33 males) could be followed for a one-year period. Exclusion criteria were: suspicion of ACS and/or a recent myocardial infarction. The predialysis levels of hscTnT, CK and CK-MB were measured monthly for 12 months with a Cobas 6000 analyzer (Roche Diagnostics).

Results
The figure shows the monthly evolution of the studied biomarkers, showing small non-significant fluctuations of the means values. The mean (±SD) level of hs-cTnT during the study year was 84.8±59.7 ng/l, much higher than the normal range (N <14), and the individual values were higher than normal in 99% of the measurements. For CK and CK-MB the mean levels remained within the normal range and were respectively 88.4±69.5 U/l (N <170) and 15.7±5.8U/l (N <25), with higher than normal values in 8.8% and 4.2% of the measurements.

Conclusions
These results show that the hs-cTnT are almost always higher than normal, and often much higher, in all HD patients. This was not the case for the third generation cardiac troponin I assay previously used in our institution. Obviously the standard algorithm for the diagnosis of an ACS based on hs-cTnT kinetics cannot be used in HD patients and alternative diagnostic strategies have to be developed.

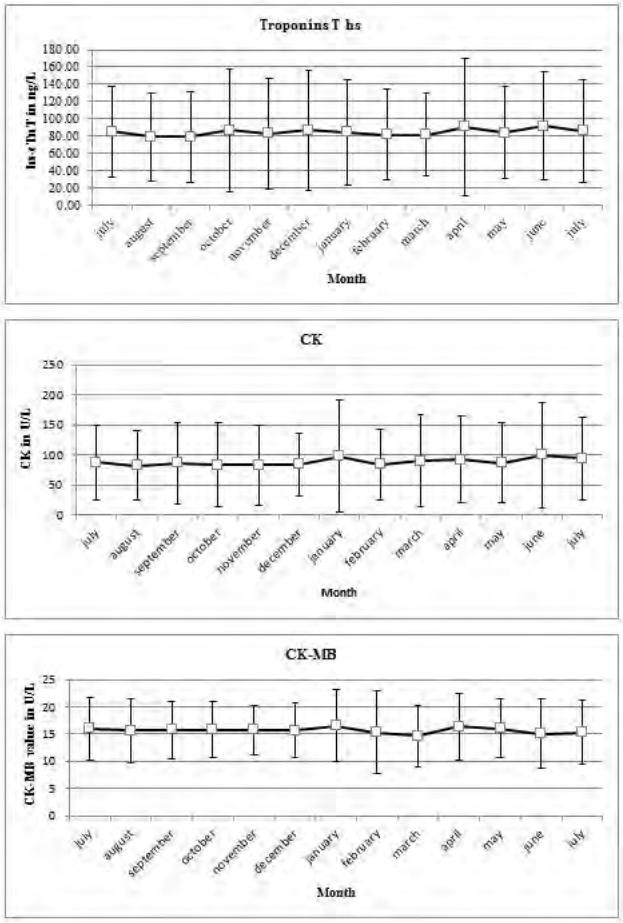

Figure 1:
Mean ± SD levels of hs-cTnT, CK and CK-MB, and their fluctuations during time.

OC 20

Plasma proteomics identifies VEGFD as a biomarker of fluid overload in hemodialysis patients

Dr. Seraina von Moos[1], Prof. Stephan Segerer[2], Prof. Andrew Davenport[3], Mrs. Malha Sadoune[4], Mr. Kerem Gerritsen[1], Prof. Julien Pottecher[5], Prof. Frank Ruschitzka[6], Prof. Alexandre Mebazaa[4], Dr. Mattia Arrigo[6], Dr. Pietro Cippà[7]

[1]University Hospital Zurich, Nephrology, Zurich, Switzerland, [2]Kantonsspital Aarau, Nephrology, Aarau, Switzerland, [3]Royal Free Hospital, University College London Medical School, London, Great Britain, [4]INSERM UMR-S 942, MASCOT, Université de Paris, Paris, France, [5]Hôpitaux Universitaires de Strasbourg, Department of Anaesthesiology and Intensive Care, Strasbourg, France[6]University Hospital Zurich, Cardiology, Zurich, Switzerland, [7]Regional Hospital of Lugano, Nephrology, Lugano, Switzerland

Background
Improved understanding and assessment of the complex physiology of volume regulation in hemodialysis (HD) patients is required to improve patient care and reduce mortality associated with fluid overload (FO).

Methods
We searched for FO-related biomarkers among 184 cardiovascular peptides by applying an unbiased analytical approach in a cohort of 30 HD patients. First, we assessed the direct impact of HD on cardiovascular peptides by comparing plasma concentrations before and after treatment. Then, we compared cardiovascular peptide profiles between patients with and without FO as defined by bioelectrical impedance measurement (BCM). Plasma concentration of selected candidate biomarkers for FO was determined by ELISA and correlated with previously described FO related clinical and laboratory parameters. For validation, results were confirmed in an
independent cohort of 144 HD patients.

Results
We found 7 peptides positively (NT-proBNP, BNP, VEGFD, TRAIL-R2, GDF15, TNFSF13B, CHI3L1) and 5 negatively (LEP, REN, EGFR, IL1RA, PRTN3) correlated to FO. In addition to NTproBNP and BNP, VEGFD emerged as third peptide highly correlated with BCM results (rho 0.619, p <0.0001). In line, VEGFD concentration by ELISA correlated with BCM, BNP and sCD146 but not with VEGFC. Notably, levels of VEGFD were unrelated to cardiac systolic function (p = 0.63) contrary to BNP (p = 0.0003). Finally, we observed that 1-year all-cause mortality was higher in patients with high BNP (p = 0.0002), FO (defined by BCM, p = 0.04), and high VEGFD (p = 0.02), but not with high VEGFC (p = 0.48).

Conclusions
VEGFD is a novel FO-related biomarker with unique diagnostic and prognostic properties.

OC21

Incremental hemodialysis : a single center experience

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Background
Preservation of residual renal function (RRF) in maintenance hemodialysis (HD) patients is associated with better survival and quality of life. RRF may be more preserved with an incremental HD regime in patients starting HD. Since 2013, incremental HD (frequency <3x/week) has been used in our center.

Methods
Incremental HD is suggested for incident HD patients who have a daily residual diuresis >600 ml, an urea clearance >3 ml/mn and an interdialytic weight intake <2,5 kgs. Patients are clinically assessed every week and a 24 hr-urine sample is collected every other month in order to measure residual diuresis and RRF.

Results
From January 2000 to December 2017, 583 patients started chronic HD in our center. Among them, 25 patients started maintenance HD with an incremental regime (22 since 2013). These patients did not differ from those with a thrice-weekly HD regime in terms of age, comorbidity score and GFR at dialysis initiation. Among those 25 patients, two could retrieve a sufficient RRF to become dialysis-independant . Among the remaining 23 patients, residual diuresis and urea clearance at incremental HD initiation were respectively 1676 + 645 ml and 4.1 + 2.3 ml/mn. Duration of incremental HD until transition to a thrice-weekly HD regime or death was 20 (8-35) months (median + IQR). Within the first dialysis year, survival (81 vs 90% ; p = 0.17) and hospital-free days (321 (220-350) vs 335 (285-356) ; median + IQR) did not differ between patients with a thrice weekly HD regime and those with incremental HD.

Conclusions
These preliminary results may suggest that incremental HD can be implemented in patrients with an adequate RRF but with subsequent regular RRF measurements and clinical examinations. However, randomised clinical trials assessing long-term survival and quality of life in incremental HD are necessary prior to its large-scale implementation.

OC 22

Hepatitis E virus prevalence in a small rural dialysis unit

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Background
Hepatitis E virus prevalence is generally higher in dialysis patients than in the general population with OR up to 2.47. The seroprevalence in Swiss blood donors is declining over two decades from 30.3% in 1997/98 to 27.0% in 2006 and 22.3% in 2015/6. The older the population the higher the seroprevalence with a 3% higher prevalence in male subjects. About 10% of pork liver sausages and raw meat sausages test positive for Hepatitis E DNA in Switzerland. Most isolates are genotype 3. Limited data is available on seroprevalence in dialysis patients in Switzerland.

Methods
In 2016 all 15 dialysis patient were tested for the presence of IgG, IgM and viral load. All new and all negative patients had a yearly control. For two patients data were not available (n.a.) in the year 2017 and 2018 respectively. They were counted as negative.

Results
6 of 15 (40%) dialysis patients tested positive for IgG. One immunosuppressed patient was positive for IgM only and died before PCR testing

could be performed. No viral load could be detected in positive patients. The total number of 46.7% positive patients ranges in a worldwide comparison at the highest level for dialysis patients. In contrast to published data less men were seropositive for hepatitis E than women (male 3/9, female 4/6). In 5 patients followed for at least one year no seroconversion could be observed. No difference of the duration of dialysis could be detected between the two groups (seropositives median 20 month, range 211, seronegatives median 23.5 month, range 54).

Patient	Sex	Age (2016)	Month dialysis	2016	2017	2018
1	m	66	2	neg	neg	neg
2	m	66	6	positiv	positiv	positiv
3	f	75	32	neg	neg	
4	m	56	15	neg	n.a.	n.a.
5	f	66	217	positiv	positiv	positiv
6	f	63	15	neg	neg	n.a.
7	m	79	48	positiv	positiv	
8	m	87	56	neg		
9	m	84	50	neg	neg	neg
10	f	82	73	positiv	positiv	positiv
11	m	68	19	positiv	positiv	
12	f	79	19	positiv	positiv	positiv
13	m	73	23	neg		
14	f	34	20	IgM pos/IgG neg		
15	m	59	24	neg	neg	neg
16	f	46			neg	neg
17	m	63			neg	neg
18	m	67				positiv
19	m	73				neg
20	m	70				neg
21	m	59				neg
22	m	86				neg
Median		67.5	23			
Positive				7/15 (46.7%)	6/14 (42.9%)	5/16 (31.3%)

Conclusions
In a rural area of the Canton of Berne one third to almost one half of the dialysis patients tested positive for hepatitis E. No seroconversion could be observed. The reason for the higher prevalence of hepatitis E in dialysis patients is not known.

OC 23

Identifying factors associated with mortality in young patients on chronic hemodialysis – a machine learning approach

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Background
Mortality in pediatric end-stage renal disease patients is significantly higher than in healthy children, and higher on chronic dialysis than after kidney transplantation. We aimed to identify factors associated with mortality in pediatric and young adult patients on maintenance hemodialysis (HD).

Methods
Data originate from a cohort of patients <30 years on chronic HD since childhood (≤19 years), having received thrice-weekly HD between 2004 and 2016 in outpatient DaVita dialysis centres. Patients with 5-year follow-up since initiation of HD, or death within 5 years, were included. A total of 105 variables relating to demographics, HD treatment and laboratory measurements were evaluated as predictors for 5-year mortality utilizing a machine learning approach (random forest). Among correlated predictors (ρ >0.7) the variable with higher clinical significance was retained.

Results
A total of 363 patients were included in the analysis. In 84 patients HD was initiated <12 years, in 279 patients between 12-19 years of age. Low albumin and increased lactate dehydrogenase were the two most important predictors of 5-year mortality. Other predictors included (a) increased: red blood cell distribution width and blood pressure and (b) low: red blood cell count, hemoglobin, albumin/globulin ratio, ultra-filtration rate, zscore weight for age, and spKt/V (below target). Mortality was predicted with an accuracy of 81%.

Conclusions
Mortality in pediatric and young adult patients on chronic HD is associated with multifactorial markers of nutrition, inflammation, anemia and dialysis dose. This highlights importance of multimodal intervention strategies besides adequate HD treatment as determined by Kt/V alone. The association with elevated lactate-dehydrogenase was not expected, but may indicate relevance of blood-membrane interactions, organmalperfusion or hematologic and metabolic changes during chronic HD treatment.

OC 24

Anemia management in dialysis patients in Switzerland

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Background
Anemia is highly prevalent in dialysis patients and is associated with increased morbidity and mortality. The purpose of the present analysis is to evaluate current anemia management in dialysis patients in Switzerland collected from the Swiss Dialysis Registry (srrqap), which covers all dialysis patients in Switzerland

Methods
All medical establishments in Switzerland (both public and private; N = 92) providing chronic treatment by either hemo- and/or peritoneal dialysis, had to provide relevant data for the year 2018. All individuals being on chronic dialytiy therapy in the year 2018 were enrolled (N = 4646). To calculate survival probabilities, all deaths from incident dialysis patients between 2014 and 2018 were analyzed.

Results
65 percent of all dialysis patients receive iron and EPO. Regardless of anemia management, 82% of patients reach target hemoglobin levels of 10 g/dl. In 18% of patients inadequate management to reach Hb targets may be suspected. The distribution of iron and EPO substitution is similar in all age groups. However, 26% of the age group 20-44 years receive EPO, but no iron, compared to only 15% in the other age groups. Survival analysis by Cox Regression adjusted for age, Charlson score and treatment modality revealed that patients with Hb levels equal or greater than 11 g/dl have the best survival (reference group). In comparison, patients in the Hb categories below 9, 9-9.9 and 10-10.9 g/dl have an odds ratio of 3.9, 2.0 and 1.3, espectively, to die.

Table 1: Overview of iron and EPO substitution in dialysis patients, stratified by hemoglobin concentration

		Hemoglobin (Hb), g/dL			
Iron / EPO-Substitution	All	<= 8.9	9-9.9	10-10.9	>= 11.0
Iron no / EPO no, %	8.5	2.6	8.3	20.2	69.0
Iron no / EPO yes, %	16.6	9.3	13.6	28.7	48.4
Iron yes / EPO no, %	9.8	0.7	3.8	17.2	78.3
Iron yes / EPO yes, %	65.1	7.3	13.0	26.3	53.4

Conclusions
Anemia management to reach Hb target levels following KDIGO guidelines seems to be adequately implemented among dialysis patients in Switzerland. In 18% of patients treatment might be optimized to achieve Hb targets. As expected, patients with Hb levels equal or greater than 11 g/dl have better survival rates compared to patients with lower Hb values.

POSTER PRESENTATIONS – BASIC SCIENCE / GENETICS / EXPERIMENTAL NEPHROLOGY

P 1

Metabolomic study can predict long term renal function

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Background
Metabolomics could be used as a tool to assess kidney function in a routine and non invasive way. This could lead to earlier detection of kidney disease by the identification of new biomarkers. We measured serum and urinary metabolites at the beginning of an eGFR time series to search for candidate metabolites that could be predictive of eGFR evolution. Herein we would like to propose metabolites which could be associated with changes in glomerular filtration rate (eGFR).

Methods
We measured metabolites in urine and serum with nuclear magnetic resonance (NMR) in a subset of 837 participants of the Colaus cohort together with eGFR estimated by CKD-EPI to assess renal function and other clinical parameters. Most participants had repeated eGFR measurements during a period of up to 10 years. A metabolite wide association study was run with eGFR as outcome and the nmr peaks as predictor with adjustments for sex, uric acid, calcium and urinary creatinine. The resulting nmr pseudospectrum contains features that are associated with eGFR and can be matched to specific compounds whose concentrations have significant outcome determination.

Results
We have identified candiate metabilites in serum and urine that are associated with eGFR changes over 10 yeares. The most relevant serum hits are: tyrosine , myoinositol , 1-methylhistidine, tryptophan and acetylcarnitine. The most relevant urinary hits are: N-acetylneuraminate, 3-aminoisobutyrate, 3-methyl-2-oxovalerate, glucarate and arabinose, some of which have already been described in the literature.

Conclusions
With the method described and the time course chosen we have obtained a list of candidate metabolites that might be predictive for future kidney function decline. In comparison with the majority of case control studies comparing metabolites of healthy and diseased at a fixed time point our results might help develop a score to delineate patients that are at high risk of developing ckd with age.

P 2

Pharmacological inhibition of H2S synthesis protects against renal crystallopathy

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Background
Renal crystallopathies is a group of diseases characterized by deposits of crystals within the renal tubules that eventually induce an inflammatory response, fibrosis and terminal renal insufficiency. Hydrogen sulfide (H2S), a gaseous signaling molecule, is a mediator of inflammation. Cystathionine-gamma-lyase (CSE), one key enzyme contributing to local production of H2S, is expressed in the renal cortex and the medulla. Cse-/- mice showed a strong reduction in renal inflammation and fibrosis in a mouse model of renal calcium oxalate nephropathy. Now, we hypothesize that pharmacological inhibition of H2S may be beneficial in renal crystallopathy.

Methods
In vitro, inhibition of H2S synthesis by DL-propargylglycine (PAG) was assessed by the methylene blue method in kidney lysates. In vivo, 12 week-old C57BL/6N male mice were exposed to either crystal-forming diet (1.5% hydroxyproline, 1.5% CaCl2) or to control diet. Further, each diet group received daily i.p. injection of either PAG or PBS. After 10 days of treatment, liver, intestine, urine, blood and kidney were harvested. Inflammation and fibrosis were evaluated by Masson trichrome staining of kidney sections and by qPCRs.

Results
In vitro, PAG inhibited H2S synthesis in a dose response manner. In vivo, after 10 days on crystal forming diet, mice developed renal calcium oxalate crystallopathy, characterized by crystal deposition and by the upregulation of inflammation and fibrosis markers. Pharmacological inhibition of CSE by PAG induced a reduction of crystal deposits in the kidney. Adhesion molecules (Cd44, Anxa2), inflammation (Tnf) and fibrosis markers (Col1a1) were decreased in the kidney.

Conclusions
These data show that pharmacological inhibition of CSE by PAG protects against calcium oxalate nephropathy. This new therapeutic pathway opens new venue for the treatment of renal crystallopathies.

P 3

Prolonged fetal hypoxia activates survival mechanisms in the developing kidney at the cost of premature cellular senescence

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Background
A low number of nephrons at birth increases the risk for chronic kidney and cardiovascular diseases later in life. Such nephron under-endowment is a common finding of intrauterine growth retardation (IUGR) and chronic hypoxia as occurs at high altitude (>2500 m) was described as one of the most critical and clinically relevant intrauterine stress factor disturbing nephrogenesis. In this study, we investigated the molecular mechanisms by which prolonged hypoxic exposure affects fetal kidney development in mice, using a proteomic approach.

Methods
Hypoxia-driven IUGR was induced by exposing gravid mice to chronic hypoxic conditions (10% oxygen) from E11.5 for 7 days. Freshly isolated E18.5 kidneys were lysed, enzymatically digested and submitted to bottom-up proteome profiling using a nano-LC system coupled to a high-resolution orbitrap mass spectrometer. Identified proteins were stratified per GO terms by means of the DAVID and Reactome databases.

Results
We identified a total of 6307 proteins, of which 436 were significantly differentially regulated in normoxic vs. hypoxic samples. GO term stratification of these proteins revealed solid mechanistic evidence explaining the constrained nephron formation in IUGR fetuses based on 1) Warburg-like metabolic adaptations, 2) responses to oxidative stress including enhanced expression of proteins mediating the translocation of proteins of the inner mitochondrial membrane, but also DNA repair enzymes and 3) aging and reduced cellular proliferation, which was characterized by diminished expression of ribosomal subunits and proteins involved in DNA replication, but also highly reduced levels of the proliferation marker Ki67.

Conclusions
Chronic fetal hypoxia led to a bipartite response in the developing kidney, on the one hand facilitating survival, but on the other promoting cellular senescence and reduced proliferation. By shifting the balance away from the unfavorable effects of this double-edged reaction, novel intervention venues could be found that might restore proper renal development in hypoxia-induced IUGR.

P 4

Short-term low protein, high carbohydrate regimen protects against kidney ischemia-reperfusion injury

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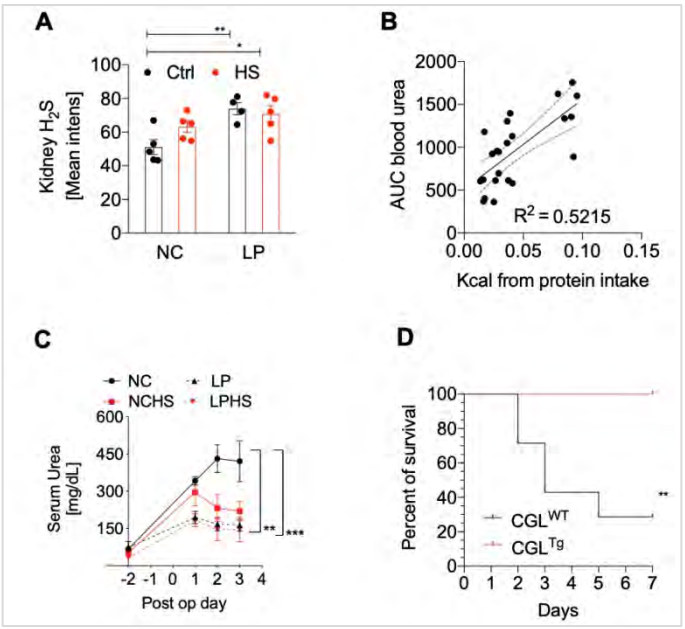
(CTO), University Hospital of Lausanne (CHUV), Lausanne, Switzerland, [3]Harvard University, Cambridge, United States

Background
Both caloric restriction and low protein dietsincrease longevity, improve glucose homeostasis and enhance metabolic fitness. Surprisingly, preoperative administration of energy and carbohydrate rich drinks (carboloading) is advocated before surgery. We hypothesized that protein restriction can be achieved by diluting protein with carbohydrate rich drinks. Protein dilution should improve metabolic fitness and stress resistance, despite increased total energy intake.

Methods
Mice were randomized into four regimens: regular diet (17.6% protein, NC), or low protein diet (5.6% protein, LP), with or without high sucrose water (50% sucrose, HS) for 7 days. At the end of the preconditioning, glucose tolerance and resistance to renal failure following a bilateral renal ischemia-reperfusion were evaluated. Renal function was assessed by measuring serum urea and creatinine levels, as well as kidney histology. The importance of hydrogen sulfide (H2S) in the benefit conferred by the LPHS diet was tested usingmice overexpressing cystathionine γ-lyase (CGL, CGLTg).

Results
Weight remained stable. Total energy intake was doubled in mice given 50% sucrosewater. Compared to the NC group, all three groups (LP, HS and LPHS) ate less protein. The reduction in protein intake resulted in improved glucose tolerance, increased kidney H2S production (Fig. 1A) and protection against renal ischemia-reperfusion injury (Fig. 1B). Protein intake, but not fat, carbohydrate or total energy intake, was correlated with susceptibility to renal ischemia reperfusion in mice (Fig. 1C). Mice overproducing H2S (CGLTg) were protected from ischemia reperfusion injury (Fig. 1D), suggesting that CGL and H2S protect from acute kidney damage.



Conclusions
Here we showed that protein dilution in ad-libitum fed animals protects against kidney ischemia-reperfusion injury, independently of calorie intake. LPHS boosted kidney H2S levels, while CGL transgenic mice were protected from kidney injury independent of diet. Pre-operative administration of low protein/high carbohydrate diets and/or H2S, is an attractive strategy to improve the recovery of patients after surgery.

P5

The long non-coding RNA H19 overexpression in mouse kidney attenuates ischemia/reperfusion injury through the modulation of miR-30a-5p expression

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Background
H19 is a long non-coding RNA expressed on one parental allele and transcribed from the maternal allele. It harbors the microRNA miR-675. It is largely expressed during development and virtually shut down in adults. The H19 gene is located downstream of the insulin-like growth factor 2 (Igf2) gene. H19 exerts its functions primarily through two distinct mechanisms 1) releasing miR-675 as its primary precursor or interacting with several partners such as proteins and miRNAs. In addition, dysregulation of H19 is reported in many types of cancers.

Methods
H19 expression levels in HUVEC were modulated by infection with a lentivirus vector or by anti-sense oligomediated knock down. The expression level was analyzed by qPCR. The cells were analyzed for migration, proliferation and apoptosis. Cell lysates were collected and analyzed by Western blot. Angiogenesis assay was performed using 3D fibrin gel and images were taken using fluorescent microscope. Kidney ischemia reperfusion injury in mice was performed by unilateral clamping and kidneys were collected after 1 and 7 days post clamping.

Results
H19 overexpression increased cellular proliferation, migration, and decreased cellular apoptosis. In addition H19 increased endothelial cells angiogenic response to VEGF. There was a noticeable increase in AKT and ERK1/2 phosphorylation. In addition, the MAPK kinase pathway p38 was dysregulated with persistent activation that went unchecked. Moreover, we identified two transcription factors SPI1 and LHX8 that may be involved in H19 induction under hypoxia. siRNA knockdown of SPI1 and LHX8 significantly reduced H19 expression. We showed that H19 interacts with miR30a-5p and regulates its function. Overexpression of H19 in vivo conferred protection against ischemia/reperfusion injury in mice.

Conclusions
Our data indicate a wide-reaching effect of H19 in endothelial cell function and can be potentially used to develop therapeutic approach to regenerate endothelial cells.

P 6

Effect of Vitamin D supplementation on atherosclerosis development in ApoE knockout mice with adenine induced nephropathy

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Background
In CKD patients, vitD deficiency is a strong predictor of disease progression and death due to cardiovascular events. Higher amounts of vitD supplementation are required in CKD patients to achieve normal plasma 1,25(OH)2D3 values. We hypothesize that in the kidney, local cholesterol and vitD metabolism by the enzymes sterol 27-hydroxylase (CYP27A1) and 25-Hydroxyvitamin D3 1-alpha-hydroxylase (CYP27B1) has an atheroprotective effect which is lost upon decline of renal function. To prove this, CKD was induced in Apolipoprotein E (ApoE) KO mice prone to develop atherosclerosis, and metabolic parameters and renal function were analysed.

Methods
ApoE KO mice (n = 8 per group) were fed for 2 weeks with Western diet (WD) ± vitD (2000U/kg) and CKD was induced by adding 0.15% adenine to WD for 5 weeks. Urine was collected in mice placed in metabolic cages. Plasma lipoproteins, kidney histology and expression of genes involved in lipid and vitD metabolism were assessed.

Results
VitD and adenine, alone or in combination, had no effect on body weight, liver and kidney size. Macroscopic changes induced by adenine in the kidney were more severe with vitD. Mice treated with adenine drunk 2x more water, excreted 4x more urine (P <0.001). Urinary pH decreased

in CKD mice with vitD (P <0.05). Urinary excretion of sodium, potassium, calcium, magnesium, inorganic phosphate and urea tended to increase with adenine, independently of vitD. Plasma glucose, LDL, HDL and triglycerides remained unchanged in all groups. In mice with healthy kidney, vitD slightly decreased plasma cholesterol but in mice with CKD, it increased (P <0.05). In kidney tissues, adenine significantly decreased Cyp27a1 and increased Cyp27b1 mRNA levels (P <0.01).

Conclusions
VitD supplementation induces specific changes in plasma and urine of ApoE KO mice with CKD. Quantification of atherosclerotic lesions will clarify the role of local metabolism of cholesterol and vitD by the kidney.

POSTER PRESENTATIONS – TRANSPLANTATION

P7

Living Related Kidney Transplantation (LRKT) Program in Armenia: A 17-year single-center experience

Dr. Milena Voskanyan[1], Dr. Helen Nazaryan[2], Dr. Emma Shahinyan[2], Dr. Sergey Babloyan[1], Dr. Poghos Geyikyan[2], Dr. Sahak Arakelyan[2], Dr. Khachatour Kyurkchyan[2], Prof. Ara Babloyan[1], Prof. Ashot Sarkissian[1]

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Background

One of the most difficult problem nephrology faces in countries with limited resources is the management of patients with renal failure. Renal replacement therapy constitutes a heavy financial burden. Among different modalities kidney transplantation (KT) is the best cost-effective option. The **aim** of this study is to evaluate results of the living related KT (LRKT) program in Armenia, strongly supported by Antwerp and Zurich.

Methods
Between 2002 and August 2019 overall 166 LRKT were performed (4 second and 7 preemptive KTs). All donors and recipients were ABO-compatible and cross-match negative. HLA mismatches (A, B and DR loci) were taken into consideration. We evaluated the frequency of complications, patients (pts) and graft survival by Kaplan-Meier method. Mean age of recipients (males - 67.5%) was 35.8 ± 13.4 years (7.1-65.7), and of donors 44.8 ± 8.1 years with female predominance (65.7%). Initial immunosuppression was with prednisone, cyclosporine A or tacrolimus and azathioprine or MMF. Induction with Basiliximab was used only in high risk cases.

Results
Prophylaxis of cytomegalovirus (CMV) infection was not applied (high cost). Overall, 28 pts (16.9%) had CMV disease that was successfully treated. Eleven pts (6.6%) had oncological complications. Twenty-two (13.2%) pts lost their grafts due to non-compliance (7), rejection (4), chronic transplant nephropathy (4) and surgical complications (3). One, 5- and 10-year graft survival rates were 96.3%, 92.3% and 87.1% - respectively. Fourteen pts (8.4%) died with functioning grafts mainly due to cardio-vascular (4) and oncological complications (4). Pts' 1-, 5- and 10-year survival was 98.7%, 96.1% and 89.2%, respectively.

Conclusions
Results are acceptable given the limited possibilities. Kidney transplant activity in Armenia at present is far from the existing demand. It should be expanded and complemented by a deceased donor program. It is a good example of fruitful international cooperation.

P 8

Preservation of kidney function in kidney transplant recipients by alkali therapy (Preserve-Transplant Study)

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Background
Kidney transplantation is the treatment of choice for patients with ESRD. Short- and long-term graft survival after kidney transplantation have significantly improved within the last decades but declining transplant function or even graft loss is still a common issue. Metabolic acidosis (MA) is highly prevalent in renal transplant patients and a recent study has shown that MA may be a significant risk factor for graft loss and mortality. However, no data exist yet on the role of alkali treatment in the prevention of graft loss in renal allograft recipients. An alkali treatment study in kidney transplant patients is of prime importance and has the potential to show that such treatment may reduce the progression towards graft failure.

Methods
This study is a multi-center, prospective, single-blinded, randomized, placebo-controlled interventional trial (RCT) to test the superiority of alkali treatment in comparison to placebo for preservation of kidney function in 240 kidney transplant recipients. The duration of the study is two years for each individual participant. Patients are randomized into two arms: an intervention arm (sodium hydrogen carbonate) and a placebo arm. The study is supported by the Swiss National Science Foundation as an investigator-initiated clinical trial.

Results
Patient recruitment has started on June 12th, 2017. By the end of the recruitment phase on July 14th, 2019, 243 patients had been randomized. In the preliminary baseline data (mean (sd)), 69.3 percent of the participants are male. Patient age is 55.38 (13.52) years, eGFR (CKD-EPI) 47.91 (16.01) ml/min/1.73 m^2 and serum bicarbonate level 21.14 (2.65) mmol/l. So far, the study medication is tolerated well.

Conclusions
The Preserve-Transplant Study has been launched successfully and the recruitment goal of 240 patients was achieved. The Preserve-Transplant Study is the first RCT investigating the role of alkali on graft function and may have an impact on future treatment of kidney transplant patients.

P 9

Daratumumab for treatment of antibody-mediated rejection after ABO-incompatible kidney transplantation

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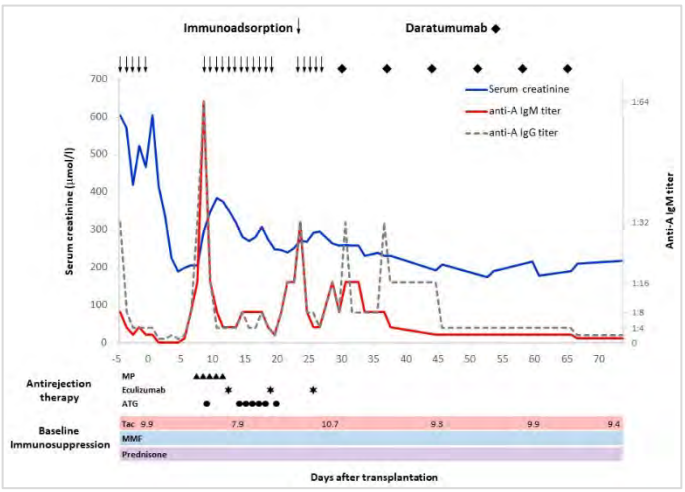
Background
Antibody-mediated rejection (AMR) has been recognized as one of the most important causes of graft loss. Although less frequent than donor specific HLA-antibodies, antibodies against ABO blood group antigens can be the cause of AMR. To date, our armamentarium to treat AMR is still incomplete. For this reason, new therapeutic options to reduce the burden of AMR are urgently needed.

Methods
We report the effectiveness of daratumumab, a human IgGκ monoclonal antibody targeting CD38 on plasma cells, for therapy-refractory AMR due to blood group antibodies in a 59-year-old man who received a living ABO-incompatible kidney transplantation. Daratumumab was administrated at a dose of 16 mg per kg of body weight in weekly intervals beginning on day 30 after kidney transplantation (totally six infusions).

Results
On day 7 post-transplant, our patient developed biopsy-proven early active AMR despite following established therapeutic strategies for ABO-incompatible kidney transplantation, and immediate treatment with anti-human T-lymphocyte globulins, high-dose methylprednisolone, blocking the complement-mediated effector mechanisms of tissue injury by eculizumab and immunoadsorption for the removal of circulating blood group antibodies. After administration of daratumumab as a rescue therapy, blood group antibody titers decreased and remained at low levels without further immunoadsorption and allowed kidney graft function to recover (Figure 1).

Conclusions
As therapeutic options for AMR are limited, an anti-CD38 agent such as daratumumab may be a new treatment option to be evaluated in patients with no response to so far utilized anti-rejection therapies for AMR. As large clinical trials evaluating new treatment regimens for AMR are unlikely to be performed in the nearer future, case reports may be a more practical way to evaluate treatment response. Nevertheless, the immunomodulatory effects of daratumumab need to be taken into account. To address this issue, further studies are warranted.



P 10

Outcome of pre-existing and de novo Tumors in Kidney Transplantation – a retrospective analysis of 1400 transplantations over 40 years

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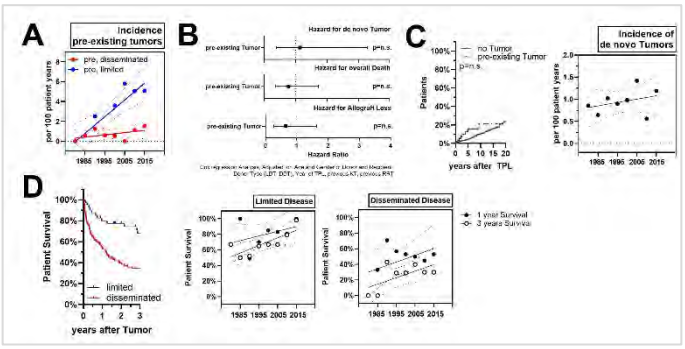
Background
Previously, pre-existing tumors were considered a contraindication for kidney transplantation. With emerging diagnostic and therapeutic options and improved outcome of patients with active malignancy, these concepts need reevaluation.

Methods
As a single center retrospective study, we analyzed the incidence and outcome of de novo tumors in kidney transplant recipients with and without pre-existing cancers from 01.01.1981 through 31.12.2018.

Results



We demonstrate, that the prevalence of de novo transplanted patients with pre-existing malignancy has increased in the last 40 years, primarily due to diagnosis of asymptomatic and limited disease during pre-TPL evaluations (Figure A). When compared to patients without pre-existing malignancy, the outcome is favorable with similar Overall and allograft survival and similar risk for recurrent/de novo cancer (Figure B) We further assessed the outcome of patients with de novo cancer after transplantation. Tumor incidence was 1 per 100 patient years and incidence increased by 30% in the last 40 years with similar contribution of limited and disseminated disease at diagnosis (Figure C). Outcome was poor, notably in patients with disseminated disease; yet 1 and 3 year survival increased over time (Figure D).

Conclusions
In summary, the incidence of pre-existing and de novo solid Tumors increased within the last four decades in our transplant cohort. Patients with pre-existing tumors have an excellent outcome and – if well selected – should not be withheld from transplantation. Meanwhile, de novo tumors after transplantation are associated with poor outcome.

P 11

Successful plasmapheresis-free treatment with eculizumab of acute antibody-mediated rejection (AMR) in a highly sensitized kidney transplant recipient

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Background
Acute AMR early after transplant remains a therapeutic challenge. Most reports have focused on preventive protocols that combine thymoglobulin induction and plasmapheresis/immunoadsorption, intravenous immunoglobulins (IVIG) or rituximab. We present the case of an early acute AMR episode in a kidney transplant recipient that was successfully treated with upfront eculizumab, without the need of plasmapheresis/ immunoadsorption.

Methods
The patient is a 58-year-old woman that suffered terminal kidney failure due to reflux nephropathy that had been on dialysis since 2014. Her first kidney transplant failed because of primary non-function due to arterial complications/thrombosis. One year later, she received a second kidney allograft from a deceased donor. At day 0, there was only one donor specific antibody (DSA) anti-DQ7 with a negative CDC crossmatch (T&B). Induction immunosuppression with thymoglobulin had to be interrupted after the first dose because of an acute respiratory distress syndrome. Basiliximab induction was thus administered. After initial excellent allograft function, her serum creatinine increased rapidly on days 7-9. Results of day 7 anti-HLA antibody measurements revealed a significant increase in her DSA anti-DQ7 and 4 de novo DSA (table 1). Allograft biopsy was performed that showed “pure” acute AMR (table 2).

Table 1: DSA evolution

DSA	Day 0 (MFI)	Day 7	Day 17	Day 25
Class I	-	anti-A11 (4’808 MFI) anti-A33 (10’922 MFI)	anti- A11(3130 MFI) anti-A33 (5466 MFI)	anti-A33 (1310 MFI)
Class II	Anti-DQ7 (1316 MFI)	anti-DP2 (17’698 MFI) anti-DQ7 (18’847 MFI) anti-DR11 (20’508 MFI)	Anti-DQ7(7846 MFI)	-

Table 2: Allograft biopsy finding

Light microscopy and immunofluorescence
• Glomerulitis
• Peritubular capillaritis
• Diffuse complement C4d deposits in peritubular capillairies
• No T-cell infiltrate or tubulitis
• No arteritis

Results
The severe acute AMR episode was treated with daily methylprednisolone boluses and upfront eculizumab (900 mg IV) was administered and repeated 8 days later with excellent CH50 blockade over 20 days (<10% CH50). Rituximab and IVIG was given over the following days. There was an excellent response to eculizumab administration, as her urine output and kidney function improved rapidly. No plasmapheresis was necessary.

Conclusions
Eculizumab administration rapidly reversed the acute AMR episode after kidney transplantation, without the need for DSA removal by plasmapheresis/immunoadsorption or T-cell depletion. More studies are needed to evaluate the efficacy of a short course of eculizumab therapy to overcome early acute AMR in highly sensitized recipients.

P 12

Diffusion-MRI detects an increase in interstitial fibrosis earlier than the decline of renal function

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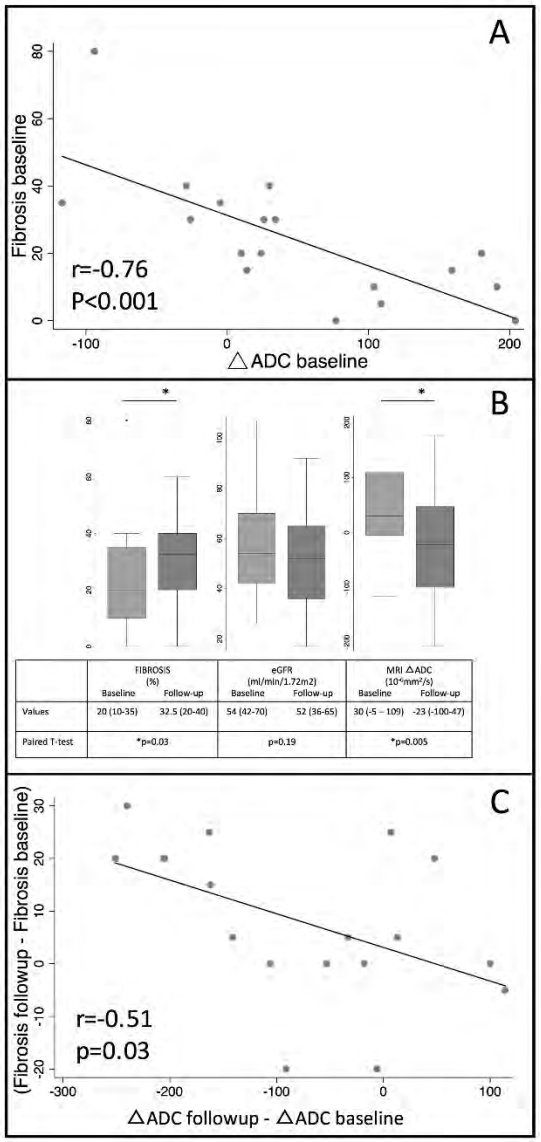

	FIBROSIS (%)		eGFR (ml/min/1.72m2)		MRI ΔADC (10^{-6}mm²/s)	
	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up
Values	20 (10-35)	32.5 (20-40)	54 (42-70)	52 (36-65)	30 (-5 – 109)	-23 (-100-47)
Paired T-test	*p=0.03		p=0.19		*p=0.005	

Background
Interstitial fibrosis (IF) is one of the major predicting factors in CKD. Diffusion Weighted Magnetic resonance imaging (DWI-MRI) is a new important tool for non–invasive IF assessment, but its value for IF follow up is unknown. We recently adapted a DWI sequence, allowing for the discrimination between the kidney cortex and medulla. The cortico-medullary ADC difference (ΔADC) was better correlated to histological IF than absolute ADC. We aimed at analyzing the use of DWI-MRI for the follow up of IF in patients having undergone repeated biopsies in comparison to renal function evolution.

Methods
In this prospective study, we included patients having undergone repeated biopsies for clinical purpose and who agreed to undergo repeated DWI-MRI at the time of biopsy.

Results
19 kidney allografts patients had repeated biopsies for clinical purposes and parallel MRI examinations. The average interval between the two biopsies was 1.7 year. There was no significant correlation between eGFR and IF at baseline (r = -0.39, p = 0.10), whereas baseline ΔADC correlated negatively with IF (r = -0.76, p <0.001) (Figure 1A). Between the two visits, IF as estimated from the renal biopsy, increased significantly from a fibrosis score of 20% to 32.5% (p = 0.03) in individual patients, whereas estimated renal function remained stable (eGFR 54 to 52ml/min/1.73 m^2; p = 0.19). ΔADC decreased significantly from 30 to -23 x10-6mm^2/S (Figure 1B). Considering the difference between the basal and follow-up values, there was a good correlation between the evolution of IF and ΔADC (r = -0.51, p = 0.03) (Figure 1C) but not between the evolution of IF and eGFR (r = 0.24, p = 0.34).

Conclusions
Thus modifications of ΔADC derived from DWI-MRI outperformed eGFR to follow IF evolution within a given patient. ΔADC may be more reliable than eGFR to allow earlier detection of an increase in IF longitudinally.

P 13

Technical considerations and confounders for urine CXCL10 chemokine measurement

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Background
The urine chemokine CXCL10 is a promising screening biomarker for renal allograft rejection. The aim of the study was to investigate important technical and biological aspects, as well as potential confounders when measuring urine CXCL10.

Methods
We analyzed 595 urine samples from 117 patients, who participate in a randomized controlled trial investigating the clinical utility of a urine CXCL10 monitoring for post-transplant management. Urine CXCL10 was measured by an immunoassay using electrochemiluminescence.

Results
Intra-assay CV was 2.5%, inter-assay CV 10%. Urine CXCL10 remained stable (i.e. <10% degradation) for 8 hours at 25°C or 37°C and for 3 days at 4°C. CXC10 concentrations [pg/ml] strongly correlated with urine CXCL10 / creatinine ratios [ng/mmol] (r2 = 0.98; p <0.0001). Leucocyturia and active BK-polyomavirus infection are associated with higher CXCL10 concentrations, while allograft function, serum CRP, patient age, proteinuria, urine pH, hematuria, squamous epithelia cell count and bacteriuria did not correlate with urine CXCL10 concentrations. In 145 paired samples obtained within 1-2 weeks, 80% showed a CXCL10 / creatinine ratio change of less than ±2ng/mmol or ±50%, respectively.

Conclusions
Urine CXCL10 measurement on the used platform is accurate and robust. Leucocyturia and active BKpolyomavirus infection are major confounders, which can be easily detected, but represent important diagnostic 'blind spots' when using urine CXCL10 to screen for allograft rejection. The intra-individual biological variability of urine CXCL10 within 1-2 weeks is mostly below ±50%, which is still much higher than the technical variability due to sample handling/processing (<20%).

P 14

Reduced expression of proximal acid-base transporters in kidney transplant patients with metabolic acidosis

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Background
Metabolic acidosis (MA) is a frequent complication of chronic kidney disease and an independent risk factor for kidney disease progression and mortality. MA is highly prevalent after kidney transplantation. However, no data are available on the underlying pathomechanisms involved in MA in renal allografts. Thus, we wanted to investigate the expression of key acid base transport proteins in kidney biopsies of kidney transplant recipients with and without MA.

Methods
We evaluated 22 kidney transplant biopsies including 9 biopsies from kidney transplant recipients (KTR) with MA, nine biopsies from KTRs without MA (control) and four biopsies from KTRs that were subjected to alkali therapy (Alkali therapy). Immunofluorescence staining was used to identify key renal acid-base transport proteins.

Results
In the proximal tubule, we observed reduced immunostaining for the sodium bicarbonate cotransporter NBCe1 (SLC4A4) in the MA group compared to the control and alkali group, whereas the alkali group demonstrated the strongest staining of all three groups. In the distal nephron, expression of the chloride/bicarbonate exchanger Pendrin (SLC26A4) and the B1 subunit of the V-ATPase (ATP6V1B1) were markedly stronger in the alkali and control group compared to the MA group. Expression of other acid base proteins such as Renal ammonia transporter RhCG (SLC42A3), Carbonic Anhydrase II, Glutamate dehydrogenase, anion exchanger AE1 (SLC4A1) and the B2 subunit of the V-ATPase (ATP6V1B2) showed no difference among all groups. Interestingly, the B2 subunit was absent in the proximal tubule in transplant biopsies of all groups.

	Metabolic acidosis	Alkali therapy	Control	p
n	9	4	9	
Gender = Male (%)	5 (55.6)	1 (25.0)	4 (44.4)	0.853
Body Mass Index (BMI) [kg/m²] (median [IQR])	22.1 [20.0, 24.3]	25.9 [25.6, 28.6]	22.5 [21.9, 23.6]	0.206
Bicarbonate [mmol/L] (mean (sd))	17.4 (2.9)	24.0 (1.6)	23.8 (1.3)	<0.001
eGFR [mL/min/1.73 m²] (mean (sd))	31.9 (17.7)	38.5 (11.4)	48.0 (11.6)	0.085
Repeated transplantation = Yes (%)	3 (33.3)	1 (25.0)	5 (55.6)	0.617
Age of patient at time of biopsy [years] (mean (sd))	43.7 (11.2)	40.0 (16.5)	52.0 (13.7)	0.255
Age of patient at time of kidney transplantation [years] (mean (sd))	36.7 (13.3)	36.2 (18.8)	45.9 (17.7)	0.428
Transplantation vintage at time of biopsy [years] (median [IQR])	6.1 [1.1, 7.8]	3.4 [0.9, 6.2]	4.2 [2.1, 6.4]	0.78
Immunosuppressive therapy (%)				1
Ciclosporine	3 (33.3)	2 (50.0)	4 (44.4)	
None	1 (11.1)	0 (0.0)	0 (0.0)	
Tacrolimus	5 (55.6)	2 (50.0)	5 (55.6)	

Conclusions
These data suggest that MA may affect the expression of several key acid base transport proteins in the kidney of transplant recipients and treatment with alkali may have the potential to reverse or prevent the altered protein expression in the kidney.

P 15

kinetic gfr outperforms ckd-epi in the immediate period following kidney allograft for renal function evaluation

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Background
Evaluation of renal function during the post ischemic phase of a kidney allograft is suboptimal since usual formulas such as CKD-EPI are not validated to estimate Glomerular Filtration Rate (eGFR) when serum creatinine levels are unstable. Using serum creatinine measured at two different timepoints, Kinetic eGFR (KeGFR) equations are emerging as interesting tools to evaluate renal function when creatinine levels are unstable

Methods
We retrospectively evaluated eGFR post transplantation using both CKD-EPI and KeGFR equations in all consecutive kidney allograft patients transplanted at the University Hospital of Geneva between august 2005 and September 2015. We included 311 patients with a median age of 53 years old. Serum creatinine as well as timing of measurements were extracted and renal function was calculated according to keGFR and CKD-EPI equations. Acute low graft function (ALGF) was defined here by a decrease in the serum creatinine levels less than 25% within the first week following transplantation

Results
keGFR stabilized 24 hours following surgery and did not significantly change over the next 5 days. CKD-EPI eGFR was initially much lower and progressively increased up to day 3. When considering eGFR at postoperative day 1, keGFR predicted ALGF with a good accuracy (AUC 0.79, 95% CI [0.71;0.87]), outstanding CKD-EPI performance (AUC O.59, 95% CI [0.52;0.67], p <0.001). Both keGFR and CKD-EPI showed low accuracy in predicting 6 months
eGFR.

Conclusions
We show that keGFR may be used from the first day after transplantation to predict a slow recovery of renal function during the first week with a better accuracy than CKD-EPI. Both equations were however not accurate to predict 6 months eGFR.

P 16

Role of rituximab for isolated de novo donor specific anti-HLA antibodies in renal transplant recipients

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Background
Post-transplant de novodonor-specific anti-HLA antibodies (dn DSA) are associated with an increased incidence of antibody-mediated rejection (ABMR) and a decreased graft survival. Nowadays, no therapeutic consensus exists for isolated dnDSA. To prevent further renal damage, we administered Rituximab (RTX), an anti-CD20 antibody, as a monotherapy and followed: reduction/disappearance dnDSA, C1q binding dnDSA, renal function, histopathological lesions and patients and grafts survivals, after RTX treatment.

Methods
This is a single-centre observational study retrospectively analysing the clinical, biological and histopathological data of a cohort of 25 renal transplant recipients (RTR) who required one or more intravenous infusions of RTX following the detection of dnDSA. The exclusion criteria were pretransplant DSA and subclinical or clinical ABMR. Anti-HLA antibody determination was performed in all patients on D0 and at 1, 3, 6, 9, 12 months after transplantation and thereafter on an annual basis. Sera were analysed by Luminex® (LABScreenTM MIX and/or Single Antigen)and by C1qScreenTM.MFI ≥ 1'000 was chosen to define positivity.

Results
A significant depletion of class II dnDSA was observed at 6 and 12 months after RTX administration. Class II dnDSA with an initial MFI >10'000, dnDSA C1q+ and/or class I dnDSA showed resistance to RTX. At 24 and 36 months post-RTX, no significant reduction in dnDSA was observed anymore. At 4.5 years follow-up, renal function was stable with no histological progression, with 88% graft and 100% patient survivals.

Conclusions
To our knowledge, we report the first study analysing the effects of RTX monotherapy on the evolution of isolate dnDSA in RTR. RTX appears to be potentially an effective immunomodulatory agent in dnDSA suppression in the short delay and thus helps to delay the occurrence of acute and chronic ABMR. Resistance to treatment could be attributed to specific intrinsic pathogenicity of dnDSA. Multiple doses of RTX may have beneficial effect on long-term dnDSA reduction.

P 17

Longitudinal metabolomic analysis for the evaluation of kidney transplantation

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Background
A proper monitoring is crucial for the success of renal transplant both in recipients and donors. Currently, evaluation is based on measurements that do not reflect the complexity of kidney transplantation. In this context, biopsy is the gold standard for the diagnosis of transplant rejection, but it is invasive and suffers from complications and sampling error. The extensive analysis of metabolite levels offered by metabolomics might help to monitor the restoration of a "normal" renal function, improve the detection of rejection and better evaluate risks for healthy donors. The present study highlighted the benefits provided by metabolomics in the context of transplant patients and voluntary donors monitoring.

Methods
Plasma samples were collected from 42 kidney recipients and 24 living donors. In recipients, we had three times points: before, one week, and one month after transplantation. For donorssamples were collected before, one week and one year after donation. In order to provide extended metabolome coverage, each sample was analysed using complementary liquid chromatographic conditions coupled to QTOF-MS in negative and positive ESI mode. Data analysis was performed using ANOVA Multiblock Orthogonal Partial Least Square (AMOPLS) to account for the multilevel data structure.

Results
More than 250 plasma metabolites were identified using multi-platform analytical setup and were monitored using two specific AMOPLS models for graft patients and donor volunteers. This data modelling strategy efficiently handles longitudinal metabolomic data by considering the intrinsic experimental design and by decomposing the metabolic alterations related to transplantation. This approach allowed a clear visualization of the shortand medium-term benefits of transplantation for recipients and the low negative impact on donor volunteers on the renal function.

Conclusions
In addition to providing extensive metabolite profiling, metabolomics is a powerful tool for patients monitoring. Clinical investigation could benefit from this non-invasive monitoring to allow for a better evaluation of transplant patients.

P 18

FEP/FGF23 ratio, Klotho and T50 did not predict evolution of renal function at 4 years in kidney transplant recipients

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Background
Serum creatinine, proteinuria and interstitial fibrosis have been reported to be predictors of kidney function evolution. Moreover, fractional excretion of phosphate (FEP)/FGF23 ratio is a independent risk factor for renal progression in CKD patients. Serum calcification propensity (T50) is an independent determinant of graft failure in renal transplant recipients. Low serum Klotho levels are significantly associated with an increased risk of poor kidney outcomes. We aimed at analyzing the use of FEP/FGF23 ratio, klotho and serum T50 in prediction of renal function in kidney transplant patients.

Methods
We included 129 kidney allograft recipients with a serotheque and an available transplant biopsy in a retrospective study. We analyzed the associations and predictive values of FEP/FGF23, klotho and T50 for renal function evolution at 4 years. Rapid decline of renal function was defined as eGFR decline >3 ml/min per year.

Results
Patients were mainly Caucasian (95%) and male (60%) of 57years old in median (IQR: 46-69). At baseline, FGF23 (r = -0.40, p <0.001), Klotho (r = 0.36, p <0.001) and T50 (r = 0.21, p = 0.016) correlated with renal function. FEP/FGF23 ratio did not correlated at baseline with renal function (r = 0.09, p = 0.35). During follow-up of 4 years, 38 patients (38/103 = 37%) had rapid decline renal function. Tertile of FEP/FGF23 (HR:0.92, 95%CI: 0.6-1.4, p = 0.71), Klotho (HR: 0.84, 95%CI: 0.57-1.24, p = 0.40) and T50 (HR: 0.88, 95%CI: 0.6-1.3, p = 0.54) were not associated with increased risk of renal progression in kidney transplant recipients.

Conclusions
In summary, we demonstrated that FEP/FGF23, Klotho and T50 are not associated with renal function evolution in kidney allograft recipients. Other factors as vascular lesion due to anticalcineurin or history of rejection may be more relevant than phosphocalcic markers in this population.

P 19

Allograft Loss, Acute Kidney Injury and functional deterioration in Patients with newly diagnosed Tumors after Kidney Transplantation

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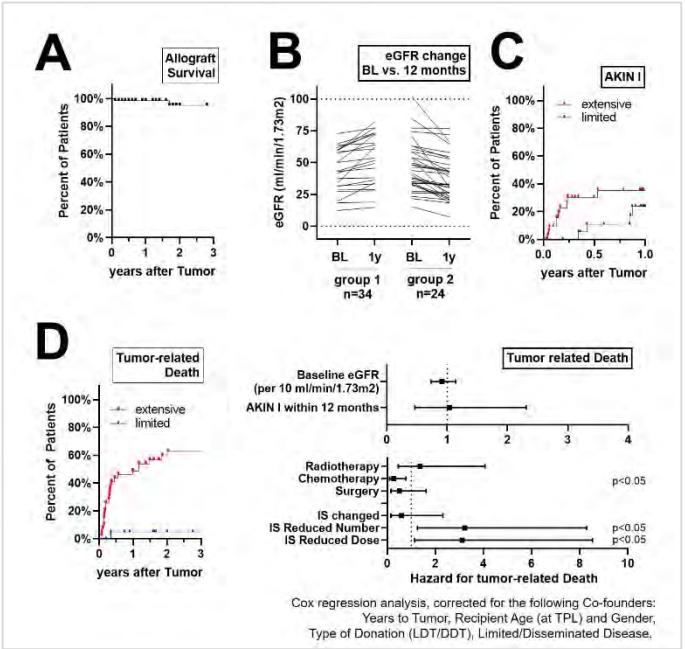
Background
De novo tumors are a frequent complication after kidney transplantation and associated with poor patient outcome. After tumor diagnosis, immunosuppression regimens are frequently altered to improve anti-tumor immunity and prevent treatment-associated side effects. These changes bear a risk for AKI, functional allograft deterioration and loss.

Methods
We investigated the renal function and outcome of 60 kidney transplanted patients diagnosed with malignant tumors from 01.01.2008 through 31.01.19. Median vintage from transplantation to malignancy was 10 years (0.1-44.4 years).

Results
observation period. 34/58 (58%) patients had a stable or increasing eGFR within the first 12 months after tumor diagnosis, in 24/58 (42%) patients, eGFR decreased. AKIN I was infrequent and occurred in 16/59 (27%) of patients within the first year of tumor diagnosis, predominantly in patients with disseminated disease. Meanwhile, tumor-related death was substantial, notably in patients with disseminated tumors at presentation and reached 40% after 3 years. Baseline eGFR and AKIN I within the first 12 months did not predict tumorrelated death outcome after correction for relevant co-founders. Meanwhile, reduction of immunsuppression (number or classes) increased the risk for tumor-related death. Here, further analysis of larger cohorts and correction for further potential cofounder is needed to draw a definitive conclusion.



Conclusions
In summary, allograft loss outcome after de novo tumor diagnosis is good. Baseline allograft function and AKIN
events do not correlate with tumor-related Outcome.

P 20

Cytomegalovirus (CMV) enteritis associated with life-threatening bleeding 21 years after kidney transplantation

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Background
Cytomegalovirus is a widespread virus that becomes latent following primary infection but frequently reactivates after transplantation. Although gastrointestinal manifestation is common, severe bleeding from small intestinal involvement is a very rare complication.

Results
We report a case of an 82- year old male with severe lower GI bleeding requiring repeated blood transfusions (total 19 RBC concentrates and 2 FFP). He also required an intensive care due to hemodynamic instability. He has been transplanted with a kidney 21 years agofor end-stage renal disease secondary to vascular nephropathy and pyelonephritis, and was currently on an immunosuppression with cyclosporine (target trough level 50 – 100 ug/l) and mycophenolate mofetil (1000 mg/day). His serostatus was positive (CMV R+), however he had no history of CMV reactivation since the transplantation. Despite an extensive search with repeated upper- and lower GI ndoscopies, push-enteroscopy, capsule endoscopy, and CT-angiography, the bleeding origin remained unknown and the patient unstable. We therefore decided to perform an explorative laparotomy with on-table endoscopy, although the perioperative mortality risk, after an NSTEMI 4 months ago, was assumed to be very high. Approximately 80cm proximal to the iliocecal valve four coarse lesions were palpated, which were identified as ulcers using on-table endoscopy after enterotomy. The histologic examination of the resected segment revealed deep ulcers with granulation tissue, atypically enlarged stromal cells with prominent eosinophilic inclusion bodies and surrounding halo, immunohistochemically positive for CMV and no evidence of malignancy. The viral replication in the PCR was low (585 IU/ml). He has been treated with ganciclovir and later valganciclovir for 4 weeks and remains stable 4 months after the diagnosis.

Conclusions
Our case demonstrates that even 21 years after transplantation, CMV enterocolitis should be considered as a differential diagnosis of GI bleeding, and that aggressive search combining endoscopic and surgical procedure may be required to make a diagnosis.

P21

PREEMPTIVE THERAPY VERSUS UNIVERSAL PROPHYLAXIS WITH VALGANCICLOVIR IN MINIMIZING THE RISK OF CYTOMEGALOVIRUS DISEASE IN KIDNEY TRANSPLANT RECIPIENTS

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Background
The aim of this study is to compare the preemptive therapy versus universal prophylaxis with valganciclovir in minimizing the risk of cytomegalovirus (CMV) disease in kidney transplant recipients.

Methods
This cohort study was conducted at Renal Transplant Unit, Dow University of Health Sciences, Karachi, Pakistan. A total of 94 kidney transplant recipients were enrolled in the study. Of them, 40 (42.6%) patients (high risk kidney transplant recipients) were treated with universal prophylaxis with valganciclovir for the early months of transplant with the daily and alternate dosage and remaining 54 (57.4%) patients (low risk kidney transplant recipients) were given preemptive therapy by regularly monitoring the CMV viremia which is defined as positive antigenemia (DNA PCR or phosphoprotein 65 [pp65]) for CMV disease without symptoms

Results
The mean age of recipients was 38±1.23. The variables that could affect the CMV disease development were introduced into the regression model: gender, age, immunosuppressive therapy, lymphocyte depleting antibodies at transplantation and underlying disease. Significant differences were found in the use of universal prophylaxis with valganciclovir versus preemptive therapy (P >0.05). The occurrence of CMV disease was found to be 7.40% (4 of 54) in the low risk group with preemptive therapy and no incidence of CMV disease; 0% (0 of 40) in the high risk group with universal prophylaxis of valganciclovir within one year of kidney transplant was observed.

Conclusions
In conclusion, universal prophylaxis with valganciclovir in high risk group is the effective treatment modality to reduce the burden of post-transplant CMV disease compared to preemptive therapy in low risk group. Therefore, it is highly recommended to initiate universal prophylaxis with valganciclovir in the low risk group as well

P 22

FREQUENCY OF URINARY TRACT INFECTION BY MULTIDRUG RESISTANCE ORGANISMS AND ITS EFFECT ON GRAFT FUNCTION IN RENAL TRANSPLANT RECIPIENTS

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Background
Urinary tract infection is a recurrent complication post renal transplant. It is frequently associated with poor graft outcomes and greater health related expenditures. The objective of this study is to determine the frequency of urinary tract infection by multidrug resistance organisms and its effects on allograft function in renal transplant recipients.

Methods
In this prospective, cross-sectional study, we screened post renal transplant patients visiting outpatient department with clinical signs and symptoms of urinary tract infection (UTI), defined as fever, frequent micturition, dysuria and urine discoloration. Multidrug resistance (MDR) or extensively drug-resistant (XDR) infections were determined by culture and sensitivity (C/S) and are defined as the organisms resistant to three or more types of antimicrobial drugs.

Results
We enrolled 97 renal transplant recipients of which 72 (74.2%) were diagnosed with clinical UTI. The mean age was 50±8 years. Out of 72 UTI patients, 28 (38.9%) were positive for MDR gram-negative UTI infection.Eschericia coliwas found to be the most frequent (n = 13, 46.4%) pathogen of MDR UTI in post renal transplant recipients and was significantly associated with antimicrobial MDR which included amikacin, amoxicillin, ampicillin, cefixime, cefuroxime, trimethoprim/sulfamethoxazole, fosfomycin, levofloxacin, nitrofurantoin, tazobactam and vancomycin. Other gram-negative organisms wereKlebsiella pneumoniaeandPseudomonas aeruginosa. Recurrent UTI occurred in 7 (9.7%) patients. Graft pyelonephritis was found to be among 3 (10.7%) patients who had creatinine above 1.5 mg/dL during the early months of post-transplant.

Conclusions
Gram-negative organisms were the most frequent pathogens associated with MDR UTI and were responsible to affect graft function in renal transplant recipients. Therefore, adequate and vigilant antimicrobial prophylaxis

POSTER PRESENTATIONS – CLINICAL NEPHROLOGY / HYPERTENSION / MINERAL / ELECTROLYTES

P 23

Estimated glomerular filtration rate predicts 30-day mortality in medical emergency departments: results of a prospective multi-national observational study

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Background
Renal failure is common in patients seeking help in medical emergency departments. Decreased renal function is associated with increased mortality in patients with heart failure or sepsis. Herein, we focused on the association of renal function with clinical outcome in more heterogenous patients on admission to medical emergency departments (ED).

Methods
We used data from a prospective, multi-national, observational cohort of patients treated in medical emergency departments of three tertiary care centers, to investigate associations of kidney function (reflected by estimated glomerular filtration rate [eGFR] CKD-EPI equation) and mortality. The eGFR was calculated from creatinine at the time of admission. Uni- and multivariate regression models were used to examine the associations of eGFR with 30-day mortality, in hospital mortality, length of stay and intensive care unit admission rate.

Results
Of the 6983 patients included, 4.7% died within 30 days of admission. 30-day mortality within eGFR cut-offs of >90, 60-89, 45-59, 30-44, 15-29, and <15 ml/min/1.73 m^2 increased stepwise from 1.8% to 3.5%, 6.9%, 11.1%, 13.6%, and 14.2%, respectively. Multivariate regression analysis adjusted for important confounders showed an odds ratio of 0.87 (95% confidence interval 0.82 to 0.91, p <0.001) per eGFR increase of 10 ml/min/1.73 m^2 with regard to 30-day mortality. Regarding eGFR groups as compared to the reference group with best kidney function (>90ml/min/1.73 m^2), the adjusted OR for the lowest group (<15ml/min/1.73 m^2) was 3.73 (95%CI 2.04 to 6.84), p <0.001). Similar results were shown for the association of impaired eGFR with in-hospital mortality, ICU-admission, and longer hospital stay. No differences were shown for hospital readmission within 30 days.

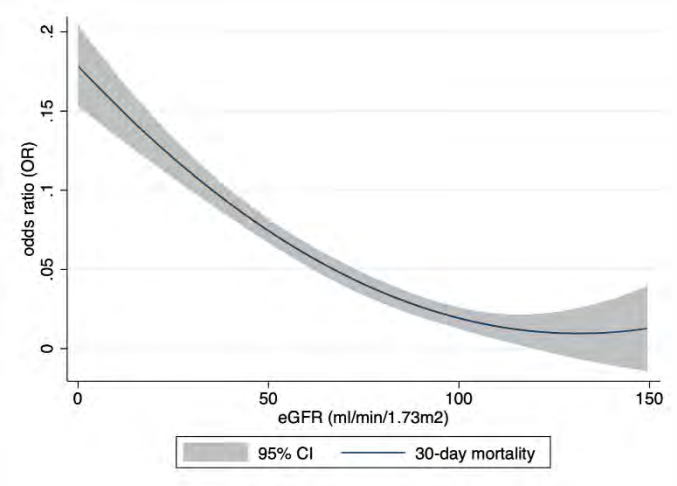

Table 1: Characteristics (given as mean ± SD or percentage) in dialysis patients according to their geographical region

	German, n=3118	French, n=1163	Italian, n=365
Prevalence, per 1000 people	0.42	0.43	0.85
Age, yr	67.9 ± 15.4	68.2 ± 14.7	74.0 ± 12.2
Sex (male), %	64.2	66.9	64.9
Caucasian, %	93.6	86.4	98.6
Swiss, %	78.5	71.2	78.2
Private establishments, %	23.8	38.1	20.0
Home dialysis, %	12.8	6.6	9.9
Dialysis vintage, months	49.3 ± 52.0	47.2 ± 52.4	49.5 ± 47.1
BMI	25.8 ± 5.5	26.1 ± 5.8	26.6 ± 5.6
Dialysis duration per week (h)	11.6 ± 1.2	11.4 ± 1.7	11.3 ± 1.1
Kt/V	1.62 ± 0.43	1.60 ± 0.40	1.55 ± 0.53
Catheter, %	30.2	38.1	32.1
Comorbidities, N	2.4 ± 1.9	2.6 ± 2.1	3.4 ± 2.1
Charlson Comorbidity Score*	4.4 ± 2.1	4.6 ± 2.3	5.2 ± 2.2
Hypertensive, %	82.4	80.0	86.0
Antihypertensive therapy, %	73.2	68.0	60.9
Hemoglobin, g/dL	11.1 ± 1.4	11.1 ± 1.4	10.8 ± 1.4
Ferritin, ng/mL	478.9 ± 418.6	428.5 ± 389.1	463.4 ± 280.7
Calcium, mmol/L	2.21 ± 0.24	2.23 ± 0.19	2.22 ± 0.20
Phosphate, mmol/L	1.64 ± 0.49	1.53 ± 0.44	1.58 ± 0.47
PTH, ng/L	383.3 ± 333.1	363.4 ± 348.6	315.1 ± 236.9
Iron substitution, %	72.9	78.3	80.7
EPO substitution, %	79.9	85.4	86.5

Conclusions
Reduced eGFR at time of admission is a strong and independent predictor for adverse outcome in this large and heterogeneous medical ED population. This information may aid for risk stratification and medical resource allocation in medical ED patients.

P 24

General characteristics in dialysis patients in different parts of Switzerland

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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 aim of this present analysis is to compare the characteristics in dialysis patients based on their geographical location.

Methods
All individuals being on chronic dialytic therapy (hemo- and/or peritoneal dialysis) in the year 2018 were enrolled (N = 4646). Patients were divided into 3 groups according to the location of their dialysis center in one of the three main language regions (German, French, Italian). To calculate survival probabilities, all deaths from incident dialysis patients between 2014 and 2018 were analyzed.

Results
Prevalence of dialysis patients in Tessin is twice as high compared to other parts of Switzerland, and patients are significantly older and have a significantly higher CCI and more comorbidities than dialysis patients in other parts of Switzerland. Dialysis duration per week is markedly higher in the German part than in the rest of Switzerland. In the French part almost 40% of dialysis patients are dialyzed in a private center, whereas in Tessin only every fifth patient is treated at a private Institution. Remarkably, Tessin has the highest number of hypertensive patients (86%), however the lowest number of patients treated with antihypertensives (61%). Kaplan Meier analyzes shows the worst 4-year-survival of incident dialysis patients in Tessin. However, after adjusting for age and CCI (Cox-Regression), this difference is no longer significant.

Figure 1: Geographic regions due to their language and the percentage of patients

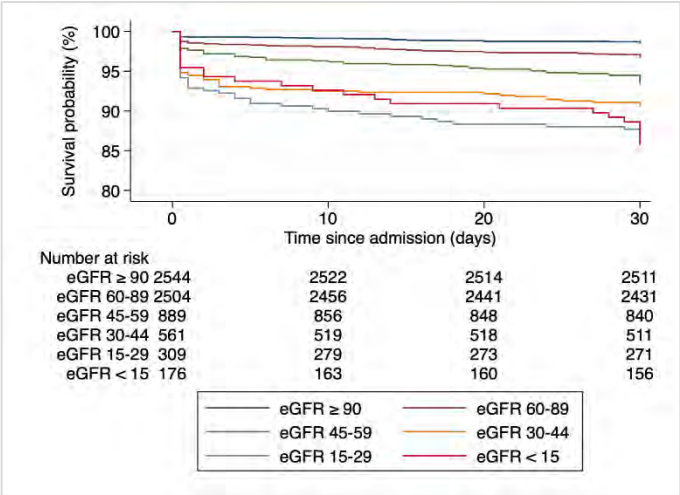

Table 2: One-, two-, 3- and 4-year survival probability (%) of incident dialysis patients, stratified by geographical region

		1 year	2 year	3 year	4 year
German	(N=3026)	90.7	79.9	70.8	61.1
French	(N=1158)	91.7	81.5	72.4	60.9
Italian	(N=341)	87.3	74.6	63.9	56.1

Conclusions

Analysis of regional characteristics of the Swiss dialysis population revealed a surprisingly diverse picture for a country the size of Switzerland. This may be partly explained by regional differences in ethnic composition. Other findings, as for example the two-fold higher prevalence of dialysis patients in Tessin, however, warrant further consideration.

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Fabry`s disease at a second glance: a case report of a patient presenting with later onset Fabry cardio- and nephropathy

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Background

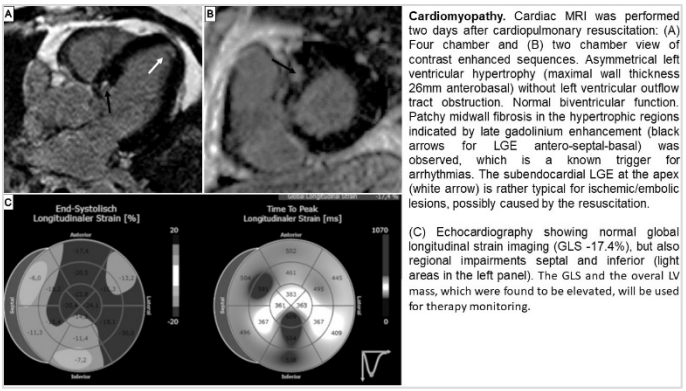
Fabry's disease (FD), an X-linked lysosomal storage disorder caused by deficiency in the alpha-galactosidase A (GLA) enzyme, is a rare cause of progressive cardio- and nephropathy (incidence 1:40.000). While the "classical" early-onset phenotype results in multiorgan manifestations at a young age, late-onset FD usually leads to isolated organ manifestations in older patients and is often misdiagnosed.

Methods

Dried blood spot analysis was used to test for FD.

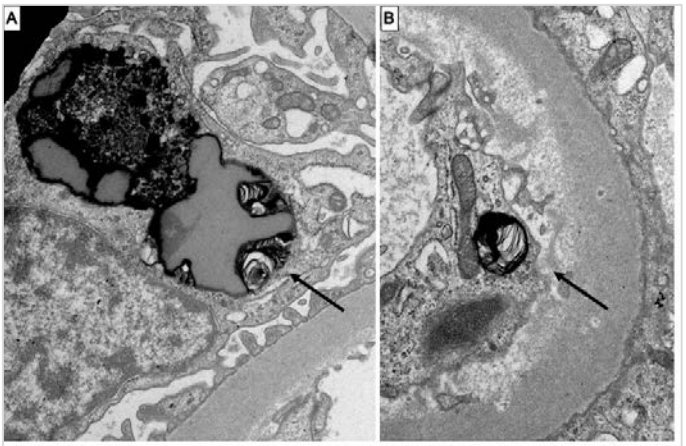
Results

A 60-year old man with mild hypertension and diabetes mellitus type 2 was diagnosed with hypertrophic cardiomyopathy in 2016 after cardiopulmonary resuscitation due to sustained ventricular tachycardia. He had normal coronaries, the cardiac MRI showed patchy fibrosis (figure 1a/b) and a genetic panel analysis for hypertrophic cardiomyopathy reported no relevant mutations. The patient was treated with an implantable cardioverter defibrillator and antiarrhythmics. Two years later he presented with progressive chronic renal failure (KDIGO G3bA1) of unknown etiology. A renal biopsy showed a few zebra and myelin bodies in podocytes and glomerular endothelial cells at electron microscopy (figure 2). Patient history further revealed fatigue, tinnitus and chronic diarrhea and the examination a cornea verticillata and a few angiokeratoma (figure 3a/b). The family history was unremarkable. A dried blood spot analysis showed the mutation c.937G >T;p.Asp313Ty, a significantly reduced alpha-galactosidase A level (7.8umol/L/h, normal >15.3umol/L/h) and normal Lyso-Gb3 value. The asymptomatic daughter tested positive for the mutation (figure 3c). To date this variant was asymptomatic in some case reports while in a large series of patients (Koulousios et al., BMJ Open, 2017) it was associated with renal and cardiac manifestations.

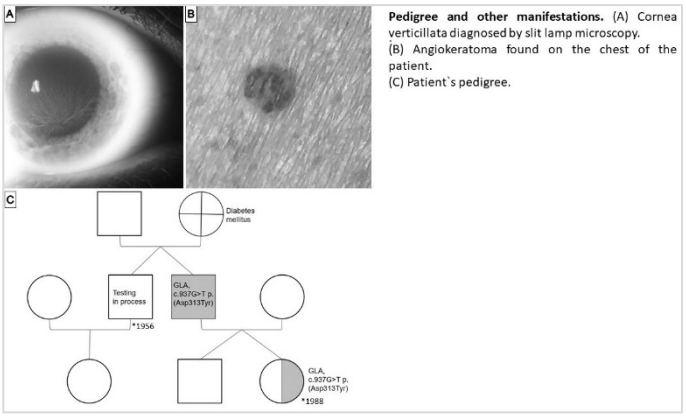


Cardiomyopathy. Cardiac MRI was performed two days after cardiopulmonary resuscitation: (A) Four chamber and (B) two chamber view of contrast enhanced sequences. Asymmetrical left ventricular hypertrophy (maximal wall thickness 26mm anterobasal) without left ventricular outflow tract obstruction. Normal biventricular function. Patchy midwall fibrosis in the hypertrophic regions indicated by late gadolinium enhancement (black arrows for LGE antero-septal-basal) was observed, which is a known trigger for arrhythmias. The subendocardial LGE at the apex (white arrow) is rather typical for ischemic/embolic lesions, possibly caused by the resuscitation.

(C) Echocardiography showing normal global longitudinal strain imaging (GLS -17.4%), but also regional impairments septal and inferior (light areas in the left panel). The GLS and the overal LV mass, which were found to be elevated, will be used for therapy monitoring.



Electron microscopy of renal biopsy. Few lysosomal osmophilic and Zebra body inclusions (arrow) in podocytes (A) and glomerular endothelial cells (B) are shown. Light microscopy (not shown here) revealed no signs of FD.



Pedigree and other manifestations. (A) Cornea verticillata diagnosed by slit lamp microscopy. (B) Angiokeratoma found on the chest of the patient. (C) Patient`s pedigree.

Conclusions

We present a case of late-onset FD that argues for genetic testing in cases of high clinical suspicion and provides further evidence for the pathogenicity of the D313Y mutation. We intend to start enzyme replacement therapy with monitoring by echocardiography (figure 1c), proteinuria and patients related outcomes.

P26

The solute carrier SLC16A12 is critical for creatine and guanidinoacetate handling in the kidney

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Background

A heterozygous mutation (p.Q215X) in the creatine transporter SLC16A12 was proposed to cause a syndrome with juvenile cataracts, microcornea and glucosuria in one Swiss family. However, we discovered a digenic syndrome in this family and demonstrated that the glucosuria was due to a concomitant SCL5A2 mutation. We found that SLC16A12 is expressed at the basolateral membrane of proximal tubular cells and patients with the heterozygous SLC16A12 mutation displayed significantly reduced plasma levels and increased fractional excretion rates of guanidinoacetate - a creatine precursor synthesized in proximal tubular cells.

Methods

To further explore the role of SLC16A12 in renal physiology and decipher the mechanism underlying the heterozygous SLC16A12 mutation in humans, we studied SLC16A12 deficient rats.

Results

SLC16A12 KO rats had lower plasma levels and increased urinary excretion rates of creatine and guanidinoacetate compared to WT. SLC16A12 KO rats also displayed lower plasma creatinine levels, but urinary creatinine excretion rates were reduced in parallel compared to WT rats. The phenotype of heterozygous rats was indistinguishable from WT rats. Metabolic cage experiments revealed no additional signs of tubular dysfunction in SLC16A12 KO rats. In addition, glomerular filtration rate was unaltered in SLC16A12 KO rats. Selective renal artery and vein sampling showed similar A-V differences in guanidinoacetate concentrations between WT and SLC16A12 KO rats, indicating incomplete compensation of urinary guanidinoacetate losses by renal synthesis in SLC16A12 KO rats.

Conclusions

Our results reveal that SLC16A12 is critical for tubular reabsorption of creatine and guanidinoacetate. In the absence of SLC16A12, ongoing urinary losses of guanidinoacetate are not adequately compensated by increased intrarenal synthesis, possibly caused by AGAT feedback inhibition due to impaired basolateral exit of creatine from the proximal tubular cell. Furthermore, the lack of a phenotype in SLC16A12 heterozygous rats suggests a dominant-negative mechanism underlying the phenotype observed in humans with the heterozygous p.Q215X SLC16A12 mutation.

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Tubular injury patterns differ between acute kidney injury subtypes in acute heart failure

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Background

Current data suggest that the prognostic significance of acute kidney injury (AKI) in acute heart failure (AHF) is not dictated by the serum creatinine increase per se but rather by the underlying pathophysiological mechanism. However, the separation of true, structural AKI from hemodynamic, pseudo-AKI remains a clinical challenge.

Methods

Basics in Acute Shortness of Breath Evaluation Study (NCT01831115) prospectively enrolled adult AHF patients at presentation to the emergency department. We assessed urine NGAL values for detection of renal tubular injury. Hemoconcentration was used as a surrogate parameter of adequate decongestion and its prognostic information on survival.

Results

Overall, a total of 253 patients were included and 111 patients(44%) suffered from an episode of AKI. Of these, 30 patients(12%) presented to the ED with community-acquired AKI(CA-AKI), whereas 81 patients(32%) developed AKI during the in-hospital period. At presentation, NGAL ratio concentrations were significantly higher in patients presenting with CA-AKI compared to in-hospital AKI patients or no-AKI patients (CA-AKI 8.5[IQR 6.6-13.0], in-hospital AKI 5.9[IQR 3.5-10.3]; P <0.01, no-AKI 5.7[IQR 3.8-9.6]; P <0.01). Importantly, NGAL ratio concentrations normalized during AHF treatment in patients presenting with CA-AKI(P versus no AKI = 0.56). In contrast, NGAL ratio concentrations remained unchanged between presentation, the time of AKI and discharge in inhospital AKI patients. Hemoconcentration was equally common in patients presenting with CA-AKI(33%) and in-hospital AKI(30%). Independent of the timing of AKI, hemoconcentration improved the 2-year survival of AKI patients towards the survival of no-AKI patients(P = 0.94).

Baseline Characteristics	No AKI (n=142)	CA-AKI (n= 30)	In-hospital AKI (n= 81)	P value
Age, years	80 (68-86)	79 (67-85)	81 (75-85)	0.17
Male gender n(%)	81 (57)	15 (50)	46 (57)	0.53
Medical history n(%)				
Hypertensive heart disease	47 (33)	11 (37)	27 (34)	0.82
Myocardial infarction	46 (33)	13 (43)	33 (41)	0.83
Diabetes	38 (27)	9 (30)	24 (30)	1
COPD	27 (19)	7 (23)	20 (25)	1
Stroke	21 (15)	5 (17)	19 (24)	0.60
Chronic kidney disease	46 (32)	20 (67)	51 (63)	0.83
Clinical signs on admission n(%)				
Jugular venous distension	67 (49)	12 (41)	45 (59)	0.078
Oedema	96 (68)	23 (77)	51 (63)	0.26
Systolic blood pressure	134 (120-146)	113 (100-133)	136 (119-150)	***0.001***
Rales	100 (70.9)	18 (60)	55 (68)	0.50
Laboratory assessments on admission				
Protein g/l	68 (64-72)	70 (66-73)	70 (67-75)	0.38
Hemoglobin g/l	131 (116-144)	122 (106-134)	123 (113-133)	0.47
Hematocrit	0.38 (0.34-0.41)	0.35 (0.32-0.4)	0.365 (0.34-0.39)	0.29
Albumin g/l	35 (33-38)	34 (33-35)	36 (33-38)	***0.042***
Creatinine µmol/l	90 (76-117)	140 (112-206)	123 (82-159)	***0.005***
NT-proBNP ng/l	4752 (2591-8395)	9777 (3826-17204)	7290 (4030-11584)	0.28
BNP ng/l	1111 (668-1860)	1527 (825-2255)	1209 (888-1998)	0.71
Baseline GFR ml/min/1.73m^2	66 (49-83)	55 (34- 81)	45 (36- 75)	0.39
Change during hospitalization				
BNP	-473 (-970- - 33)	-281 (-.1251- - 51)	-485 (-990- - 157)	0.42
NT-proBNP	-2150 (-4800- -576)	-3544 (-6249- -816)	-2613 (--4926- -83)	0.23
Weight loss kg	-2.5 (-5.8- -0.4)	-3.0 (-5.5- 0.1)	-2.9 (-5.7- -1.1)	0.99

Table 1 Baseline characteristics of patients presenting with no-AKI, community-acquired AKI and in-hospital AKI. Values are median (interquantile range) and numbers (percentages). P- Values are calculated between community-acquired AKI and in-hospital AKI using a Mann-Whitney-U test for continuous variables and Fisher's exact test or chi-square Test for categorical variables.

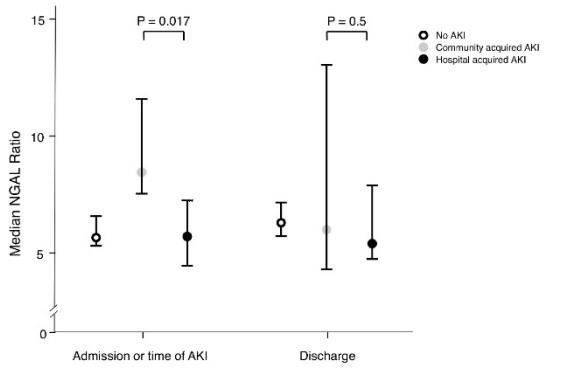

Figure 1 Error bars displaying median NGAL ratio with 95%-confidence interval in patients with no AKI (white), community-acquired AKI (grey) and in-hospital AKI (black) stratified by admission or time of AKI and discharge.

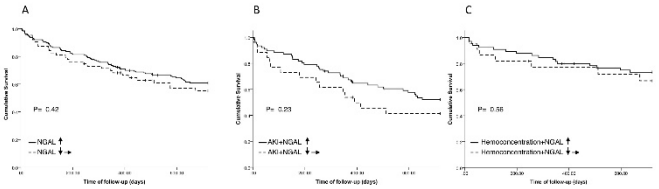

Figure 2 Kaplan–Meier curves displaying 2-year survival according in-hospital NGAL ratio changes. Solid lines signify patients experiencing in-hospital NGAL increases, dashed lines signify patients experiencing stable or decreasing in-hospital NGAL ratio concentrations. Panel A displays the overall population according to NGAL ratio changes. Log rank test indicating no difference (P=0.42). Panel B displays AKI patients according to NGAL ratio changes. Log rank test indicating no difference in patients with AKI (P=0.23) and without AKI (P=0.92, Kaplan Meier not shown); Panel C displays hemoconcentration (HC) patients according to NGAL ratio changes. Log rank test indicating no difference in patients with hemoconcentration (P=0.56) and without hemoconcentration (P=0.48, Kaplan Meier not shown).

Conclusions
CA-AKI is marked by significant tubular injury, probably reflecting prolonged tubular ischemia due to renovenous congestion and/or forward cardiac failure and contrastingly tubular injury does not occur in-hospital AKI, suggesting a hemodynamic increase in serum creatinine. Independent of the timing of AKI, adequate decongestion as assessed by hemoconcentration improves the survival of AKI patients towards the survival of no-AKI patients.

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Anticoagulant-related nephropathy: myth or reality?

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Background
The new oral anticoagulants (NOAC) have become very popular in medical practice since their appearence in the market. At the present time, they are frequently the molecule of choice for the prevention of systemic embolization and stroke due to atrial fibrillation, for the treatment of venous thromboembolism or even due to their simpler use in comparison to warfarin. However, recent literature recognizes an increased risk of renal failure with both NOACs and warfarin.

Methods
VigiAccess database is an international pharmacovigilance database from 134 countries from all around the world that are members of the World Health Organization (WHO) Program for International Drug Monitoring. We researched VigiAccess database from 1968 until December 2018 for any evidence associating renal side effects with the use of anticoagulants, including all the NOACs as well as warfarin, phenprocoumanone, acenocoumarol, heparin and enoxaparin.

Results
The data retrieved from VigiAccess shows that all anticoagulants can induce renal failure but particularly NOACs. Table 1 shows that out of a total of 235,457 side effects reported for NOACs since 2003, 7,725 cases were renal side effects, the majority being acute kidney injury (49.1%) or unspecified type of renal failure (36.3%). Comparatively, since the first case reported for both antivitamin K and heparin in 1968 only 2,145 and 2,263 cases, respectively, of renal side effects have been reported (table 1). Among NOACs, dabigatran and rivaroxaban were the drugs with the higher proportion of kidney-related adverse events: 4.4% and 3.3%, respectively, compared to 1.9% for apixaban and 1.7% for edoxaban (data not shown).

Table 1 – Frequency and type of renal side effects for NOACs, antivitamin K and heparin retrieved from VigiAccess database from WHO Program for International Drug Monitoring. Available in: http://www.vigiaccess.org/.

	NOACs	AVKs	Heparin
Total number of reported side effects	N=235,457	N=117,015	N=80,508
First case reported	2003	1968	1968
Renal side effects, n(%)	7,725 (3.3)	2,145 (1.8)	2,263 (2.8)
Acute kidney injury	3,796 (49.1)	904 (42.1)	915 (40.4)
Renal failure unspecified	2,802 (36.3)	704 (32.8)	843 (37.3)
Renal haemorrhage	553 (7.2)	147 (6.9)	68 (3.0)
Chronic kidney disease	209 (2.7)	75 (3.5)	195 (8.6)
Tubulointerstitial nephritis	55 (0.7)	36 (1.7)	18 (0.8)

All NOACs (rivaroxaban, apixaban, edoxaban and dabigatran) were included. Acenocoumarol, warfarin and phenprocoumone were regrouped as AVKs. Heparin group includes heparin and enoxaparin. AVKs, antivitamin K; NOACs, new oral anticoagulants.

Conclusions
All anticoagulants can induce renal injury, being NOACs the most concerned. Therefore, medical doctors must be aware of the risk of renal side effects when prescribing a long-term anticoagulation to their patients and consider anticoagulant-related nephropathy in the differential diagnosis of renal dysfunction occurring in patients receiving these drugs.

P 29

Effect of ageing on the decline of renal function over time: a cohort population-based study

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Background
Since a long time, “natural” kidney ageing has been described with a natural decline in eGFR of 1ml/min per year starting after 30-40 years. Only few longitudinal studies have analysed the long-term decline in renal function in the general population. We analysed the effect of age on renal function decline (RFD) in a population-based cohort with a 10-year follow-up.

Methods
Caucasian participants from the CoLaus study having a prospective 10-year follow-up data were included. RFD was computed from the difference in eGFR over the follow-up period. Models with age in tertiles were used because of a non-linear effect. Interactions with gender and hypertension were tested. Multivariate analyses were performed accounting for gender, education levels, dyslipidemia, hypertension, diabetes, smoking, body mass index, chronic kidney disease, C Reactive Protein and Uric acid levels, as well as albuminuria.

Results
We included 4163 participants with mean age of 52.3 (±10.4) years and mean baseline eGFR of 85.9 (± 14.6) ml/min/1.73 m^2. The median unadjusted eGFR decline was -0.48 (-1.06 to +0.16) ml/min/1.73 m^2 per year, with 70% of the sample presenting a confirmed decline in eGFR. The decline was non-linear across age tertiles as quicker decline was observed in the older tertile or decade. In the full-adjusted model the RFD in the older group was -0.82 (95%CI: -1.06; -0.57) compared to -0.61 (95%CI: -0.84; -0.37) ml/min/.172 m^2 in the younger one (pvalue <0.001). Hypertension modified the effect of age on RFD: in hypertensive participants there was still an ageeffect in older strata on RFD compared to younger groups, but this difference was reduced in non-hypertensive subjects.

Conclusions
Over a 10-year follow-up, we confirmed a RFD was confirmed in most of the participants. However, this decline was not similar across age categories: older subjects were more at risk of a steeper decline, with hypertension accelerating the kidney ageing process

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Dietary advice reduces urinary supersaturation in idiopathic calcium oxalate stoneformers – the dilution-promotion-inhibition program

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Background
Few controlled data are available on direct effects of dietary advice (DA) on urine supersaturation in calcium oxalate stone formers.

Methods
We selected 75 (66 men, 9 women) with truly idiopathic calcium oxalate stones, based on results of stone analyses. The goals of the simple three-component DA were 1) urine dilution, 2) reduced crystallization promotion, and 3) increased crystallization inhibition. Thus, increased fluid intake, increased calcium intake with meals for lowering intestinal oxalate absorption, and decreased acid and increased alkali consumption for raising urinary citrate were recommended. After 3 months, the desired effects of DA were increases in volume, calcium (U-Ca), and citrate (U-Cit), and decreases in oxalate (U-Ox) and uric acid U-(UA). An adherence score was calculated by awarding +1 point for parameters altered in the desired direction, whereas 1 point was deducted for changes towards higher stone risk. CaOx supersaturation was calculated using Tiselius' AP (CaOx) index EQ. Parameters before and after DA were compared by paired t-test, and linear regression analysis for correlating supersaturation with urine parameters was performed.

Results
DA induced significant changes ($p < 0.0001$) in volume (2057 +/- 79 vs. 2573 +/- 71 ml/d), U-Ca (5.44 +/- 0.24 vs 7.98 +/- 0.38 mmol/d), U-Ox (0.334 +/- 0.012 vs. 0.263 +/- 0.013 mmol/d) and U-UA (3.46 +/- 0.12 vs. 3.13 +/- 0.10 mmol/d). U-Cit increased hardly significantly (3.06 +/- 0.17 vs. 3.36 +/- 0.23 mmol/d, $p = 0.06$). After DA, AP(CaOx)index EQ dropped from 0.93 +/- 0.05 to 0.73 +/- 0.05 ($p = 0.0003$). This decrease positively correlated with adherence scores ($R = 0.470$, $p < 0.0005$), i.e. patients with highest adherence scores lowered their urine supersaturation most.

Conclusions
In idiopathic calcium oxalate stone formers, simple dietary advice targeting only 5 relevant urinary parameters is able to significantly reduce CaOx urinary supersaturation, calculated by Tiselius' AP(CaOx)index EQ.

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Incidence of biopsy-proven glomerulonephritis in the Western part of Switzerland over the last decade

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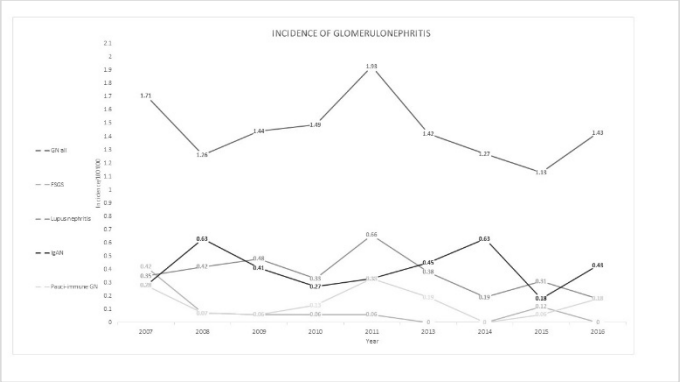
Background
Glomerulonephritis (GN) is a rare yet serious group of diseases with a high risk of progression to end-stage renal disease. For optimal health care planning, detailed epidemiological and demographic data are essential. Despite their clinical relevance, these data are largely lacking in Switzerland. The objective of this study was to assess the incidence of the different forms of glomerulonephritis in the Western part of Switzerland and its changes over the last ten years, compared to international data.

Methods
We listed all renal biopsy reports analyzed between 2004 and 2016 at the University hospital of Lausanne, the renal pathology reference center of all hospitals in the cantons of Vaud, Fribourg, Valais, and Neuchâtel. Biopsies with a first diagnosis of primary glomerulonephritis were included in the analysis. The incidence was calculated as the number of patients newly diagnosed with glomerulonephritis divided by the number of inhabitants of all the above-mentioned cantons during the year under review, as retrieved from the federal statistical office of Switzerland.

Results
We collected biopsy reports from 403 patients between 2006 and 2016; 271 biopsies met the inclusion criteria. The most common primary glomerulonephritis was IgA nephropathy (IgAN) with 23.6% of cases, followed by lupus nephritis (23.3%) and focal segmental glomerulosclerosis (FSGS) (13.7%). Overall, the mean incidence of glomerulonephritis was 1.4/100'000/year. Between 2007 and 2016, the incidence of all glomerulonephritis taken together remained stable. The same was true for the incidence of IgA nephropathy, lupus nephritis and pauciimmune glomerulonephritis (see figure). In contrast, the mean age at the moment biopsy increased significantly over this 10-year period, with a trend of higher creatinine-levels, proteinuria and degree of interstitial fibrosis at diagnosis (see table).

	2007	2016	p-value
Number of biopsies	26	30	
Incidence of all GN (/100'000/year)	1.71	1.43	
Women (%)	38	30	0.52
Age	49.7±19	59.2±16	*0.05
Creatininemia (µmol/L)	196±155	329±383	0.13
Proteinuria/creatininuria ratio (g/mol)	388±516	646±676	0.21
Glomerulosclerosis (%)	16.2±19	21.2±24	0.4
Interstitial fibrosis (%)	24.8±21	31.5±22	0.27



Conclusions
The incidence of glomerulonephritis in the western part of Switzerland was low and remained stable over time, in line with European data, whereas the age at diagnosis increased.

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Contrast-enhanced and Doppler ultrasound to assess renal microcirculation in healthy subjects and patients with chronic kidney disease before and after vasodilatation with nitroglycerin

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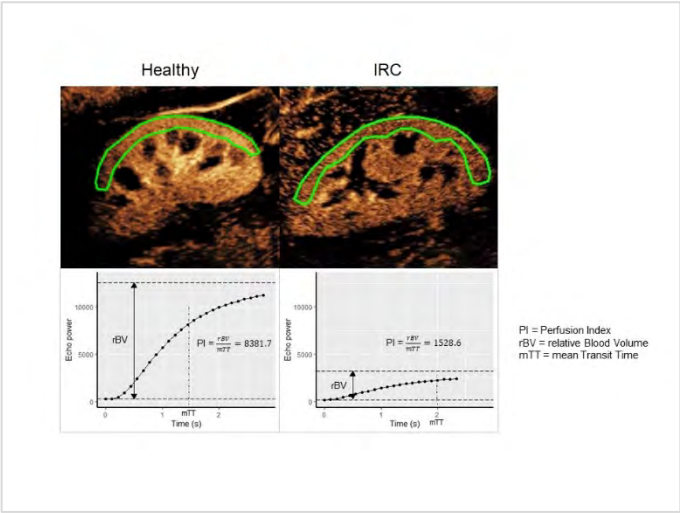
Background
Vascular factors such as capillary rarefaction, increased vascular stiffness and reduced vasodilatation due to endothelial dysfunction probably play an important role in the pathophysiology of chronic kidney disease (CKD). However, our understanding of the underlying mechanisms is hampered by the lack of non-invasive techniques to quantify renal microvasculature in humans. The aim of this study was to assess whether contrast-enhanced ultrasonography (CEUS) can identify (1) differences in renal microperfusion and (2) the degree of nitroglycerininduced vasodilatation as a measure of renal flow reserve between healthy volunteers and CKD-patients.

Methods
All participants underwent CEUS before and five minutes after the sublingual administration of nitroglycerin (0.2mg). Sonovue© (0.015

ml/kg/min) was perfused as contrast product until a steady state was obtained, followed by four destruction-refilling sequences. Outcome measure of CEUS was the mean (change in) perfusion index (PI) of the outer renal cortex (see figure). Renal resistive index (RRI) as a measure of vascular stiffness was also measured at each time point with Doppler ultrasound.

Results

A total of 13 healthy volunteers (mean age 46±8 years, 30% men, eGFR 98±11 ml/min/1.73 m², BMI 26±4 kg/m²) and 10 CKD patients (aged 59±16 years, 70% men, eGFR 60±33 ml/min/1.73 m², BMI 30±8 kg/m²) were included. At baseline, RRI was significantly higher and PI slightly lower in CKD patients. RRI decreased moderately in healthy but not in CKD patients after SL nitroglycerin whereas PI did not alter (see table).



	Healthy			CKD		
	pre-NTG	post-NTG	p	pre-NTG	post-NTG	p
Renal Resistive index	0.64±0.03	0.61±0.02	0.01	0.73±0.1*	0.72±0.12*	0.68
Renal Perfusion index	3096±2555	2848±1607	0.88	1982.09±1213.73	2075±1012	0.63
Systolic BP (mmHg)	115±12	112±10	0.56	131±17*	128±19*	0.84
Diastolic BP (mmHg)	70±10	63±14	0.19	77±15	71±16	0.29
Heart rate (beat/min)	61±10	63±9	0.35	67±11	67±11	0.93

*p<0.05, Healthy vs CKD

Conclusions

Although there was a trend towards a lower CEUS-assessed renal microperfusion in CKD patients, this difference did not reach statistical significance in this small pilot study. Sublingual Nitroglycerin induced only small changes in ultrasound-derived parameters of renal circulation and seems to have limited potential as a new test of renal flow reserve.

P 33

Successful treatment of immunotactoid glomerulopathy exhibiting nephrotic syndrome with rituximab

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Background

As immunotactoid glomerulopathy (ITG) is a very rare primary glomerular disease, no standard treatment has been established. It has been reported that ITG progresses to end-stage renal disease at a high rate. Here, we report a case of ITG exhibiting nephrotic syndrome treated by rituximab.

Methods

We report a case of a 53-year-old male with nephrotic syndrome and normal kidney function. Initially kidney function was normal with a creatinine of 82 µmol/l (eGFR CKD-EPI 94 ml/min/1.73 m²), proteinuria was 4 g/d and serum albumin was 24 g/l. Kidney biopsy was preformed which showed signs of a membranous glomerulopathy and mesangioproliferative glomerulopathy. Clinical and laboratory there was no hint for any underlying systemic autoimmune disorder or malignancy. Since the membranous pattern was predominant in the kidney biopsy the patient was treated conservative with diuretics and antiproteinuric therapy. Kidney function stayed stable and proteinuria decreased to 3g/day and albumin was 25 g/l. However, after two years proteinuria increased to 6g/day and albumin decreased to 20 g/l. Another kidney biopsy was performed which revealed now immunotactoid glomerulopathy. There was still no sign of underlying systemic or lymphoproliferative disorder.

Results

After treatment with 1g rituximab initially followed by another 1g after 14 days, we observed a continuous decrease of proteinuria to 2 g/day and an increase of albumin to 33 g/l over a period of 18 month.

Conclusions

ITG is difficult to treat and there are no randomized controlled trails to guide optimal therapy. However, given the generally poor prognosis associated with this disorder, it is reasonable to offer a trial of immunosuppressive therapy. In this case, partial remission was achieved through depletion of B cells by administration of rituximab.

P 34

A non-steady state adaptation of the CKD-EPI equation

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Background

The CKD-EPI equation is one of the most widely used estimates of kidney function. It is commonly calculated whenever a plasma creatinine (pcr) is measured, although only valid when pcr is stable. Chen proposed a “kinetic eGFR” (JASN 24, 877-888 (2013)) for non-steady state conditions. Despite its name it essentially estimates a creatinine clearance (crcl). The goal of our calculations was to develop a true kinetic eGFR estimation and to improve the underlying kinetic clearance formula by explicitly including creatinine generation rate (cgr), the creatinine distribution volume (vd), and accounting for possible changes in distribution volume (deltavd).

Methods

The pharmacokinetics of creatinine are comprehensively described by equation A. To solve it for crcl requires an iterative process, so a simplified form has been used, which we modified to allow for corrections of deltavd (equation B). In steady state, crcl is creatinine excretion rate (which equals cgr) divided by the pcr. To convert our kinetically determined crcl into CKD-EPI based eGFRs, we divided cgr by crcl and calculated a virtual steady state pcr. We then inserted this into CKD-EPI. Cgr and vd were estimated with published formulas (incorporating age, gender, race, weight and height).

Results

The comparison of crcl values obtained by equation B and the “gold standard” equation A demonstrated excellent agreement across physiologically plausible ranges of their variables pcr1, pcr2, vd, deltavd, time interval (t) and cgr. The final kinetic CKD-EPI equations were tested for sensitivity to deviations of cgr and vd from their estimated values. We show that differences within clinically meaningful ranges can have significant effects on the kinetic eGFR. Therefore, cgr and vd need to be checked for plausibility and adjusted (e.g. according to muscle mass, volume status) in individual patients.

Equation A:

$$pcr2 = pcr1 \left(\frac{deltavd - vd}{vd}\right)^{1 \frac{crcl \cdot t}{deltavd}} + \frac{cgr \left(1 - \left(\frac{deltavd \cdot vd}{vd}\right)^{-1 - \frac{crcl \cdot t}{deltavd}}\right)}{crcl \cdot \frac{deltavd}{t}}$$

Equation B:

$$crcl = -\frac{deltavd}{t} + \frac{2\left(cgr - \frac{(-pcr1 - pcr2, Vd)}{t}\right)}{pcr1 - pcr2}$$

Conclusions

We have developed a non-steady state adaptation of the CKD-EPI equation.

P 35

A case report of multiple dissections in abdominal arteries

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Background
Polyarteritis nodosa (PAN) is a necrotizing vasculitis that typically affects medium-sized arteries, i.e. visceral arteries, presenting with systemic symptoms. Microaneurysms at the mesenteric or renal arteriography are a typical finding. Immunosuppressive therapy with glucocorticoids is the gold standard, including cyclophosphamide in more severe disease. Another illness that clinically and radiologically overlaps with PAN is the segmental arterial mediolysis (SAM), a rare, non-inflammatory nor atherosclerotic arteriopathy that also affects the medium-sized splanchnic branches of the aorta. Radiological findings are dissection and aneurysm with or without organ infarction in the mesenteric or renal arteries. The absence of inflammatory markers represents one criteria for the diagnosis. The mainstay management is primarily supportive with pain control, antihypertensive and antiplatelet therapy.

Methods
We report the case of multiple abdominal arterial dissections and aneurysms.

Results
A 59-year-old woman presented with sudden onset of abdominal pain without any other symptom or sign of inflammation, with dissection of the upper mesenteric artery at the CT abdomen. Three days later, by worsening of the abdominal pain and increasing in inflammation tests, a new CT abdomen was made, observing a progression in the mesenteric artery dissection and new dissections of hepatic and renal arteries causing renal infarction. An urgent stenting of the mesenteric was required with detection during the angiography of a microaneurismatic aspect, with a suspect of polyarteritis nodosa. Taken the atypical presentation without systemic symptoms and inflammation, a segmental arterial mediolysis could not be excluded. A PET-CT demonstrated a vasculitic origin through the contrast enhancement of hepatic and mesenteric arteries. We began immunosuppression (CYCLOPS Protocol), with rapid clinical and chemical response.

Conclusions
In cases of systemic dissection with microaneurisms of medial arteries, a differential diagnosis with the more rare segmental arterial mediolysis should be considered, as the treatment completely differs. We demonstrated that the diagnosis is possible through the PET-CT.

P 36

Urinary lithogenic risk profile in ADPKD patients treated with Tolvaptan

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Background
Nephrolithiasis is a common health problem in autosomal dominant polycystic kidney disease (ADPKD) and significantly contributes to patient morbidity. In observational studies, prevalence rates of up to 36% have been reported. Kidney stones of ADPKD patients are typically composed of uric acid or calcium oxalate and hypocitraturia and low urinary pH have been reported as the main prolithogenic abnormalities. Recently, Tolvaptan has been introduced for the treatment of ADPKD, but its impact on the lithogenic risk profile in ADPKD patients remains unknown.

Methods
We conducted an analysis of patients enrolled in the Bern ADPKD registry, a prospective longitudinal observational cohort study. Inclusion criteria were age ≥ 18y, clinical diagnosis of ADPKD, informed consent. The main exclusion criterion was need for renal replacement therapy. Twenty-four hour urine analyses were performed at baseline and then at yearly follow-up. Relative supersaturation ratios (RSS) for CaOx, CaP and UA were calculated with EQUIL2. Univariable and multivariable mixed-effects linear regression models adjusted for age, sex, BMI, eGFR and endogenous acid production, estimated by net acid excretion, were used to assess the impact of Tolvaptan treatment on urinary composition.

Results
38 patients treated with Tolvaptan (60.5% males) were included in the analysis. Six patients (15.8%) had a history of symptomatic stone events. In multivariable analysis, Tolvaptan treatment was significantly associated with reductions of CaOx (β:-0.394, 95%CI: -0.597 to -0.192, P <0.01), CaP (β:-0.155, 95%CI: -0.257 to -0.054, P <0.01) and UA (β:-0.316, 95%CI: -0.445 to -0.189, P <0.01) RSS and increased urinary citrate (β:0.041, 95%CI: 0.009 to 0.073, P = 0.02) and calcium (β:0.054, 95%CI: 0.015 to 0.093, P <0.01) excretion. In contrast, Tolvaptan treatment was not associated with alterations in urinary oxalate excretion or urinary pH.

Multivariable models

Outcome variables	N	β	95% CI	*P* value
RSS Calcium Oxalate*	254	-0.3941	-0.5969 to -0.1924	< 0.001
RSS Brushite*	255	-0.1550	-0.2566 to -0.054	0.003
RSS Uric acid*	255	-0.3164	-0.4454 to -0.1894	< 0.001
Urine citrate / creatinine ratio (mmol/mmol/day)*	255	0.0409	0.0087 to 0.0734	0.015
Urine phosphate / creatinine ratio (mmol/mmol/day)	255	-0.0145	-0.1734 to 0.1416	0.86
Urine oxalate / creatinine ratio (mmol/mmol/day)*	253	0.0120	-0.0028 to 0.0268	0.12
Urine calcium / creatinine ratio (mmol/mmol/day)*	255	0.0544	0.0154 to 0.0927	0.007
Urine uric acid / creatinine ratio (mmol/mmol/day)	255	0.0020	-0.0166 to 0.0203	0.84
Urine pH*	255	0.0248	-0.0053 to 0.0554	0.11
Plasma copeptin (pmol/L)**	233	1.1621	0.9736 to 1.3444	< 0.001

Table 2: Associations between the explanatory variable Tolvaptan treatment with risk factors of kidney stone formation as outcome variables, adjusted for age, sex, BMI, eGFR and NAE. NAE = net acid excretion, eGFR = estimated glomerular filtration rate* = square root transformed, ** = natural logarithm transformed. Number of observations (N), beta coefficients (β), 95% confidence intervals (95% CI) and *P* values are indicated for the presence of Tolvaptan treatment.

Univariable models

Outcome variables	N	β	95% CI	*P* value
RSS Calcium Oxalate*	265	-0.5355	-0.7431 to -0.3286	< 0.001
RSS Brushite*	264	-0.1827	-0.2904 to -0.0769	< 0.001
RSS Uric acid*	266	-0.4350	-0.5859 to -0.2827	< 0.001
Urine ammonium / creatinine ratio (mmol/mmol/day)*	270	-0.1063	-0.1943 to -0.0186	0.018
Urine citrate / creatinine ratio (mmol/mmol/day)*	275	0.0208	-0.013 to 0.0543	0.22
Urine phosphate / creatinine ratio (mmol/mmol/day)	274	-0.1533	-0.3086 to 0.0004	0.051
Urine oxalate / creatinine ratio (mmol/mmol/day)*	273	0.0178	0.0032 to 0.0323	0.017
Urine calcium / creatinine ratio (mmol/mmol/day)*	277	0.0073	-0.0312 to 0.0452	0.71
Urine uric acid / creatinine ratio (mmol/mmol/day)	275	-0.0038	-0.0217 to 0.0139	0.68
Urine pH*	268	0.0520	0.0119 to 0.0916	0.011
NAE / urine creatinine (mEq/mmol/day)	236	-0.1988	-0.3345 to -0.062	0.004
Urine volume (mL/day)*	291	3.3965	2.0933 to 4.7028	< 0.001
Plasma copeptin (pmol/L)**	261	1.1497	0.9848 to 1.3155	< 0.001

Table 1: Univariate associations between the explanatory variable Tolvaptan treatment with risk factors of kidney stone formation as outcome variables. NAE = net acid excretion, * = square root transformed, ** = natural logarithm transformed. Number of observations (N), beta coefficients (β), 95% confidence intervals (95% CI) and P values are indicated for the presence of Tolvaptan treatment

Conclusions
Tolvaptan significantly reduces RSS for CaOx and UA. Future studies are needed to assess the impact of Tolvaptan
treatment on stone recurrence in ADPKD patients.

P 37

Memo is required for FGF23 expression during osteoblast differentiation (NCCR-Kidney.CH project)

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Background

Memo ablation in mice caused a bone disease with diminished osteoblast and osteoclast serum biomarkers (Moor, JBMR Plus 2018). This biomarker profile resembles alterations occuring during adynamic bone disease in humans with renal failure, and those found in klotho-deficient mice (Kawaguchi, J Clin Invest 1999). FGFR signaling is impaired in Memo-deficient osteoblasts (Moor, JBMR Plus 2018) because Memo modulates FGFR (Marone, Nature 2004; Haenzi, FASEB J 2014). In health and in kidney disease, FGF23 expression by bone requires feedback regulation involving FGFR/Klotho signaling (Kaludjerovic, FASEB J 2017). Therefore, we hypothesized that the FGF23 expression regulation is disturbed in Memo-deficient bone cells. **Methods**
Osteoblast progenitors were isolated from nenonatal calvaria of control mice and of inducible whole-body Memo KO (wbKO) as previously described (Moor et al., JBMR Plus 2018). Memo1 exon2 was excised using 4OHtamoxifen, and cells were differentiated to osteoblasts using beta-glycerophosphate and ascorbic acid. Gene expression of FGF23 and of TNAP encoding alkaline phosphatase (ALP) and Bglap (osteocalcin) were measured by qPCR. ALP activity was measured and stained in these cells.

Results
FGF23 gene expression was detected in control osteoblast-like cells, but not in Memo-deficient osteoblasts. Conversely, during osteoblast differentiation ALP activity and its corresponding gene expression were more increased in Memo-deficient osteoblasts. Similarly, Bglap expression was increased in Memo-deficient osteoblasts. Intriguingly, Memo-deficient osteoblasts showed ALP activity staining occuring in nodules, whereas control osteoblasts showed more uniform staining.

Conclusions
Under Memo deficiency, FGF23 gene expression is impaired in primary osteoblasts, since it is controlled by FGFR-mediated signaling. With ascorbic acid as a strong antioxidant in culture medium, the opposite phenotype appears in Memo-deficient osteoblasts regarding FGF23 and ALP compared with the in vivo Memo wbKO phenotype, where a disturbed bone redox homeostasis is present with low NAD+/NADH ratio (Moor, JBMR Plus 2018), resembling metabolism in cancer cells (da Veigo Moreira, Metabolites 2016).

P 38

Memo1 modulates renal Rho-GTPase signaling at resting state and in response to FGF23 (NCCR-Kidney.CH project)

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Background
Memo is an intracellular redox protein that modulates receptor tyrosine kinase-driven cellular signaling (Mac- Donald, Science Signal 2014). Mice with postnatally-induced deficiency in Memo showed a phenotype resembling Klotho and Fgf23-deficient mouse models (Hänzi, FASEB J 2014). FGF receptor signaling modifies the activity of cytoskeletal Rho-GTPases to support FGF-driven downstream effects on a cell (Eun-Young, J Biol Chem 2003). However, several drugs used in humans with kidney disease affect Rho-GTPase activity, such as lipidlowering statins (Rashid, Circ J 2009) or bisphosphonates (Kuiper, Br J Pharmacol 2012). Here, we investigated the effect of Memo1 deletion on small Rho-GTPase signaling at resting state and upon FGF23 treatment in mice.

Methods
Exon 2 of Memo1 gene was postnatally deleted in mice to obtain whole-body knockout (wbKO) mice. Littermates without Cre served as controls. Kidney tissue was harvested after intraperitoneal injection with FGF23 or vehicle. Kidney lysates were used in immunoblotting and probed with antibodies against Rho-GTPase relateda proteins. RhoA and Rac1 activity were measured in renal cortical lyates.

Results
FGF23 caused an increased renal Rac1 activity compared to vehicle in controls, but this was absent in kidney from Memo wbKO. Rac1 protein quantity was comparable across conditions. However, renal RhoA activity and protein quantity were excessive in Memo wbKO animals but were not significantly affected by FGF23. The renal quantity of regulator protein Rho-GTPase dissociation inhibitor 1 was unaffected by genotype and treatment.

Conclusions
FGF23-dependent induction of Rac1 activity in controls was similar to what has been reported in cells treated with FGF2 (Eun-Young, J Biol Chem 2003). Renal RhoA was excessive in Memo wbKO, similarly as in Memodeficient nematodes (Ewald, eLife 2017). Further studies should determine the drug side effects on the renal responses to FGF23 during kidney disease, and assess to which extent the Memo- dependent cell signaling phenotype is mediated via the disturbed small Rho-GTPases.

P 39

From rats and guinea pigs

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Background
Leptospirosis is the most important zoonosis in the world and frequently associated with acute kidney injury in tropical countries, but not in developed countries. The major histological findings are pathogen-induced tubulointerstitial nephritis and acute tubular necrosis. Although antibiotic treatment is efficient in resolving the infection, some patients have incomplete renal recovery and progress to CKD due to sustained tubulointerstitial nephritis. The question is whether corticosteroids are a useful therapy for the treatment of the pathogeninduced acute tubulointerstitial nephritis.

Case
A 54-year-old man was hospitalized in the intensive care unit due to septic shock with acute anuric renal failure, hepatic injury, respiratory failure, thrombocytopenia and rhabdomyolysis. Based on the history - dealing with dead guinea pigs and rats 20 days ago - the suspicion of leptospiral infection was raised. We started ceftriaxone and doxycycline, carried out continuous hemodiafiltration, and in the course intermittent hemodialysis therapy for anuric renal failure. The diagnosis was confirmed by a positive urine- and serum-PCR. Antibiotic treatment resulted in improvement in his general condition. After three weeks, we were able to stop hemodialysis. Despite an improvement in the patient's condition and most laboratory data, renal impairment persisted. Therefore, we performed a renal biopsy, which revealed an acute tubulointerstitial nephritis. Since the infection subsided under antibiotic therapy, oral administration of corticosteroids at 0.8 mg/kg body weight for sustained tubulointerstitial nephritis was started in accordance with the colleagues of the infectiology ward. Gradual tapering of the corticosteroids was performed over two months. Eight weeks later, his serum creatinine levels returned to the normal range.

Conclusions
Renal biopsy should be performed if renal function does not improve after successful treatment of leptospiral infection. If persistent tubulointerstitial nephritis is present, oral corticosteroids may be a therapeutic option to prevent progression to CKD.

P 40

LYMPHOCYTE PHENOTYPE AND FOXP3+: A POTENTIAL TOOL FOR CLINICAL MANAGEMENT IN SYNDROME OF TUBULOINTERSTITIAL NEPHRITIS WITH UVEITIS (TINU)

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Background
TINU syndrome is rare and clinical management remains uncertain. A lymphocyte-mediated immune mechanism has been suggested to ex-

plain the pathogenesis of idiopathic TINU. Regulatory T cells (Tregs) express the x-linked transcription factor FOXP3+ as a major regulator of the function of T lymphocytes. Few reports have addressed the issue of whether Tregs may dampen alloimmune responses thus limiting tissue damages in TINU; the interpretation of the level FOXP3+ is also not yet validated in TINU (1). Our case evaluates the lymphocyte phenotype and the density of FOXP3+ T cells in the renal biopsy of a TINU syndrome.

Methods
A 39-year-old female was admitted for a left ocular pain, redness and photophobia 1 month before. Anterior uveitis was diagnosed by slit lamp examination.

Results
Laboratory findings showed: ESR 9 mm/h, BUN and serum creatinine were 8.1 mmol/l and 170 µmol/l respectively. ANA, ANCA, anti s-DNA, anti-Sm antibody, ACE were all-negative. CD4+ T lymphocyte 36% (normal 25%– 54%) and CD8+ T lymphocyte 37% (normal 23%–56%). HLA typing revealed DQA1*01 and 02:01 and DQB1*02:02 and 05:01 genotypes. Urinalysis results were unremarkable and her kidneys appeared normal by sonography. A renal biopsy showed: interstitial mononuclear inflammatory component (20% of the cortical surface) and interstitial fibrosis (30% of the cortical surface). No deposit was revealed by immunofluorescence. The number of cells CD4+ or FOXP3+ was then automatically quantified by color segmentation. FOXP3+ density was measured at 243 cell/mm^2. Based on the ocular and renal findings, TINU syndrome was diagnosed.

Conclusions
The immunopathology of TINU could implicate a delayed-type hypersensitivity reaction, with skewing to a Thelper cell type 1. FOXP3-expressing cells in the kidney may correlate with the clinical or pathological feature. Studies are needed to evaluate if the persistence of lymphocytes in the plasma and the density level of FOXP3+ in the kidney could predict the evolution of TINU.

P 41

NOSTONE Trial: Randomized double-blind placebo-controlled trial assessing the efficacy of standard and low dose hydrochlorothiazide treatment in the recurrence prevention of calcareous nephrolithiasis

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Background
Nephrolithiasis is a global healthcare problem with a current lifetime risk of up to 18.8% in men and 9.4% in women. Without specific treatment, 5- and 20-year recurrence rates are 40% and 75%, respectively. Given the high cost of medical treatments and surgical interventions as well as the morbidity related to symptomatic stone disease, medical prophylaxis for stone recurrence is an attractive approach. Nowadays, thiazides are widely used in the treatment of recurrent nephrolithiasis and arterial hypertension. In the case of recurrent nephrolithiasis, however, this practice is not supported by randomized evidence. Thus, evidence for benefits and harms of low dose thiazides in the prevention of calcium-containing kidney stones in general remains unclear.

Methods
The NOSTONE clinical trial is a multicenter, randomized, placebo-controlled, double-blind, parallel-group trial with the purpose to assess the dose-response relationship for three different dosages of HCTZ (placebo, 12.5mg, 25.0mg, 50.0mg). The primary outcome is the incidence of stone recurrence (a composite of symptomatic or radiologic recurrence), a low-dose CT will be performed at beginning and at the end of the trial. A total of 416 patients from 12 hospitals in Switzerland will be included in the study.

Results
Recruitment started in Bern on the 9th of March 2017, all study sites are operative since June 30th2017. The recruitment for all sites with the exception of Bern closed on the 31st of August 2019, 396 patients were randomized in the trial (regular updates: www.nostone.ch). Baseline data concerning the study population and stones composition will be available after the end of recruitment in Bern.

Conclusions
The NOSTONE study will provide critical information to physicians for the treatment of kidney stones. The impact of the results of this study will affect many patients currently treated with hydrochlorothiazide for the prevention of recurrent nephrolithiasis.

P 42

Integrated Efficacy Results from the Phase II and Phase III Studies with Caplacizumab in Patients with Acquired Thrombotic Thrombocytopenic Purpura

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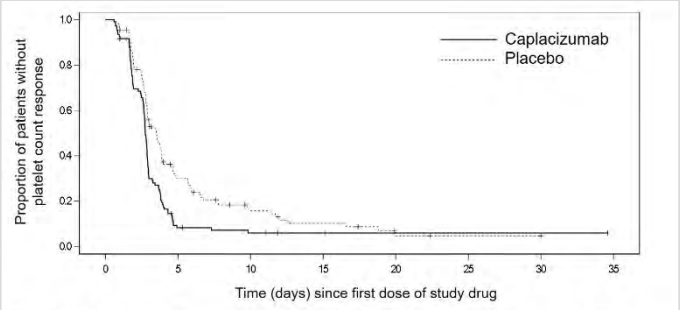
Background
Acquired thrombotic thrombocytopenic purpura (aTTP) is a rare, lifethreatening thrombotic microangiopathy. The efficacy of caplacizumab in aTTP, in conjunction with plasma exchange (PE) and immunosuppression, was demonstrated in placebo-controlled Phase II and III studies. Here, we present the integrated efficacy results of these studies.

Methods
All randomized subjects in the studies were included in the analysis. Phase III study subjects could have an openlabel caplacizumab treatment. The primary endpoint was time to platelet count response. Secondary endpoints included mortality rate; the number of PE days; the proportion of subjects with TTP-related death, recurrence of TTP or at least one treatment-emergent major thromboembolic event during treatment (composite endpoint); a recurrence of TTP; refractory TTP.

Results
220 subjects were randomized, 108 to caplacizumab and 112 to placebo. There was a significant difference in favour of caplacizumab in time to platelet count response (p <0.001). Treatment with caplacizumab resulted in a 72.6% reduction in the composite endpoint during the DB/SB treatment period (p <0.0001). Treatment with caplacizumab reduced recurrences of TTP by 84.0% during the DB/SB treatment period (p <0.0001), and by 49.5% during the overall study period (p <0.005). No patients died in the caplacizumab group vs. 4 in the placebo group during the DB/SB treatment period (p <0.05). There was a reduction in the mean number of PE days of 3.9 days in the caplacizumab vs. placebo group.



TITAN: Response was defined by a recovery of platelets count ≥150,000/µL. This response had to be confirmed at 48 hours after the initial reporting of platelet count recovery equal to or above 150,000/µL by a de novo measure of platelets count ≥150,000/µL and LDH ≤2 x upper limit of normal range.
HERCULES: Response was defined as initial platelet count ≥150,000/µL with subsequent stop of daily PE within 5 days.

Conclusions
This integrated efficacy analyses confirmed results from Phase II and III studies showing that caplacizumab significantly reduces time to platelet count response, and resulted in clinically meaningful and significant reductions in the proportion of subjects with TTP-related death, a recurrence of TTP, or at least one major thromboembolic event; the rate of death due to TTP a recurrence of TTP; refractory TTP; and the mean number of PE days, during the treatment period.

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Evaluation of Etio-Pathology and Risk Factors Prevailing in Hypertensive Patients of Rural Bangladesh

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Background
Hypertension is a widely prevalent health problem. Identifying hypertension and its prevalent etiologies with associated metabolic risk factors will help managing this group.

Methods
This was an observational study. Subjects were randomly selected from a rural population in Bangladesh. Results from an early group are presented here. Baseline demographic, anthropometric and clinical information was recorded in WHO STEPS Instrument. (Core and Expanded). Blood Pressure was measured by digital blood pressure monitor (Omron) with standard sized cuff after 10-15 minutes of rest in sitting posture and mean of two readings. A fasting blood sample and spot urine was collected. BP ≥140/90mmHg, FBS >5.6 mmol/l and HbA1c ≥6.5%, LDL 150 mg/dl , Cholesterol >200 mg/dl , eGFR <60ml/min (MDRD equation) or urine positive for ACR >30 mg/g was taken as diagnostic cut-offs for hypertension, diabetes, dyslipidemia and nephropathy.

Results
Mean age of the participants was 40+14 years, bmi 24+3 kg/m^2 with over weight to obese 50%, 80% had up to primary education, tobacco user was -smoke/smokeless- 22/14%. Prevalence of hypertension was 27% (systolic 23% & diastolic 17%). Secondary causes of HTN were DM (23%) and nephropathy (7%). Cholesterol was >200mg% in 57% and LDL >150 mg% in 31%. High incidence of parental hypertension (35%) and diabetes (28%) was seen. Fruit and vegetable intakes were low (3 serving/day in only 12%), 80% were ingesting added salt with food, 80% had moderate to sedentary lifestyle and only 50% were aware of their hypertension. All subjects had low urinary K+ excretion 47+24mmol/l.

Conclusions
Hypertension is highly prevalent in rural community. Modification of lifestyle specially healthy eating, limiting salt intake and exercise need to be emphasized. Frequent monitoring of blood pressure and its risk factors should be implemented in primary care facilities

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Is there a practical role for bone biopsy in CKD patients?

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Background
Compared with the general population, fracture incidence rates are more than fourfold higher in CKD patients, the risk increasing with progressive CKD. As alterations to bone morphology in CKD-MBD comprise a heterogenous group of metabolic bone disorders it seems important to discern them in order to choose the appropriate treatment. Bone biopsy should help to accurately assess the type of renal steodystrophy and the responses to therapeutic interventions.

Methods
In 2014 we started to perform bone biopsies in selected CKD patients to gain knowledge and expertise about the procedure. After written approval, the patient had to ingest tetracycline for bone labeling in order to determine bone turnover rate. Transiliac crest biopsies were performed by fluoroscopic technique under local anesthesia and analgosedation, using an electrical drill [Acculan 3TI] with a special manufactured drill sleeve (internal diameter 4 mm, length 140 mm).

Results
A total of 21 bone biopsies in 17 patients were performed: the main findings are summarized in Table 1 through 3 for demographic, histological and outcome data, respectively.

Table 1: Demographics

	Number
Patients	17 (Female: 52.9%)
Mean age (years)	62.4
CKD Stage	
G5D	11
G5	1
G4	2
G3	2
G2	1
History of fractures	6
DXA results	12
Osteoporosis	5
Osteopenia	7
Diabetes mellitus 2	3
History of parathyroidectomy	4
History of calciphylaxis	3
History of kidney transplantation	1

Table 2: Histology

	N (%)
Bone biopsies	21 (100)
Repeated biopsies	4 (19.0)
Representative material	17 (80.9)
Good quality	7 (33.3)
Reduced assessment due to destroyed spongiosa	10 (47.6)
No representative material	4 (19.0)
Tetracycline labeling done	15 71.4)
High turnover osteopathy due to HPT	8 (47)
Low turnover due to adynamic bone disease	4 (23.5)
Mixed uremic osteodystrophy	1 (5.8)
Osteomalacia	1 (5.8)
No definite diagnosis*	
* 1 patient agreed on a second bone biopsy	3 (17.6)

Table 3: Outcome

	Patients	
	N	%
Biopsy confirmed clinical diagnosis	10	58.8
Biopsy corrected clinical diagnosis	4	23.5
Biopsy with no definite result	3	17.6
Treatment modality after bone biopsy:		
Teriparatide 20 mcg s/c per day	4	23.5
Bisphosphonates	2	11.7
Parathyroidectomy	2	11.7
Cinacalcet/Paricalcitol	6	35.3
Vitamine D3 (25-OH) i.m.	2	11.7
Kidney transplantation	2	11.7
Follow-up > 2 years	11	64.7
Outcome measured by:		
Bone markers	17	
Fracture incidence	2	
DXA follow-up	4	
Bone biopsy	3	
Death	4	23.5

Conclusions
The get an representative bone biopsy in a CKD patient is not an easy task as a kidney biopsy: the spongiosa is easily destroyed by the intervention itself. In most instances the presumed osteologic diagnosis could be confirmed by the histologic findings. Nevertheless the identification of the underlying bone metabolism can be of crucial importance when a CKD patient with manifest osteoporosis has inconclusive bone formation and resorption markers: the question is whether an antiresorptive or an osteoanabolic treatment would be harmful / beneficial for increasing his bone strength. Because of the scarcity of evidence in the treatment in CKD-MBD an interdisciplinary approach is needed to discuss the treatment options and to determine the monitoring of the outcome (fracture, BMD, virtual bone biopsy, bone biopsy) for assessing efficiency.

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An unexpected cause of nephrotic-range proteinuria

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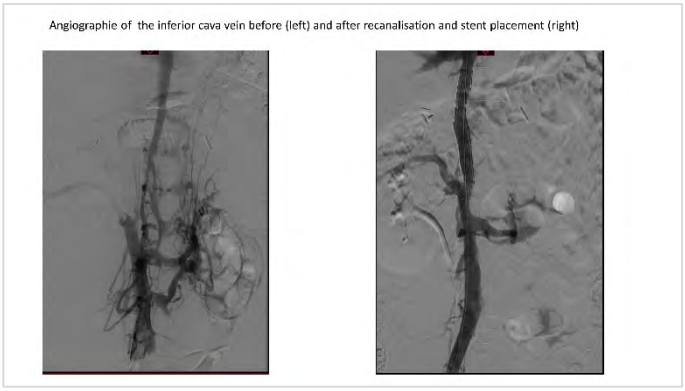
Background
Nephrotic-range proteinuria is a common reason for nephrological consultation in clinical practice. The differential diagnosis is wide, and generally focuses on different forms of glomerulonephritis.

Methods
We report 2 female patients who presented with nephrotic-range proteinuria. In the first patient, known with extreme obesitas(BMI 75kg/m²), nephrotic-range proteinuria was discovered during an emergency visit for acute abdominal pain due to cholecystits. The second patient developed stage 4 chronic kidney disease and progressive proteinuria (10-18 g/l) after accidental rupture of the inferior vena cava (IVC) during a gastric bypass operation that was prematurely interrupted hereafter.

Results
On split-urine collection, both had a much higher degree of proteinuria during the day as compared to the night, compatible with orthostatic proteinuria. At further work-up, inferior vena cava (IVC) thrombosis was diagnosed in both patients, without renal vein thrombosis. After respectively anticoagulation in the first case and anticoagulation plus endovascular recanalization in the second (see Figure), there was a complete resolution of the orthostatic proteinuria and a strong improvement of the estimated glomerular filtration rate in both cases.



Conclusions
These cases highlight that nephrotic-range proteinuria is not always caused by glomerulonephritis, and that a split-urine collection may unravel an underlying problem in the post-renal venous circulation.

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FOCAL AND SEGMENTAL GLOMERULOSCLEROSIS FOLLOWING SHORT-TERM BILASTINE ADMINISTRATION: A CASE REPORT

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Background
Drug-induced nephrotoxicity is often associated with tubulointerstitial injury, causing either acute tubular necrosis or acute interstitial nephritis. Though less common, drugs may induce glomerular injury by targeting visceral epithelial, endothelial and/or mesangial cells. Focal and Segmental Glomerulosclerosis (FSGS) has been described following administration of some drugs such as IFN-a, pamidronate, sirolimus, anabolic steroids, lithium and following heroin abuse. Whether FSGS may occur secondary to selective H1-receptor antagonist administration is unknown.

Methods
Case-Report: We report a case of an 84 year old Caucasian man with no H/O of renal disease, who presented with onset of generalized oedema and uncontrolled severe hypertension (BP 200/105 mmHg). The symptoms appeared 2 weeks after the beginning of a treatment with Bilastine (BilaxtenR) for allergic rhinitis. Except for a treated essential hypertension, medical history and physical examination were otherwise unremarkable.

Results
Initial laboratory data revealed normal renal function (serum creatinine 64mcmol/L), hypoalbuminemia (serum albumin 27 g/L), normal total cholesterol (4.75mmol/L) and heavy proteinuria (protein excretion of 4.43 g/day). Anti-histone antibodies were elevated while PLA2 was normal. Further laboratory and CT-scan evaluation excluded the presence of systemic, collagenous and/or neoplastic disease. After normalisation of the blood pressure a renal biopsy was performed. The histology showed a pattern consistent with FSGS with TIP-lesion type in 1/29 glomeruli and a moderate atherosclerosis. The therapeutic regime was potentiated with an AII-receptor blocker. After 4 months of treatment there was no remission of the proteinuria.

Conclusions
In absence of any underlying systemic and/or neoplastic disease a drug-induced nephrotoxicity should be suspected. Though tubulointerstitial injury due to medications is more common, drug-induced glomerular disease should be included in the differential diagnosis in all patients presenting with proteinuria, haematuria and/or renal failure. A careful medical history of medication is therefore mandatory in any patient with suspected glomerular disease.

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Chronic inflammatory demyelinating polyneuropathy and concurrent membranous nephropathy associated with anti-contactin-1 autoantibodies

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Background
Membranous nephropathy (MN) is a common cause of nephrotic syndrome in nondiabetic adults, accounting for up to one-third of biopsied cases of nephrotic syndrome. Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired disorder of peripheral nerves. Antibodies directed against the paranodal axonal cellular adhesion molecule contactin-1 and its binding partner neurofascin have been identified in some severe cases of CIDP. Case reports of patients with co-existing MN and CIDP have been published, but an underlying disease mechanism has not been described in these patients.

Methods
A 45-year old male was diagnosed with CIDP in March 2015. He was treated with prednisone, IVIG and azathioprine with good clinical and electrophysiologic response. In March 2016 he was diagnosed with pulmonary embolism and treated with rivaroxiban. In September 2016, he presented with nephrotic syndrome with 22 g/day of protein, anasarca, hypoalbuminemia, and hypercholesterolemia. He underwent a renal biopsy which showed stage 2 MN. Renal function was normal and anti-phospholipase 2 antibody (found in the majority of primary MN patients) was negative. Malignancy, infectious, and routine autoimmune investigations were negative. Additional serology was positive for IgG4 anti-contactin-1 antibody. Neurofascin antibody was negative. We examined renal tissue for the presence of contactin-1 antigen by immunohistochemistry. The patient's biopsy was strongly positive for this antigen, while 2 control samples were negative. Cyclosporine was added to the patient's regimen with good resolution of proteinuria.

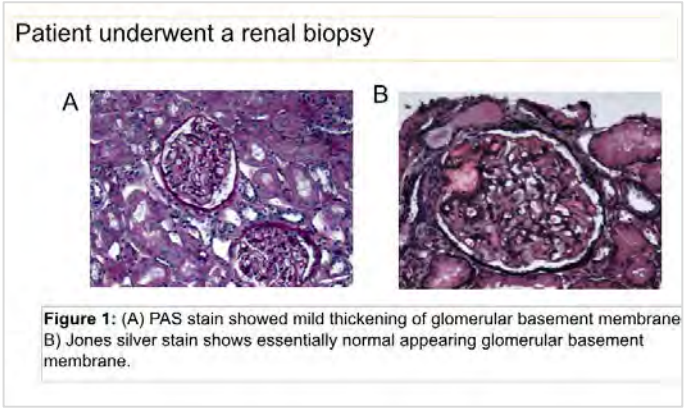

Figure 1: (A) PAS stain showed mild thickening of glomerular basement membrane B) Jones silver stain shows essentially normal appearing glomerular basement membrane.

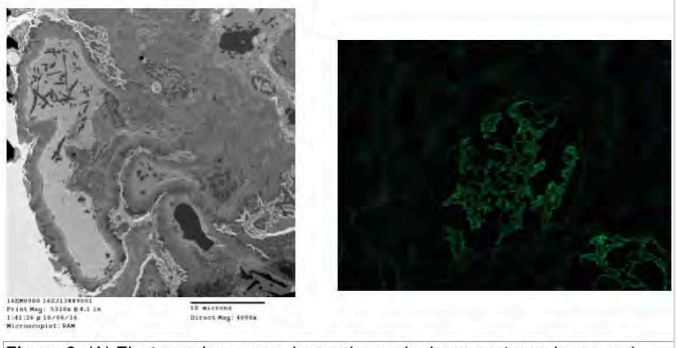

Figure 2: (A) Electron microscopy shows glomerular basement membrane and interstitial dense deposits suggestive of immune globulin. This was diagnostic of stage 2 membranous nephropathy and suggestive of secondary MN. B) Immunofluorescence shows positive staining for IgG.

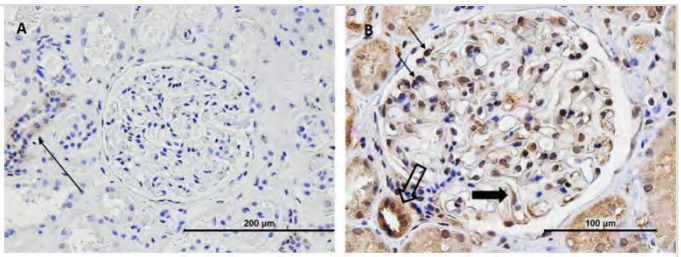

Figure 4: A) Normal control renal tissue (nephrectomy sample) shows minimal or non-specific contactin-1 staining in tubules (arrow). B) Patient biopsy sample shows extensive contactin-1 antibody staining in glomerulus (podocytes – thin arrows, thick arrow is an endothelial cell, open arrow is distal tubule.

Results
This is the first case report of anti-contactin-1 as a possible cause of MN in the setting of CIDP

Conclusions
Anti-contactin-1 antibodies have been identified as a cause of CIDP. This is the first report of these antibodies being identified in a case of secondary membranous nephropathy.Anti-contactin 1 antibody may be a novel diagnostic test in this condition, and may allow determination of therapeutic response

P 48

An unexplained case of acute kidney injury: would you consider orellanine ?

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Background
The diagnosis of out-patient acute kidney injury (AKI) can often be made rapidly with clinical and laboratory investigations. Sometimes, however, the etiology remains unclear even after a complete workup including a kidney biopsy.

Methods
We report a case of severe AKI in which the etiology could be identified only one year after admission when the patient finally confessed that she had consumed Cortinarius mushrooms in a suicidal attempt.

Results
A 46-years woman previously investigated for suspected multiple sclerosis was admitted end-september for nausea and vomiting with dizziness and stupor. A relapse of MS was suspected but a complete neurological workup (LP, MRI and EEG) was normal. An oliguric AKI was also present (Table 1). Renal morphology was normal. The patient was not taking any treatment at admission and repeatedly denied the consumption of nonprescribed medications or drugs. A toxic screening in urine was negative (benzodiazepine, opioids). In the following days the renal function worsened and hemodialysis (HD) was started. A kidney biopsy showed signs of acute tubular necrosis suggesting a toxic origin; the glomeruli were normal. With supportive care the mental status normalized but the patient developed anxio-depressive symptoms. The renal function also improved and HD could be stopped after 6 weeks. The creatinine stabilized thereafter at ≈200 µmol/l. Only one year later the patient finally admitted that in order to suicide she took three Cortinarius orellanus (CO) mushrooms 5 days before hospitalization.

Table 1: laboratory data at admission

Urea	15,4 mmol/l	Haemoglobin	145 g/l
Creatinine	424 µmol/l	Leucocytes	9,6 G/l
Sodium	138 mmol/l	Platelets	259 G/l
Potassium	4,5 mmol/l	pH	7,35
Ion. calcium	0,98 mmol/l	Bicarbonates	14 mmol/l
Phosphate	1,84 mmol/l		
Total proteins	70,4 g/l	**Urinanalysis**	
Albumin	39.8 g/l	Erythrocytes	3-5 /field
CRP	30 mg/l	Leucocytes	< 3 /field
CK	441 U/l	Sodium	111 mmol/l
LDH	487 U/l	Potassium	14 mmol/l
GOT	32 U/l	Creatinine	5,1 mmol/l
GPT	16 U/l	Proteins	3,55 g/l
gamma-GT	12 U/l	FE Na	6,7 %

Table 2: THE ORELLANUS SYNDROME

- Delayed symptom (> 6 hours after ingestion)
- Serious and potentially lethal toxicity

6-12 hours	Gastroenteritis	Nausea, vomiting, diarrhea, abdominal pain
1-4 days	Aspecific symptoms	Headache, general malaise, myalgias, dizziness, stupor
3-20 days	Orellanine	Acute renal failure with interstitial nephritis and tubulointerstitial fibrosis

Conclusions
Every year in Switzerland, ≈500 cases of accidental - or sometimes voluntary - mushroom poisoning are reported, only rarely due toCO. Cortinarius orellanus contains orellanine that can cause delayed nephrotoxicity. The 3 phases of the orellanus-syndromeare reported in Table 2. Once dialysis has to be instituted the prognosis is rather poor: 50% of these patients develop chronic renal failure. So far there is no causative therapy.

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Parvovirus B 19 causing severe anemia and graft dysfunction in renal transplant recipients: a report of 2 cases

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Background
Parvovirus B19 infection is a virus transmitted via respiratory secretions with a limited disease course in immunocompetent individuals. It has an affinity for human erythroid precursor cells often leading to mild anemia. In recipients of solid organ transplantation parvovirus B19 infection is associated with severe anemia/pure red cells aplasia or pancytopenia but also allograft dysfunction has been described.

Methods
Herein, we present two kidney transplant recipients who developed a severe anemia non-responsive to erythropoiesis stimulating agents (ESA) and with deterioration of renal transplant function in the early period after renal transplantation.

Results
Viremia was confirmed by polymerase chain reaction (PCR). Treatment was consistent with intravenous immunoglobulins (IVIG) initially every day for 3 and 5 days respectively, and tapered until once weekly. Immunosuppressive regimen with tacrolimus, mycophenolate mofetil was reduced in one patient. Hemoglobin levels gradually increased within 21 days after starting IVIG. Renal graft function improved to baseline 2 and 12 weeks respectively after starting IVIG-treatment.

Conclusions
Parvovirus B 19 is a common viral infection but probably underdiagnosed in renal transplanted recipients. Therefore, it should be considered in the differential diagnosis of pancytopenia or chronic anemia in the posttransplant period. Treatment with IVIG and reducing immunosuppressants is a valuable treatment option in severe cases.

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Integrated Safety Results from the Phase II and Phase III Studies with Caplacizumab in Patients with Acquired Thrombotic Thrombocytopenic Purpura

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Background
During the development of caplacizumab, safety data have been accrued from Phase I,II, and III studies in healthy subjects and patient with acquired thrombotic thrombocytopenic purpura (aTTP) . Given that caplacizumab blocks the interaction of the von Willebrand FactorA1 domain with the GPIb-IX-V platelet receptor, the main expected safety risk is bleeding.

Methods
The objective of this integrated analysis is to characterize the safety and tolerability of caplacizumab based on the pooled Phase I, II, and III data, with a main focus on data from the Phase II and III studies in aTTP. Data were analysed during the overall study including the follow-up period.

Results
Safety data for caplacizumab have been accrued in 220 aTTP patients. The median duration of exposure to study drug was 35.0 days in the caplacizumab group and 32.5 days in the placebo group. Similar percentages of subjects reported TEAEs in the caplacizumab (96.2%) and placebo (95.5%) group. Events that occurred more frequently (≥5% difference) in the caplacizumab group vs. placebo were epistaxis (29.2% vs. 5.5%; p <0.05), headache (20.8% vs 13.6%) and gingival bleeding (16.0% vs 2.7%; p <0.05). Events that occurred more frequently in the placebo group were TTP (35.5% vs 5.7%; p <0.05), hypokalaemia (20.0% vs 12.3%), and hypertension (12.7% vs 4.7%; p <0.05). A lower percentage of subjects experienced SAEs in the caplacizumab group vs. placebo. The most frequently reported SAE was TTP in both the caplacizumab (5.7%) and placebo (34.5%) group. A higher percentage of subjects experienced bleeding TEAEs in the caplacizumab group (60.4%vs. 42.7%). Bleeding TEAEs were mainly mucocutaneous, mostly selflimited and the majority resolved.

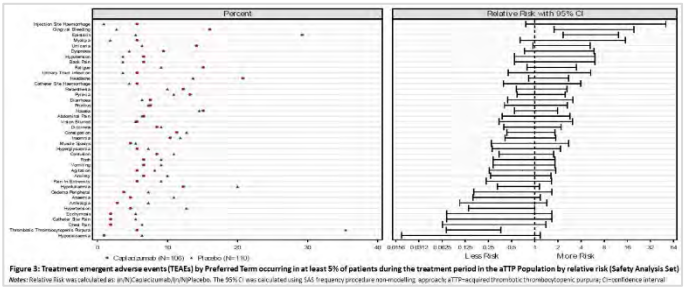

Figure 3: Treatment emergent adverse events (TEAEs) by Preferred Term occurring in at least 5% of patients during the treatment period in the aTTP Population by relative risk (Safety Analysis Set)

Conclusions
Bleeding TEAEs (epistaxis and gingival bleeding), were the most common TEAEs in subjects treated with caplacizumab. Results from laboratory tests confirmed the safety profile of caplacizumab. This integrated analysis shows that caplacizumab is well tolerated and has a favourable safety profile.

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Cognitive function in children with end stage renal disease on hemodialysis

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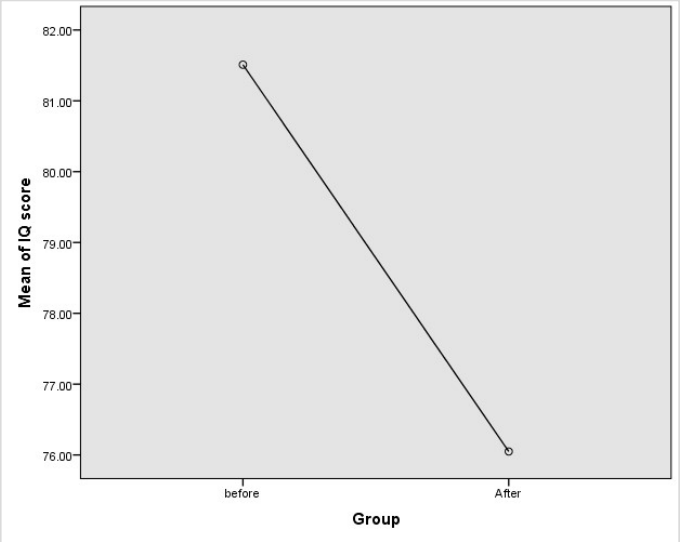
Background
Cognitive impairment is a common problem in end stage renal disease (ESRD) patients, but it is often underdiagnosed. Many studies documented impaired cognitive function in patients with ESRD both dialyzed and non-dialyzed. The aim of the present work was to assess the cognitive function in children and adolescents with ESRD on regular hemodialysis (HD) and to detect if there is deterioration in their cognitive function over time with the continuation of regular HD.

Methods
All ESRD patients on regular HD in the HD unit at the Nephrology unit, Alexandria University Children's Hospital (AUCH), Alexandria, Egypt, between May 2016 and May 2018 were included in the study. Exclusion criteria were diseases that influence the cognitive function. Intelligence was assessed using Stanford-Binet Intelligence Scale: Fourth Edition (SB4). The total IQ score and its four subdivisions: verbal reasoning (VR), abstract visual reasoning (AVR), quantitative reasoning (QR) and short term memory (STM) all were tested to all patients in two settings: at the start of the assessment (47 ESRD patients) and was repeated after one year from the first assessment to each patient separately (41 ESRD patients).

Results
72% & 85.4% of patients' total IQ, 88% & 90.2% of patients' VR, 59.6% & 80.5% of patients' AVR, 49% & 78.1% of patients' QR and 36.2% & 61% of patients' STM were below average values in the first and second assessments respectively. The total IQ and its four domains values showed decrease in the second assessment than the first assessment. All the percentage decrease between the first and second assessments were statistically significant for the total IQ and its four domains.



Conclusions
ESRD has negative effect on cognitive function of ESRD patients. This effect is not influenced by the regular HD.

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

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Background
To safely perform angioplasties in acute coronary syndromes with very low contrast volume using Cordis diagnostic catheters and thereby improve the clinical outcomes.

Methods
In 985 patients (1280 lesions/ 1440 stents) with acute coronary syndromes, angioplasty were performed with cordis 6F diagnostic catheters. Primary angioplasty was performed in 297 cases. In 76% of cases, Iodixanol was used. All contrast injections were given by hand. Regular follow-up of the patients was performed at 30 days. All the procedures were performed through femoral route . Tirofiban was used in 99% cases with adjusted dosages based on the creatinine values. The mean contrast volume used per patient was 27 ml (±6 ml) including the angiogram prior to angioplasty. Fifty-eight patients had creatinine more than 2 mg/dl before the angioplasty procedures. Forty-two patients had cardiogenic shock at presentation. 77% of the cases had diabetes. IVUS was used in only two patients. A variety of coronary stents from various companies were used. Buddy wires were used in 32 cases.

Results
Mild reversible nephropathy (CIN) was observed in five patients. Two patients had creatinine more than 5 mg/dl at presentation, and they were started on hemodialysis after the procedures. Three patients were already on dialysis. Switch-over to the radial route was seen in three cases due to associated aortic/iliac obstructive lesions. Fifteen mortality in total

was observed in this series; 10 of these patients had cardiogenic shock (3 late presenters), and two patients expired after discharge due to possible acute stent thrombosis, two patients had associated septic shock, and one patient died of severe acute respiratory distress syndrome. Groin hematoma was seen in three cases requiring one unit of blood transfusion.

Conclusions
Angioplasty and stenting could be performed safely in patients with acute coronary syndromes using Cordis diagnostic catheters using very low volume of contrast with improved cardiovascular and renal outcomes.

POSTER PRESENTATIONS – HEMODIALYSIS / PERITONEAL DIALYSIS

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Demography of the dialysis population in Switzerland in 2018

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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 Swiss dialysis population are given.

Methods
All medical establishments in Switzerland (both public and private; N = 92) providing chronic treatment by either hemo- and/or peritoneal dialysis, had to provide relevant data for the year 2018. All individuals being on chronic dialytic therapy in the year 2018 were enrolled (N = 4646). For patients alive on December 31 2018, data were gathered from this date or closest to this date. For patients who died during 2018 or were being transplanted, data refer to time of event, or to a date closest to the event.

Results
The median age of dialysis patients in 2018 increased almost by one year compared to 2016. More than fifty percent of the patients were older than 71 years, and nearly 1/4 were beyond 80 years. No relevant differences were found between female and male patients regarding mean age (68.6 vs . 68.3 years, respectively). However, women's dialysis vintage is significantly higher than men's (54.4 vs. 45.7 months, respectively) and they are significantly less comorbid than men (4.2 s. 4.7).

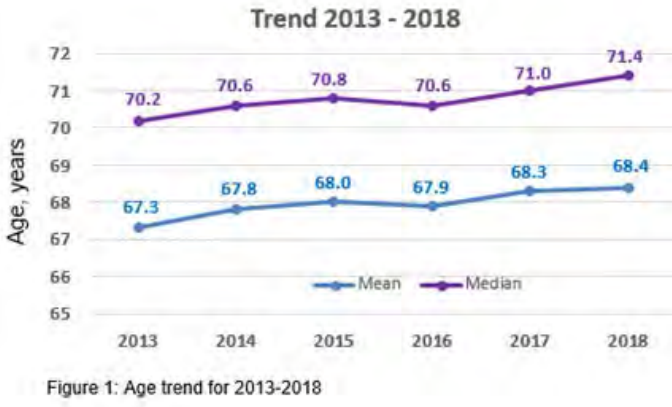

Figure 1: Age trend for 2013-2018

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

	All (100%)		In Centre (88.9%)		Home (11.0%)	
	Mean	Median	Mean	Median	Mean	Median
Age, yr	68.4	71.4	69.3	72.0	61.6	65.3
Dialysis vintage, months	48.8	34.0	50.9	36.0	31.6	21.0
Comorbidities, N	2.5	2.0	2.6	2.0	1.8	1.0
Charlson Comorbidity Index	4.5	4.0	4.6	4.0	3.7	3.0
Hypertensive, %	82.1		81.7		84.8	
Sex (male), %	64.9		64.7		66.9	

Comment: In 0.1% of patients, actual dialysis type is unknown

Table 2: Trend of incident/prevalent count and comorbidities in dialysis patients from 2014-2018

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

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 95.9 pmp is clearly lower than in most other countries. In 2018, 3789 prevalent patients (443.7 pmp) were dialyzed in Switzerland. The number of dialysis patients with diabetes increased by almost 1% from 2017, reaching 37.4%.

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Survival on dialysis: Switzerland in comparison with other countries – A follow up

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Background
Survival in dialysis patients is substantially reduced compared to the general population. The aim of the present analysis was to compare the survival of Swiss dialysis patients with other countries with an additional year of follow up and a higher number of patients.

Methods
Incident dialysis patients (hemo- or peritoneal dialysis; N = 4525) from the Swiss dialysis registry were followed up from 2014 on until December 31, 2018 (mean follow up days = 684). Deaths occurring during this time (N = 976) were recorded and survival was examined using the Kaplan Meier method, censored for transplantation.

Results
Characteristics of the dialysis population stratified according to survival status are provided in Table 1. Dialysis patients in Switzerland have an approximately 8% higher survival in the first and second year after start of dialysis compared to other European countries (Annual ERA-EDTA Report 2016). In the oldest age group, it amounts to up to 13 and 14%, in the first and in the second year, respectively. The proportion in survival rates between genders is similar in Switzerland, as well as in Europe. Dialysis patients aged younger than 45 years have a worse survival in Switzerland compared to other European countries.

Table 1: Characteristics (given as mean±SD or percentage) in incident dialysis patients according to their survival status

	Non-Survivors, n=976	Survivors, n=3550	p-value
Age, years	73.7 ± 12.5	64.8 ± 16.3	0.000
Male gender, %	67.1	66.0	0.526
Body mass index, kg/m²	24.6 ± 5.9	26.2 ± 5.6	0.430
Dialysis vintage, days	578 ± 402	713 ± 496	0.000
Dialysis duration per week (h)	11.2 ± 1.5	11.5 ± 1.4	0.000
Kt/V	1.50 ± 0.41	1.60 ± 0.45	0.024
Hemoglobin, g/dL	10.6 ± 1.8	11.1 ± 1.4	0.000
Ferritin, ng/mL	554.6 ± 622.1	452.5 ± 375.6	0.000
Calcium, mmol/L	2.21 ± 0.22	2.21 ± 0.22	0.316
Phosphate, mmol/L	1.54 ± 0.50	1.63 ± 0.47	0.021
PTH, ng/L	305.5 ± 349.8	367.1 ± 309.5	0.251
Iron substitution, %	74.2	74.0	0.909
EPO substitution, %	82.9	81.9	0.496
Comorbidities, n	3.6 ± 2.1	2.2 ± 1.9	0.000
CCI*	6.0 ± 2.7	4.1 ± 2.1	0.000

*Charlson Comorbidity Index

Table 2: One-, two-, 3- and 4-year survival probability (%) of incident dialysis patients, unadjusted, stratified by age, gender and cause of renal failure

		1 year		2 year		3 year	4 year
		srrqap	ERA-EDTA	srrqap	ERA-EDTA	srrqap	srrqap
0-19 yrs	(N=51)	88.4	97.6	88.4	94.2	88.4	88.4
20-44 yrs	(N=396)	97.3	96.7	90.5	93.4	89.0	89.0
45-64 yrs	(N=1252)	93.4	90.6	87.3	83.4	82.5	78.6
65-74 yrs	(N=1231)	90.7	83.2	79.5	71.6	69.8	60.0
75+ yrs	(N=1595)	87.3	74.0	72.9	58.1	60.7	47.8
Men	(N=2998)	90.7	83.4	79.6	71.7	70.6	61.1
Women	(N=1527)	90.8	83.6	80.6	72.6	70.7	59.6
Diabetes	(N=913)	90.3	85.2	78.9	72.8	72.0	56.2
Renal vascular disease	(N=1015)	91.1	82.4	77.6	69.3	68.1	56.5
Glomerulonephritis	(N=690)	94.1	91.2	90.1	84.3	81.4	77.9
Other causes	(N=1905)	89.4	81.7	78.2	70.7	67.5	59.8
All	(N=4525)	90.7	83.5	79.9	72.1	70.6	60.6

Conclusions
The markedly better survival in dialysis patients in Switzerland compared to other European countries could be confirmed with an additional year of follow up and more patients. With another year of follow up, data to analyze 5-year survival probability will be available for comparison with the ERA-EDTA report. In addition, we will be able to verify whether dialysis patients under 45 years in Switzerland have an increased mortality or whether this is due to the small number of patients in these two groups.

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Does hemodialysis patient's awareness of laboratory sampling schedules influence their adherence prior to sampling?

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Background
Hyperkalemia and Hyperphosphatemia represent common problems in chronic hemodialysis patients and are treated by dietary restrictions and medical therapy (phosphate binders), in addition to the hemodialysis procedure. Predialysis potassium and phosphate concentrations are monitored by regular blood sampling, which follows a defined schedule (e.g. every first Mon or Tue of the month) in most dialysis units. We hypothesized that knowledge of the blood sampling schedule by the patients might temporarily increase their adherence to dietary restrictions and medications during the interdialytic interval just prior to blood sampling. Thus, the monthly measured values might not be representative.

Methods
In a previously published study (ISRCTN12825165), iron parameters were measured at days 2, 4, 7, 14, 21 and 28 after a bolus injection (100 or 200mg) of ferric carboxymaltose. For the sub-study reported here, we also measured plasma potassium and phosphate levels in these blood samples, but the patients were not aware of these measurements. We compared the values from the scheduled monthly blood sampling (obtained after a long interdialytic gap) with the same patient's mean of all values obtained after a long interdialytic gap during the study period, using a two-sided paired t-test.

Results
A total of 31 patients were included in this analysis. The mean phosphate and potassium values at the scheduled monthly blood samplings were 1.79±0.40 mmol/l and 5.0±0.8 mmol/l, respectively. The mean values obtained during the study, that did not coincide with a scheduled monthly blood sampling, were not different (1.74±0.34 mmol/l; $p = 0.24$ and 4.9±0.7 mmol/l; $p = 0.69$).

Conclusions
Prior knowledge of dialysis patients about potassium and phosphate determination had no influence on the respective values. Hence, scheduled measurements of these values appear to be representative. However, due to the small study size, a minor effect or an effect in a subset of patients cannot be excluded.

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Peritonitis in peritoneal dialysis – when to consider acute pancreatitis

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Background
Acute pancreatitis (AP) is a recognised complication of peritoneal dialysis (PD). However, it can be challenging to efficiently establish diagnosis, as presentation is non-specific, mimics PD-related peritonitis and interpretation of serum pancreatic enzymes is not straight-forward. In addition, numerous potential aetiologies need to be considered.

Methods
Case report.

Results
A 74 years old PD patient presented with cloudy dialysate and subtle symptoms of malaise and abdominal pain. Examination revealed guarding only on deep abdominal palpation. WBC was 26.000/µl and CRP 250 mg/l. Dialysis effluent appeared cloudy and contained 2990 leucocytes/µl (90% polymorphs). Infectious peritonitis was presumed and empirical antibiotic treatment started. However, dialysate cultures remained negative, clinical condition deteriorated and effluent leucocyte count remained high. Abdominal ultrasound was unremarkable (pancreas not visible) and there was no exit-site infection or alternative foci identifiable. AP was diagnosed by elevated serum lipase (628 U/l) and CT scan (enlarged pancreas, fluid collections). Disentangling aetiological factors was challenging. The patient had gallstones, consumed alcoholic beverages regularly, was on doxycycline shortly before presentation, and dialyzed with icodextrin. In addition, PD treatment itself may have been a contributory factor. Antibiotic therapy was stopped and PD treatment with icodextrin was emporarily suspended (the patient had sufficient residual kidney function). Effluent leucocyte count was monitored via glucose 1.5% dwells every other day. Systemic and effluent markers of inflammation took 4 weeks to normalize. The patient did not regain his usual state of health until several weeks after discharge. Follow-up CT scan showed considerable pancreatic sequelae of the AP. We discuss incidence, diagnostic challenges, aetiologies, and prognosis of AP in PD.

Conclusions
AP is an important cause of PD peritonitis. Negative dialysate cultures and unsatisfactory clinical response should trigger evaluation for AP and its multiple potential causes, including PD treatment itself. Prognosis can be poor and close monitoring is recommended.

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Severe malignancy related hypercalcemia refractory to standard renal replacement therapy

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Background
Malignancy related hypercalcemia is a frequent cause of hypercalcemia and accompanies approximately 30% of neoplasms. Its presence carries poor prognosis with a mortality rate of 80% at 1 year. Parathyroid carcinoma is rare and accounts for less than 1% of primary hyperparathyroidism cases and even fewer cases of hypercalcemia. Severe hypercalcemia is a life-threatening electrolyte disorder defined by corrected calcium levels of 3.5 mmol/L or ionized calcium of 2.5 mmol/L. Most cases of severe hypercalcemia are managed by medical therapy consisting of intravenous volume expansion, calcitonin, bisphosphonates/denosumab and sometimes cinalacalcet and corticosteroids. Only few refractory cases eventually require renal replacement therapy. Refractory hypercalcemia may be managed with standard intermittent RRT or via continuous modes. To our knowledge, no cases of severe hypercalcemia have been described as refractory to standard methods of renal replacement therapy. There is no significant literature that documents or offers management strategies for such cases, where standard dialysate calcium concentrations and standard dialysate flow rates are deemed ineffective. We would like to present such a case, with a patient presenting with severe malignancy related hypercalcemia due to metastatic parathyroid carcinoma.

Methods
After standard intermittent hemodialysis was deemed inefficient, the patient was started on continuous venovenous hemodiafiltration

(CVVHDF), with modified pre-dilution and dialysate calcium concentrations at 0 mmol/L. The dialysate flow rate was increased in the process, with regular arterial blood gas monitoring to ensure safety.

Results
Target physiologic calcium levels were achieved with CVVHDF using adapted dialysate calcium concentrations at 0 mmol/L and by progressively increasing dialysate flow rate.

Conclusions
Adapting pre-dilution and dialysate calcium concentrations to 0 mmol/L, along with the increasing dialysate flow rates seems to be an effective method to lower calcium concentrations in a case of severe refractory hypercalcemia related to malignancy. The method also seems to be safe with appropriate regular arterial blood gas monitoring.

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A 2% Taurolidine dialysis catheter lock solution is easy to use, cost efficient and successfully prevents catheter related bloodstream infection as well as catheter dysfunction

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Background
In hemodialysis patients, catheter related bloodstream infection (CRBSI) and catheter dysfunction are associated with significant cost, morbidity and mortality. The ideal catheter lock solution has yet to be defined. Due to its antimicrobial and antithrombotic properties and lack of side effects Taurolidine seems promising.

Methods
21 patients receiving chronic hemodialysis and 2% taurolidine solution without citrate and heparin (TauroSept®) as intermittent catheter lock were retrospectively analyzed during the last 2 years at Spital Linth in Switzerland. The primary endpoint was catheter related blood stream infection (CRBSI), the secondary endpoints included catheter dysfunction (flow rate <200ml/min), catheter dysfunction treatment costs, catheter technical problems and adverse events. The data were compared to standard lock solutions described in the literature.

Results
No CRBSIs occured in the observation period. The average catheter dysfunction rate was 0.19 per patient and the average catheter dysfunction treatment costs were CHF 543 per patient. The average catheter technical problem rate was 0.1 per patient. No adverse events related to the use of the 2% catheter lock solution were observed. These results compare favorably with other catheter lock solutions.

Conclusions
In conclusion, in a representative Swiss cohort of dialysis patients a 2% taurolidine catheter lock solution successfully and safely prevented CRBSI and catheter dysfunction and was cost efficient.

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