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OC 1

Transcriptional trajectories of human kidney disease progression

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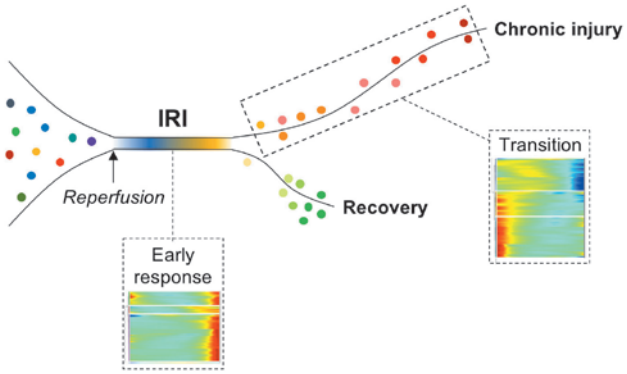
Background: The molecular understanding of the transcriptional program determining the progression from acute to chronic kidney injury in humans is limited.
Methods: We performed RNAseq-based transcriptional profiling on protocol biopsies obtained from 42 kidney transplant recipients at 4 time points (before and after reperfusion, 3 months and 12 months after transplantation) and we applied machine learning techniques to identify and group patient responses over time. Our previously described preclinical model of ischemia/reperfusion injury was used for data validation.
Results: In the first hours after renal reperfusion all patients underwent a similar transcriptional response characterized by a biphasic transcriptional program under the control of immediate early response genes. In the following months we identified two main transcriptional trajectories corresponding to kidney recovery and to a sustained injury response leading to fibrosis and renal function deterioration (figure). The molecular map generated by this unsupervised computational approach delineated the transcriptional program determining the transition from acute to chronic kidney injury: genes associated with mitochondrial dysfunction, kidney injury/repair and innate immunity were followed by the upregulation of genes related to fibrosis and adaptive immunity. Moreover, the computational model highlighted early markers of kidney disease progression (such as the transcription coactivator EP300). The characterization of a similar process in the mouse model showed evidence for substantial similarities in the response to tissue injury across species and expanded the relevance of the findings beyond kidney transplantation.
Conclusions: The integration of multiple transcriptomes from serial biopsies in advanced computational algorithms overcame the analytical hurdles related to interindividual variability and identified shared transcriptional elements of kidney disease progression in humans. For the first time, this new concept allowed an unsupervised analysis of the molecular mechanisms of kidney disease in a clinical setting.



Conceptual summary. Computational analysis of transcriptional responses in kidney tissue from renal transplant patients identified common early injury outcome with divergent longer-term outcomes: recovery versus the initiation of a chronic injury signature.

OC 2

High magnesemia protects Memo1-deficient mice from calcification propensity

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Background: Mediator of Cell Motility1 (Memo) is an ubiquitously expressed redox protein involved in extracellular ligandinduced cell signaling. We have previously reported that inducible whole-body Memo KO (cKO) mice displayed a syndrome of premature aging and disturbed mineral metabolism partially resembling klotho or Fgf23-deficient mouse models. Here, we aimed at delineating the calcification propensity of Memo cKO mice.
Methods: We used a *Memo1*exon 2 floxed mouse allele on C57BL/6 mouse background and crossed the mice with strains harboring CreERTM or Pax8-rtTA and LC1 transgenes to generate whole-body and renal-specific inducible Memo KO mouse models, as previously described. Dietary interventions and biochemical and molecular biological methods were employed.
Results: We attempted to rescue the Memo cKO mouse premature aging phenotype by dietary depletion of phosphate or vitamin D but failed to see an effect on survival. Moreover, and to our surprise, Memo cKO mice did not reveal soft-tissue calcification and displayed a lower serum calcification propensity. We identified elevated magnesemia as a putative protective factor. Concordantly, we found that genes encoding intestinal and renal magnesium transporters as well as epidermal growth factor were increased in Memo cKO. Next, we generated a mouse model of kidney-specific Memo KO (kKO), which reproduced the higher magnesemia and renal-specific increases of magnesium transporter gene expression, whereas these mice showed an intestinal counterregulation of magnesium transporter gene expression.
Conclusions: Collectively, using two different mouse models, we identified Memo as a novel regulator of magnesium homeostasis and systemic calcification propensity. These findings may prove crucial to understanding the pathophysiology of mineral disease and the role of magnesium therein.

OC 3

Primary Membranous Nephropathy: Potential novel biomarkers and therapeutic targets from glomerular RNA sequencing

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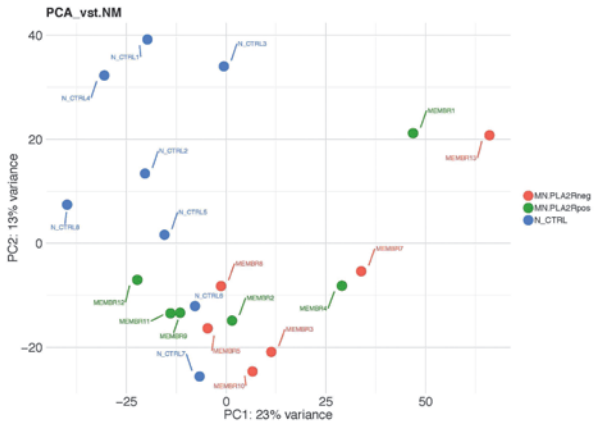
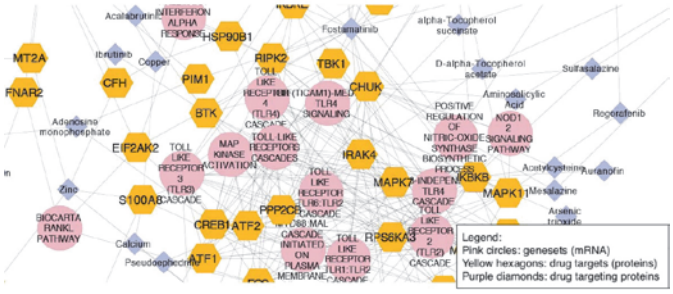
Background: Membranous Nephropathy (MN) can be divided in 80% primary MN (e.g.cancer, SLE ruled out) and 20% secondary MN. Study aim was to determine if RNA sequencing from archival kidney biopsies is feasible and if it delineates the molecular basis of primary MN.
Methods: Formalin-fixed and paraffin-embedded renal biopsies were selected from the Norwegian Kidney Biopsy Registry: i) normal tissue (n = 8, mean age 27 ± 11 years) and ii) primary MN (n = 12; equal sex distribution; mean age 55 ± 16 years; mean proteinuria 2.9 ± 3.5 g/d). When adequate, MN was grouped into PLA2R antibody positive (n = 6) and negative (n = 6) subjects. All patients had eGFR >60 ml/min/1.73 m^2. Total RNA inputs of 0.15–3 ng/sample, isolated from microdissected glomerular cross-sections, were subjected to 75 bp paired end mRNA sequencing (Illumina).
Results: Systematic mapping of transcriptional landscapes from MN versus controls delineated enrichment in gene expression associated with innate immune responses in general and Toll-like receptor-cascade activation and interferon signatures in particular. Alterations were paralleled by increased stress response and augmentation in cell cycle regulation, but by a decrease in gene expression pertaining to development and morphogenesis of kidney epithelia and metabolic pathways. While MN patients, irrespective of PLA2R-status, exhibited marked changes compared to normal controls, PLA2R positive and negative patients resembled one another to a great degree (fig. 1). Nonetheless, analyses with a focus on immune mediators indicate more pronounced inflammation in PLA2R positive patients. In these subjects, interferon regulatory factor 4 (IRF4) appeared as a most obvious transcription factor, while signal transducer and activator of



transcription 5B (STAT5B) qualified as the most significant transcription factor in PLA2R negative patients. Data visualisation depicts novel drug targets (fig. 2).



Conclusions: Our results suggest that transcriptional profiling of glomeruli from archival kidney biopsies is feasible and delivers quality data allowing in-depth data mining, which could lead to biomarker and drug target programs.

OC 4

Pharmacokinetic and pharmacodynamic evaluation of a vascular calcification inhibitor (INS-3001) in rats

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Background: Morbidity-mortality with CKD increase with the progression of vascular calcifications. In the context of the development of drugs capable of reducing pathological crystallization, myo-inositol hexaphosphate (IP6) has been shown to be a promising candidate but needs to be administered viaintravenous infusion. This study demonstrates the in vivo inhibitory effect of an IP6 analog (INS-3001), and characterizes its pharmacokinetic profile in uremic and nonuremic rats.
Methods: Efficacy of INS-3001 versus IP6 to prevent vascular calcification was studied in non-uremic rats (vitamin D3 model, $n = 5 – 11$/group), while the PK of INS-3001 was determined after after single i.v. or s.c dosing of 10 mg/kg in uremic rats (adenine diet model) and non-uremic controls ($n = 6$/group). Vascular calcifications were visualized by von Kossa staining and calcium tissue content measured by ICP-MS. INS-3001 concentrations in plasma were measured using a HILIC-MS/MS bioanalytical method.
Results: INS-3001 blunted carotid calcification reducing the amount of calcium in tissues by a factor of two compared to controls ($p = 0.017$) while only partial decrease was observed at the level of abdominal aorta ($p > 0.05$). Treatment with IP6 could not be completed due to the appearance of necrotic lesions at the injection site. INS-3001 displayed high s.c. bioavailability. In the s.c. group, uremic rats displayed higher AUC, mean residence time and Tmax than non-uremic controls (1327.1 vs 802.3 µg/mL*min; 124 vs 66 min; 23 vs 50 min, respectively) whereas Cmax remained unchanged (8348 vs 8325 ng/mL). Similar trends were observed following i.v. administration.
Conclusions: INS-3001 is a potent inhibitor of vascular calcification and has a beneficial effect on the renal function. Uremia appeared to significantly influence the plasma PK of INS-3001 after s.c. and i.v. administration. The data suggests that uremia extends plasma exposure of INS-3001 without increasing peak plasma levels and therapeutic levels can be attained following s.c. administration.

ORAL COMMUNICATIONS – TRANSPLANTATION

OC 5

Pre-transplant detection of donor-specific B cell memory improves risk assessment for antibody-mediated rejection in sensitized renal allograft recipients

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Background: Outcomes of patients transplanted across donor-specific HLA antibodies (DSA) range from indolent courses to severe antibody-mediated rejection (ABMR) with graft loss within days. Assessment of the peripheral memory B cell pool may help to better stratify the immunological risk. The aim of this study was to investigate the clinical utility of detection of donor-specific memory B cell-derived HLA antibodies (DSA-M) by using a recently developed sensitive and easy-to-perform assay.
Methods: Twenty patients with Luminex single antigen bead (SAB) assay-defined DSA but negative complementdependent cytotoxicity crossmatches were enrolled. All patients had at least two allograft biopsies (indication and/or surveillance) within the first year post-transplant. The study was conducted within the framework of the Swiss Transplant Cohort Study and took advantage of plasma and PBMC samples collected at three time points (pre-transplant, month 6, month 12). We analyzed IgG-purified, concentrated culture supernatants from polyclonally activated PBMC using Luminex SAB assays and compared HLA antibody profiles with plasma antibodies determined at the same time point.
Results: In total, plasma SAB analysis revealed 35 DSA in 20 patients pre-transplant. Of those, concurrent DSA-M were detected for 10 specificities (29%) and in 9 patients (45%). Pre-transplant DSA/DSA-M positive individuals showed a higher incidence of (sub)clinical ABMR ($p = 0.032$) and a higher extent (g≥1+ptc≥1) of microvascular inflammation (67% versus 9%, $p = 0.02$). In 17 patients (28 DSA) with post-transplant analyses, persisting DSA post-transplant had significantly more often DSA-M (6/12; 50%) than non-persisting DSA (2/16; 13%; $p = 0.04$).
Conclusions: Pre-transplant analysis of donor-directed HLA antibodies deriving from peripheral memory B cells may serve as a novel tool to predict risk for ABMR in patients with pre-transplant DSA.

OC 6

Towards defining the Immunogenicity of HLA Epitopes: Impact of Eplets on Antibody Formation during Pregnancy

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Background: Pregnancy serves as model to study antibody-responses to HLA-mismatches. Such child-specific antibodies (CSA) are induced by non-self structures of HLA-molecules of the unborn

child. Comparison of high resolution HLA-typing from mother and child reveals the Eplet-load on mismatched HLA from paternal alleles. Eplets associated with an increased frequency of CSA may indicate HLA-epitopes of higher immunogenicity, potentially relevant as well in the transplant setting. The aim of this study was therefore to determine the impact of Eplet-load on the extent and type of CSA-formation and to assign the relative immunogenicity of different HLA class I Eplets in the pregnancy setting.
Methods: 155 mothers (devoid of any pre-sensitizing events) and their first newborn children were HLA-typed at high resolution. Immediately after delivery, all sera from the mothers were tested for IgM- and IgG-type HLA class I antibodies and evaluated for Eplet associated reactivity-patterns.
Results: 397 (85%) of the 465 paternal HLA class I alleles were mismatched. CSA were detected against Eplets on 93 (23%) of these mismatched HLA, and their immunoglobulin composition was: IgM only: 14 (15%), IgM and IgG: 37 (40%), and IgG only: 42 (45%). Antibody reactive mismatched HLA-A and HLA-B (but not HLA-C) alleles epresented a significantly higher Eplet-load than non-reactive mismatched alleles of the child. The relative immunogenicity of certain Eplets was assigned according to the frequency of Eplet specific CSA responses. The ten most immunogenic Eplets (in descending order) were: 144TKH, 62GE, 163LW, 82LR, 127K, 80I, 163EW, 41T, 80K, 90D. We found two hot spots on the surface of the HLA class I molecule, located on the alpha-1 and alpha-2 domain, where most immunogenic Eplets are clustered.
Conclusions: If further studies will confirm the same Eplets to trigger an enhanced donor specific HLA-antibody (DSA) response in the post-transplant setting, they should be differently scored for pre-transplant risk assessment.

OC 7

CXCL10 measurement in late renal allograft biopsies predicts outcome even in histologically quiescent patients

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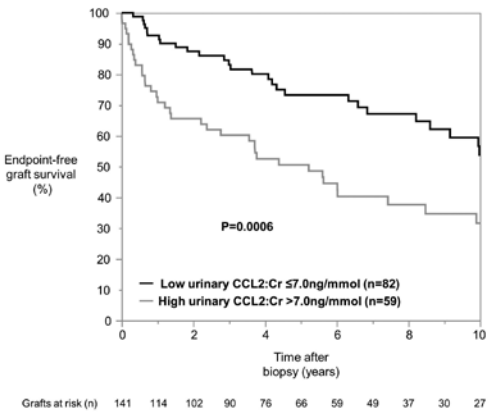
Background: Urinary-CXCL10 is a promising early non-invasive diagnostic marker for allograft rejection and predictive for long-term outcome, however its impact when measured later in the post-transplant course has not yet been analyzed. Therefore, the goal of this study was to investigate urinary-CXCL10 in patients with clinically indicated allograft biopsies performed >12 months post-transplant.
Methods: A prospective, observational renal transplant cohort (n = 141) with 182 clinically indicated allograft biopsies/corresponding urines was evaluated. The primary outcome was a composite of allograft loss/renal function decline (>30% decrease eGFR between the index biopsy and last follow-up). Secondary outcomes were patient/graft survival. Urinary-CXCL10 levels were measured by MSD® single-spot assay system (V-Plex® Human IP-10 Kit).
Results: Urinary-CXCL10 correlated with TCMR [median (IQR) 13.2 ng/mmol (6.76–117.9), p = 0.0002] as well as ABMR [median (IQR) 9.78 ng/mmol (3.75–14.2), p = 0.02] compared to no rejection [median (IQR) 4.09ng/mmol (2.13–9.37)]. Sixty-nine patients (69/141, 49%) reached the primary outcome and their urinary-CXCL10 levels were significantly higher at the time of their biopsy compared to patients with stable allograft function [median (IQR) 9.15 ng/mmol (4.05–19.0) vs. 3.50 ng/mmol (2.03–9.23), p <0.0001]. Time-to-endpoint analyses according to high or low urinary-CXCL10 demonstrated that low urinary-CXCL10 (≤7.0 ng/mmol) was associated with 75% 4-year event-free survival compared to 51% with high urinary-CXCL10 (p = 0.0006) fig. 1). Even in histologically quiescent patients (i.e. with inflammatory processes not reaching Banff classification criteria of acute rejection), high urinary-CXCL10 (>7.0 ng/mmol) was associated with inferior death-censored allograft survival (p = 0.04) as well as endpoint-free graft survival (p = 0.07). In a multivariate Cox-regression model, urinary-CXCL10 was the only independent predictor of the primary outcome in histologically quiescent patients [HR 5.02, 95%CI 1.46-17.2; p = 0.02].
Conclusions: This study confirms that urinary-CXCL10 has also a promising diagnostic performance for the detection of allograft rejection when measured >12 months post-transplant. Furthermore, it is an independent predictor of long-term renal allograft outcomes even in histologically quiescent patients.



OC 8

Immune signatures of allograft rejection and outcome after kidney transplantation

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Background: The immunosuppressive drugs (IS) currently used in clinical transplantation (Tx) mainly control naïve T-cell activation and differentiation with little effect on pre-existing memory T cells and the B-cell lineage, which are responsible for chronic rejection. Some protocols may also interfere with the expansion of regulatory T cells (Treg). Therefore, long-term patient and graft survival remains suboptimal, in particular in HLA-sensitized patients. It would thus be necessary to have specific assays to monitor the immune response and the effect of IS with time after Tx.
Methods: We used prospectively collected blood samples and clinical data from kidney Tx recipients, enrolled in the Swiss Transplant Cohort Study. Our aim was to analyze the immune repertoire during the first year after an HLA-mismatched allograft, correlating these data with graft outcome (acute cellular rejection, ACR; antibodymediated rejection, AMR; vs. stable). For this purpose, we performed single-cell analysis using mass cytometry on peripheral blood mononuclear cells (PBMC) of recipients at day 0, months 6 and 12 after Tx.
Results: Our data provide detailed PBMC characterization at phenotypic and functional levels, during the first year after Tx. We analyzed PBMC subsets dynamics in patients with well-defined clinical phenotypes, i.e. stable nonsensitized (NS), stable sensitized (S) recipients and patients who experienced an ACR episode. Comparing rejecting vs. stable patients, we observed a significant increase in effector Th1, CD4 and CD8 memory T cells early after Tx, together with very low frequencies of Treg already at baseline. There was also an important increase in plasma cells in NS and S patients with ACR.
Conclusions: Our initial data are promising and need to be validated. We believe that this could contribute to the identification of predictive signatures of graft outcome and provide a basis for a simplified panel of biomarkers for routine clinical follow-up, in order to individualize IS therapy.

OC 9

Differential impact of delayed graft function in deceased donor renal transplant recipients with and without donor-specific HLA-antibodies

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Background: Delayed graft function (DGF) after deceased donor renal transplantation is regarded as a risk factor for rejection and lower graft survival. However, the impact of DGF in patients with/without pre-transplant donor-specific HLA-antibodies (DSA) has not been studied.
Methods: We investigated 375 consecutive deceased donor kidney transplantations from 2005 to 2017, who had DSA assigned by Luminex single-antigen bead technology and who received

maintenance immunosuppression with tacrolimus, mycophenolic-acid and prednisone. These patients had 755 allograft biopsies (187 indication biopsies, 568 surveillance biopsies at 3/6 months). DGF was defined by the requirement of ≥1 dialysis post-transplant due to inadequate allograft function.
Results: Median follow-up time was 6.1 years. Eighty-five of 375 patients had DSA (23%). The incidence of DGF was similar in DSApos-patients and DSAneg-patients (40% vs 36%; p = 0.45). In DSAneg-patients, five-year graft survival was not different with/without DGF (81% vs 83%; p = 0.48). In addition, one-year incidence of (sub) clinical rejection was similar with/without DGF (26% vs 23%; p = 0.34). By contrast, in DSApos-patients, five-year graft survival was significantly lower with DGF (64% vs 79%; p = 0.01) and one-year incidence of (sub)clinical rejection was more frequent (61% vs 37%; p = 0.03). Median eGFR at last follow-up was lower in patients with DGF (DSApos-patients: 40 ml/min vs 43 ml/min; p = 0.17, DSAneg-patients: 43 ml/min vs 51 ml/min; p = 0.003).
Conclusions: DGF has a more detrimental impact in DSApos-patients compared to DSAneg-patients. Efforts to reduce DGF might be most beneficial for DSApos-patients.

OC 10

Long-term outcome of DCD kidney transplantation

Mrs. Amelie Müller[1], Dr. Kerstin Hübel[1], Dr. Pietro Cippà[1], Mr. Jonas Ehrsam[1], Dr. Christian Oberkofler[1], Dr. Kuno Lehmann[1], Prof. Markus Weber[2], Prof. Thomas Müller[1], Prof. Philipp Dutkowski[1], Prof. Rudolf P. Wüthrich[1], Prof. Pierre-alain Clavin[1], Dr. Olivier De Rougemont[1]
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Background: Donation after circulatorydetermination of death (DCD) represent up to 20% of used kidney grafts. Numerous studies have shown similar outcome compared to donation after braindeath on the short- and mid-term. Until now, long-term outcome has though neverbeen shown. The aim of this study was to complete long-term follow up and graftsurvival of a controlled-group study comparing DCD and DBD kidneys.
Methods: We retrospectively analyzed all patients transplanted at our institution between January 1985 and March 2000. All DCD, formerly known as donors without a heartbeat, recipients were matched one-to-one with patients transplanted with DBD grafts during this period. Graft survival was estimated with Kaplan-Meier method.
Results: Overall 1133 kidneys were transplanted during this period. Of these, 122 patients received a graft from a DCD donor and accordingly matched with 122 DBD recipients. Results showed similar graft-survival in both groups, with no significantdifference (p = 0.93). Median graft survival after 33-years follow-up was 25years (305 months) in DBD, and 26 years (315 months) in DCD. Delayed graftfunction occurred in 59 patients in the DCD group compared to 29 in the DBD group (p = 0.001).
Conclusions: This is the first study to show similar long-term outcome in DCD kidneys compared to DBD. Although the incidence of delayed graft function is higher after DCD, these graft are valuable resource and should probably be handled in the same way as DBD grafts.

ORAL COMMUNICATIONS – CLINICAL NEPHROLOGY / HYPERTENSION / MINERAL / ELECTROLYTES

OC 11

Prospective evaluation of complex renal cystic lesions with contrast enhanced ultrasound (CEUS) and functional magnetic resonance imaging (MRI) versus the gold standard: computer tomography (CT)

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Background: The aim of this study was to compare contrast enhanced ultrasound (CEUS) and magnetic resonance imaging (MRI) with computer tomography (CT) for the evaluation of cystic renal lesions with the Bosniak classification.
Methods: This is a prospective observational study. From July 2014 to October 2017, 48 patients with a median age of 63 years (range 36–91 years) and 65 cysts underwent CT scan, MRI, and CEUS for cystic renal lesions. CT is the gold standard to determine the Bosniak classification of cysts, in which a complex cyst is defined as a Bosniak classification BII-F, BIII, and BIV, whereas BI and BII are defined as non-complicated cysts. The sensitivity, specificity and accuracy of CEUS and MRI compared to the goldstandard CT were calculated. Results: The cystic kidney lesions were classified on CT as follows: BI (n = 5), BII (n = 31), BII-F (n = 7), BIII (n = 5), and BIV (n = 17) Thus 44.6% (n = 29) of the cysts were determined as complex cysts. The agreement for complex cysts was 50.8% (Kappa 0.389, SD 0.056) in CEUS and 80.0% (Kappa 0.708, SD 0.071) in MRI. The sensitivity of CEUS to detect a complex cyst was 100% with a specificity of 33%, and an accuracy of 64%. MRI had a sensitivity of 90%, specificity of 91%, and an accuracy of 94%.
Conclusions: The use of CEUS and MRI allows the detection and evaluation of complex cystic lesions without using CT, thereby avoiding ionizing radiation and the risks of contrast material reactions and nephropathy. MRI classification of cysts correlated well with the CT classification and should be used for this purpose. CEUS tends to upgrade the classification due to better spatial resolution and better visualisation of the enhancement.

OC 12

Estimated 24h Urinary Sodium and Sodium-to-Potassium Ratio are predictors of kidney function decline: a 5-year cohort study

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Background: The prevalence of chronic kidney disease (CKD) is increasing worldwide in part due to population ageing. Identifying risk factors for age-related kidney function decline could help in understanding underlying mechanisms for ageing kidney. Sodium and Potassium intakes are associated with CKD progression in the renal population, but little is known about their role in renal function decline in the general population. We explored the association of urinary sodium and potassium excretions with changes in estimated glomerular filtration rate (ΔeGFR) in a population-based cohort.
Methods: For this study, we used the CoLaus dataset with full available data on baseline and 5-year follow-up. We estimated 24h urinary sodium (eUNa), potassium (eUK) and sodium-to-potassium (eUNa/K) using Kawasaki formulae. We performed multivariate linear

regression models studying the association of eUNa, eUK ans eUNa/K with yearly ΔeGFR, taking several covariates into account, including baseline eGFR and albuminuria. Results were expressed using standardised coefficients [X-mean X/SD X].
Results: We included 4141 (67%) caucasians participants from which 54.3% were women. Mean ΔeGFR was –0.6 (SD1.7)ml/min/1.73 m^2 per year. In the unadjusted analyses, there was a significant linear trend accross quintiles of eNa, eUK and eUNa/K with ΔeGFR: higher quintiles being associated with steeper decline in eGFR. In the fully adjusted model, high eUNa and eUNa/K were associated with faster renal function decline with coefficients $\beta = -0.07$ and $\beta = -0.05$ (both $p < 0.001$), respectively. On the contrary eUK taken alone showed no association ($\beta = 0.02$; $p = 0.3$).
Conclusions: Our results suggest that dietary sodium and potassium intakes may play a role in kidney function decline in the general population. Whether lowering sodium and increasing potassium in the diet may help in CKD prevention needs further exploration.

OC 13

The Circular RNA ciRs-126 Predicts Survival in Critically Ill Patients with Acute Kidney Injury

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Background: Circular RNAs (circRNAs) have recently been described as novel noncoding regulators of gene expression. They might have an impact on microRNA expression by their sponging activity. The detectability in blood of these RNA transcripts has been demonstrated in patients with cancer and cardiovascular disease. We tested the hypothesis that circulating circRNAs in blood of critically ill patients with acute kidney injury (AKI) at inception of renal replacement therapy may also be dysregulated and associated with patient survival.
Methods: We performed a global circRNA expression analysis using RNA isolated from blood of patients with AKI as well as controls. This global screen revealed several dysregulated circRNAs in patients with AKI. Most highly increased circRNA-array–based transcripts as well as expression of the circRNA target miR-126-5p were confirmed in blood of 109 patients with AKI, 30 age-matched healthy controls, 25 critically ill non-AKI patients, and 20 patients on maintenance hemodialysis by quantitative real-time polymerase chain reaction.
Results: Circulating concentrations of 3 novel circRNAs were amplified in blood of patients with AKI and in controls. *Circular RNA sponge of miR-126* (or ciRs-126) was most highly altered compared to healthy controls and disease controls (fold change of 52.1). *ciRs-126* was shown to bioinformatically sponge miR-126-5p, which was found to be highly suppressed in AKI patients and hypoxic endothelial cells. Cox regression and Kaplan-Meier curve analysis revealed *ciRs-126* as an independent predictor of 28-day survival ($P < 0.01$).
Conclusions: Circulating concentrations of circRNAs in patients with AKI are detectable. ciRs-126 may potentially sponge miR-126-5p and acts as a predictor of mortality in this patient cohort.

OC 14

Quality of Life and Tolerability of Jinarc® (Tolvaptan) in Swiss ADPKD Patients

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Background: Health-related quality of life (HRQoL) is an often-neglected aspect of illness. In standardized questionnaires of general HRQoL, ADPKD patients have been found to score similarly to the general population. However, HRQoL in Swiss ADPKD patients has not been thoroughly investigated. In addition, the impact of Tolvaptan treatment on HRQoL outcomes in ADPKD patients has not been studied in detail.
Methods: HRQoL of patients included in the Bern ADPKD registry was assessed by yearly collection of QoL-data with the standardized KDQOL-SF™ 1.3 questionnaire.
Results: Baseline HRQoL data of 92 ADPKD patients (41 men, 51 women) rendered median physical (SF-12 PCS) and mental (SF-12 MCS) health composite scores of 54.2 and 52.7, respectively. This suggests that general physical and mental HRQoL of Swiss ADPKD patients is comparable to other international (EU, US, Japan) ADPKD-cohorts, as well as to the general population, although KDQOL-SF™ 1.3 questionnaire-based data from the general Swiss population are lacking. Tolvaptan treatment has been initiated in 37 patients enrolled in the Bern ADPKD registry thus far. Four patients (11 %) discontinued treatment due to polyuric side effects within the first 3 months of treatment initiation. Treatment had to be permanently discontinued due to elevated liver enzymes in 2 patients (5.4%). Of the 31 patients (84%) still on Tolvaptan, one-year HRQoL follow-up data are currently available in 15 patients (40%). Median physical and mental component scores of Tolvaptan-treated patients were 54.8 and 54.1, respectively.
Conclusions: HRQoL of Swiss ADPDK patients is comparable to HRQoL of ADPKD patients in other international cohorts and similar to HRQoL of the general population. Furthermore, our data reveal that, beyond an initial adaptation to increased aquaresis, long-term treatment with Tolvaptan does not negatively affect HRQoL of ADPKD patients.

OC 15

Short-term changes in dietary sodium intake influence muscle sodium content and sweat sodium concentration in healthy subjects

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Background: There is increasing evidence that sodium can be stored in the skin and muscles without being osmotically active, yet whether acute changes in dietary sodium intake alter skin and muscle sodium content has not been investigated previously.
Methods: In a cross-over design, we assessed muscle sodium content by 23Na magnetic resonance imaging in 38 healthy normotensive volunteers (aged 33.5 ± 11.1 years, 76.3% female) after 5 days of high sodium diet (HS) (6 g of salt added to their normal diet) and 5 days of a low-sodium diet (LS). At each study visit, a 24-hour urine collection was performed. In a sub-group of 18 participants (72.2% female) we conducted quantitative pilocarpine iontophoretic sweat collections and measured the sodium, potassium and chloride concentrations of sweat.

Table 1: Participants characteristics after high and low salt diet[1] (n = 38)

	High Salt	Low Salt	p
Weight (kg)	66.3 ± 12.2	65.2 ± 11.8	<0.001
Body mass index (kg/m^2)	23.8 ± 3.7	23.4 ± 3.7	<0.001
eGFR (CKD-EPI, ml/min/1.73m^2)	107.4 ± 13.7	102.9 ± 13.2	0.005
Serum sodium (mmol/l)	140.4 ± 1.5	139.1 ± 1.7	<0.001
24h urinary sodium excretion (mmol/day)	227.0 ± 104.2	51.7 ± 60.1	<0.001
24h urinary chloride excretion (mmol/day)	235.1 ± 80.2	39.0 ± 30.7	<0.001
24h urinary potassium excretion (mmol/day)	63.6 ± 22.8	66.6 ± 23.6	0.49
24h urinary salt excretion (g/day)	13.4 ± 6.1	3.0 ± 3.5	<0.001
Muscle sodium content (mmol/l)	10.7 ± 1.3	9.8 ± 1.0	<0.001
Sweat sodium (mmol/l)[2]	43.9 ± 18.6	34.2 ± 20.2	0.01
Sweat chloride (mmol/l)[2]	25.2 ± 13.0	17.6 ± 12.9	0.02
Sweat potassium (mmol/l)[2]	8.1 ± 1.9	10.3 ± 3.1	0.01

[1] paired t-tests expressed in mean ± SD
[2] analysis in sub-group of 18 participants

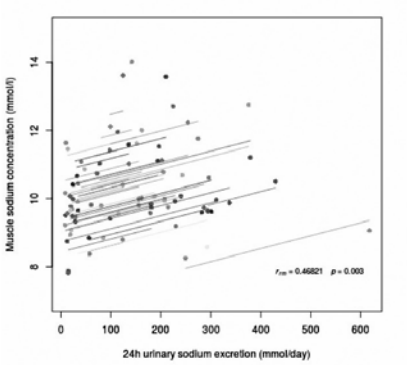

Figure 1 : Repeated measures correlation between muscle sodium concentration and 24h urinary sodium excretion. Each dot represents a single observation for a participant, with corresponding lines to show the common linear fit for each participant.

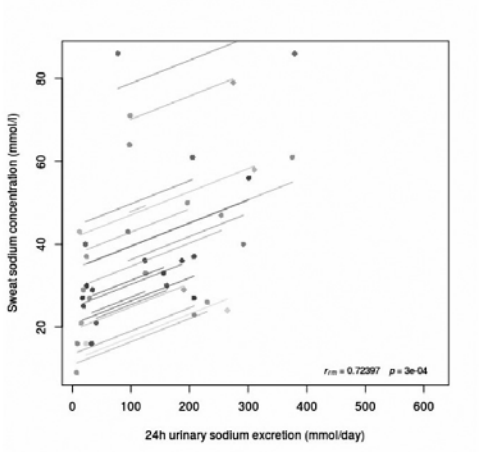

Figure 2 : Repeated measures correlation between sweat sodium concentration and 24h urinary sodium excretion

Results: Under HS conditions, serum sodium, urinary sodium excretion, muscle sodium content and sweat sodium concentration all increased significantly (table 1). Muscle sodium content (rm= 0.47, p = 0.03) and sodium sweat concentration (rm = 0.72, p <0.001) correlated positively with 24-hour urine sodium excretion (figure 1, 2). There was no significant correlation between muscle sodium content and age after LS (rs = 0.18, p = 0.26) or HS (rs = 0.09, p = 0.55). Muscle deposition of sodium was similar in female and male participants after LS (respectively 9.9 ± 1.0 versus 9.3 ± 0.9 mmol/l, p = 0.15) and HS (10.6 ± 1.3 vs 10.9 ± 1.6 mmol/l, p = 0.55) as was the change in muscle sodium content from LS to HS (0.86 ± 1.5 vs 1.1 ± 1.2 mmol/l, p = 0.63).
Conclusions: Muscle and sweat sodium concentrations are significantly higher under high salt conditions in healthy male and female subjects, suggesting that skin and muscle play a role in the dietary sodium balance in humans. Further studies are needed to investigate whether muscle and sweat sodium adaptations differ in patients suffering from chronic kidney disease and/or arterial hypertension.

OC 16

Safety and Efficacy Study of Lumasiran (ALN-GO1), an Investigational RNA Interference (RNAi) Therapeutic, in Patients with Primary Hyperoxaluria Type 1

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Background: In Primary Hyperoxaluria Type 1 (PH1), defective glyoxylate aminotransferase leads to excessive hepatic oxalate production, leading to progressive renal impairment and multi-organ damage from systemic oxalosis. Lumasiran, an investigational RNAi therapeutic suppresses hepatic glycolate oxidase, decreases the conversion of glycolate to glyoxylate, and results in reduced oxalate production.
Methods: ALN-GO1-001 is a randomized, placebo-controlled, single-blind, multicenter trial, evaluating lumasiran in patients with PH1 ≥6 years of age with urinary oxalate (UOx) ≥0.7 mmol/1.73 m^2/day and eGFR >45 mL/min/1.73 m^2. One of four patients in each dosing cohort was randomized to placebo prior to subcutaneous lumasiran. Cohorts 1 & 2 received 3 monthly doses of 1 mg/kg or 3 mg/kg, respectively; cohort 3 received 2 quarterly doses of 3 mg/kg lumasiran. An additional 4 patients received lumasiran in expansions of each of the first 2 cohorts. The primary endpoint is safety; secondary endpoints include change in 24-hour UOx from baseline. Eligible patients may continue dosing in the open-label extension (OLE) study.
Results: Patients in cohorts 1–3 had a mean age of 13.1 years (range 6–43), 7 (58%) female, and baseline UOx was 1.58 mmol/1.73 m^2/day (range 0.63–2.37). Lumasiran has demonstrated acceptable preliminary safety and tolerability with no treatment related serious adverse events or discontinuations; majority of adverse events were mild/moderate and unrelated to study drug. All patients treated with lumasiran in cohorts 1-3 experienced UOx lowering below 0.7 mmol/1.73 m^2/day, with a mean maximal decrease of 65%. Data available 85 days after initial dosing in the first 3 cohorts (n = 9) showed a mean UOx reduction of 63% (range 49–73%). Data from patients in all cohorts (n = 20), including quarterly dosing, expansions and OLE will be presented.
Conclusions: Preliminary results demonstrate acceptable safety data and lowering of UOx in patients with PH1 supporting the continued development of lumasiran as a potential therapeutic to alleviate pathologic overproduction and consequences of excess oxalate in this devastating disease.

ORAL COMMUNICATIONS – HEMODIALYSIS / PERITONEAL DIALYSIS

OC 17

Soluble CD146 and BNP dissect overhydration into functional components of prognostic relevance in hemodialysis patients

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Background: Optimal volume control is a pivotal goal in hemodialysis (HD). We tested B-type natriuretic peptide (BNP, a biomarker of cardiac dysfunction) and soluble CD146 (sCD146, a biomarker of endothelial mechanical stretch) for their potential to estimate volume status in HD patients and differentiate between cardiac and non-cardiac components of overhydration.
Methods: In a first part, BNP and sCD146 were tested in 30 HD patients (Zürich) as a biomarker of overhydration in comparison to bioelectrical impedance measurement (BCM). In a second part, the results were validated in a prospective 1-year follow-up study in 144 HD patients (London).
Results: sCD146 incrementally increased after the short and the long HD intervals (+53 ng/ml; p = 0.006 and + 91 ng/ml; p <0.001) and correlated with overhydration as determined by BCM (ROC Curve 0.72, p = 0.005). Levels of sCD146 did not significantly correlate with cardiac systolic dysfunction, while BNP levels were significantly higher when cardiac systolic dysfunction was present. One-year all-cause mortality was markedly higher in patients with high BNP (p = 0.001) but not with high sCD146. In a multivariate analysis, systolic dysfunction and BNP, but not overhydration per se were associated with reduced survival.
Conclusions: Combination of sCD146 and BNP helps to differentiate between cardiac and non-cardiac origin of overhydration, which is of prognostic relevance.

OC 18

Dialysis after graft loss: the Swiss experience

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Background: Renal transplantation is the treatment of choice for patients with end-stage renal disease. Patients, who return to dialysis after graft loss (DAGL), have a high early morbidity and mortality. Methods: As there are major differences in the treatment protocols of patients returning to dialysis, we used data from the Swiss Transplant CohortStudy (STCS) to describe current management and outcome in Switzerland.
Results: We included 1499 patients who received a renal allograft between 2008 and 2014. Of those, 78 patients lost their graft during follow up, of which 41 allografts were lost within one year after transplantation. Patient survival was 86%, 81% and 74% at 30, 90 and 365 days after graft loss. After graft loss, 90% of the patients started hemodialysis (31% with catheters, 54% with native fistulae, and 10% with vascular grafts). Starting with a permanent vascular access was associated with a decreased mortality (HR 0.32). At the time of graft loss, the majority of patients were on triple immunosuppressive therapy, which was reduced to double immunosuppression over the following year. After allograft nephrectomy, immunosuppression was significantly reduced. Allograft nephrectomy was performed within six months after graft loss in 76% patients who lost the graft within one year and in 35% of patients who lost the graft after 1 year. Three years after graft loss, 37% of the patients with early and 9% with late graft loss received another allograft, of those 20 out of 23 had an allograft nephrectomy.
Conclusions: In summary, our detailed analysis of STCS patients after allograft failure illustrate a high mortality and a high number of allograft nephrectomies. Patients commencing hemodialysis with a catheter had asignificantly higher mortality compared to patients with a native fistula. The role of immunosuppression reduction and allograft nephrectomy as interdependent factors for mortality and re-transplantation needs further evaluation.

OC 19

Hospitalizations within the first year and survival in patients aged below and above 80 who start dialysis in emergency

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Background: Implementation of dialysis in octogenarians is a debated question on account of an unfavourable short-term prognosis. We therefore analyzed what is the impact of planned implementation versus emergency dialysis on first year hospitalizations and survival in this population compared to those aged <80.
Methods: During the past 16 years, all patients who started maintenance dialysis in our unit were reviewed. Patient's demographic and clinical characteristics were collected. Emergency implementation of maintenance dialysis was defined as no prior referral to a nephrologist one month before starting dialysis.
Results: From 2000 to the end of 2016, 683 patients started maintenance dialysis in our unit, of whom 96 were aged ≥80. Mean age was 62 + 16 years. Hemodialysis and peritoneal dialysis were implemented in 95 and 5% of the patients respectively. Emergency dialysis was implemented in 44 and 26% of the patients aged ≥80 and <80 respectively (p <0.001). One-year mortalities in patients aged ≥80 and <80 were 36 and 19 % respectively in patients who had emergency dialysis and 13 and 14% in those with planned dialysis (p <0.001). In patients aged ≥80 and <80, one-year hospitalization-free days were respectively 318 (105) and 328 (90) days with planned dialysis implementation versus 271 (303) and 322 (90) days in those who had emergency dialysis (median +IQR; p <0.001).
Conclusions: Prior referral to nephrologists substantially increase one-year hospitalization-free days and survival after maintenance dialysis implementation in patients aged above 80.

OC 20

DIALFIT: Water-soluble vitamins in chronic on-line hemodiafiltration patients

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Background: The last decade has witnessed changes in dialysis prescriptions towards more intense schedules and use of hemodiafiltration (HDF). These changes may lead to increased losses of essential substances such as vitamins. Water-soluble vitamins supplementation is therefore common practice, but dosages are largely based on conventional hemodialysis techniques and shorter dialysis times. The aim of this study was to assess the status of water soluble vitamins in chronic dialysis patients receiving HDF and vitamin supplements.
Methods: This monocentric study included 40 patients on thrice weekly chronic on-line hemodialfiltration. All patients received two tablets of Dialvit (containing 50 mg of thiamine, 10 mg of riboflavin, 40 mg of pyridoxine, 3 mg of folic acid and 200 mg of vitamin C per tablet) after each dialysis session. Predialysis samples were obained and concentrations of vitamin B1, B2, B5, B6, B8 and B9 and C were measured by the Swiss Vitamine Institue.
Results: Patient and dialysis characteristic are listed in table 1. Results for the different hydrosoluble vitamins are listed in table 2. Two patients (5%) showed vitamin levels below the reference range, one for vitamin C and the second for vitamin C and B6. Both patients admitted that they had never taken Dialvit. The majority of patients were above the upper reference interval, except for vitamin C, for which most patients were in the normal range.
Conclusions: This monocentric study shows that only a small percentage of patients on HDF suffers from vitamin C deficiency. For the other hydro-soluble vitamins (B1, B2, Biotin, B6, folic acid and pantothenic acid), supranormal values of vitamin levels were found, suggesting that the actual dose of vitamin supplements can be safely lowered, with the exception of vitamin C.

Table 1: Patients characteristics

Characteristics	Mean (sd) or n (%)
Age (years)	56.1 (+/-15.7)
Female	10 (25)
Body mass index (kg/m2)	26.4 (+/-5.3)
Charlson Comorbidity index	5 (+/-2.4)
Diabetes	16 (40%)
Hypertension	31 (77.5%)
Dialysis vintage (month)	43 (+/-75)
Hemodiafiltration vintage (month)	15.6 (+/- 17.6)
eKT/V	1.6 (+/-0.3)
Weekly dialysis time (min)	711 (+/-27)
Substitution volume (liters)	22.0 (+/-6.2)
Epurated blood volume (liters)	84.9 (+/-9.4)
Ultrafiltration (ml)	2012 (+/-1065)

Table 2: Vitamin values

Vitamin	Ref range	Mean (sd)	Deficient	Normal	High
			n (%)		
Vitamin B1*	10 – 53 nmol/l	207.8 (+/-138.2)	-	4 (10)	36 (90)
Vitamin B2*	18 – 180 nmol/l	257.7 (+/-143.7)	-	10 (25)	30 (75)
Biotin	0.3 – 3.8 nmol/l	7.4 (+/-3.8)	-	5 (12.5)	35 (87.5)
Vitamin B6*	6.5 – 69 nmol/l (women) 10 – 111 nmol/l (men)	177.3 (+/-65.0)	1 (2.5)	3 (7.5)	36 (90)
Pantothenic acid	160 – 588 nmol/l	1515.6 (+/-1321.5)	-	2 (5)	38 (95)
Folic acid*	7 – 31 nmol/l	169.5 (+/-54.9)	-	-	40 (100)
Vitamin C*	26 – 97 µmol/l	64.9 (+/-39.3)	2 (5)	33 (82.5)	5 (12.5)

*Vitamins contained in Dialvit

OC 21

Incidence and prevalence of home dialysis treatment in the Swiss dialysis population between 2013 and 2017

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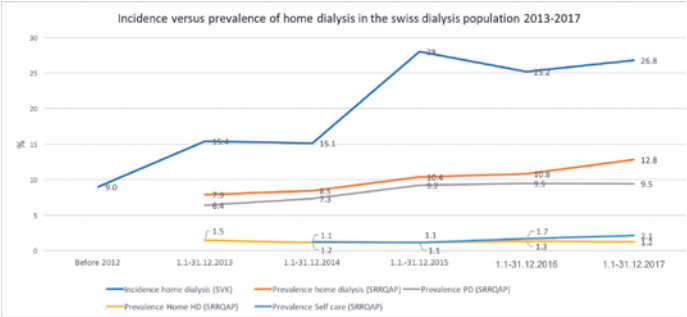
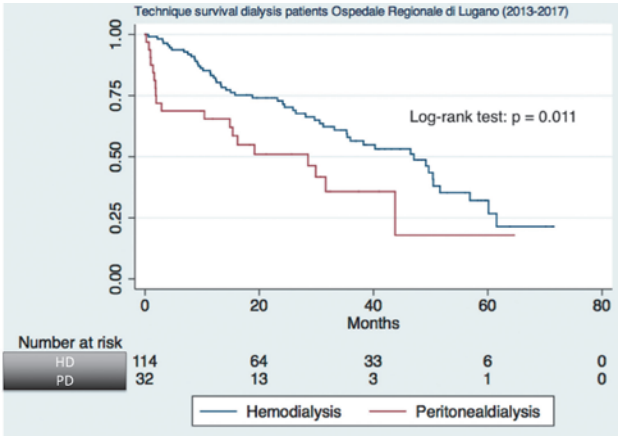
Background: In the first decennium of this millennium incidence and prevalence of dialysis home treatments were particularly low. To reduce health care costs, Swiss Hospitals (H+) and the Swiss association for joint tasks of health insurers (SVK), starting on January 1st 2012, agreed to set a minimum threshold in order to increase the incidence of patients on home dialysis (PD, home HD and limited or self-care HD). This led to a spectacular increase in the yearly incidence of home dialysis treatments from around 9% before 2012 to 26.8% in 2017. The general impression was that the prevalence of patients on PD did not increase significantly in the same time period, probably due to the shorter half-life of this modality.
Methods: Comparison of incidence data from SVK (self-declaration of all centers of the country) with prevalence data from SRRQAP (Swiss Renal Registry and Quality Assessment Program, adherence 95–100% between 2013 and 2017). To better explain the results, we compared modality half-life in our PD- and HD-patients (2012–2017; HD: n = 114, PD: n = 32). Reasons for technique failure included modality switch, kidney transplantation or death.
Results: Results are presented in figure 1 and 2. Technique survival was significantly shorter in patients on PD compared to HD (Log-rank test: p = 0.011).





Conclusions: Due to the new dialysis contract between H+ and SVK, there was not only an increase in the yearly incidence of home dialysis treatments (from around 9 to 27%, approximately 200%) but also in the prevalence (from 6.4% to 9.5%, approximately 50%) of PD patients, despite the shorter half-life of this modality compared to HD. Prevalence of home HD instead remained stable (1.5 to 1.2%). The actual contract has the advantage of both leading to a reduction of health care costs and facilitate wellbalanced information about the different dialysis modalities for patients.

OC 22

The effectiveness and safety of regional citrate anticoagulation in high cut off hemodialysis among patients with myeloma cast nephropathy

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Background: High Cut-off (HCO) hemodialysis can rapidly reduce circulating levels of serum free light chains in multiple myeloma patients with cast nephropathy, yet its benefit remains controversial. Besides, long sessions (between 5–8h) with systemic anticoagulation to prevent filter thrombosis are necessary, exposing the patients to increased bleeding risk. The primary aim of this study was to assess the safety and the influence of regional citrate-based anticoagulation as compared with systemic heparin-based anticoagulation on the rate of free light chain (FLC) removal.
Methods: This monocentric, observational study included all patients who underwent HCO hemodialysis between 2010–2016. Most patients received bortezomib-dexamethasone based chemotherapy. Hemodialysis was performed with the HCO hemodialyser Theralite 2100 (Gambro, Baxter). The use of systemic heparin or regional citrate (according to local protocol) was left to the discretion of the physician in accordance with the bleeding risk. Serum FLC were measured before and after each HCO session.
Results: A total of 19 patients (mean age 69 ± 8 years, 47% women) were included. Achieved reduction of FLC was 83.9 and 76% after 12 and 21 days. After 3 and 12 months, respectively sixteen (84%) and twelve patients (66.7%) were still alive; of these, 11 (69%) and 10 (83%) were free of dialysis. A total of 294 HCO sessions were performed. Regional citrate was mostly used during the first sessions after renal biopsy. There were no hemorrhagic complications during or shortly after HCO sessions; one bleeding episode occurred after renal biopsy and one pectoral muscle bleeding occurred due to traumatic muscle rupture.
Conclusions: Regional citrate anticoagulation in HCO hemodialysis leads to similar FLC removal as systemic anticoagulation in patients with AKI due to cast nephropathy, and has the advantage that it can be used immediately after kidney biopsy. HCO hemodialysis is a safe procedure, and was associated with high rate of hemodialysis independence in this observational study.

Table 1. Extended HCO hemodialysis sessions

Caractéristiques of HCO session	Systemic heparin	Regional citrate anticoagulation
Number of sessions (%)	151 (51.4)	143 (48.6)
Duration of sessions, n (%)		
8 h	66 (43.7)	51 (35.7)
7 h	1 (0.7)	8 (5.6)
6 h	74 (49.1)	76 (53.2)
5 h or less	5 (3.3)	7 (4.9)
Other duration	5 (3.3)	1 (0.7)
Mean duration (hours)	6.7	6.7
Blood flow (ml/min)	341.8 (29.8)	308.8 (29.1)
Urea reduction in %	87.9 (83 - 92.3)	85.9 (81.3 - 90)
sFLC (mg/l)		
before the session	1080 (510 - 2710)	2280 (1340 - 4720)
after the session	300 (90 - 780)	558.5 (338 - 1200)
Reduction in sFLC in %	74.5 (64.4 - 81.3)	74 (67.3 - 78.7)
Sessions with hypotension, n (%)[1]	6 (3.97)	8 (5.59)
Premature termination for technical issue, n (%)[2]	1 (0.66)	2 (1.4)
Cardiac arythmia, n (%)	0	3 (2.1)

[1] Drop in systolic blood pressure >20 mmHg with symptoms or intervention (sodium chloride, passive leg rising
[2] Issues including system thrombosis and catheter dysfunction.

If not otherwise specified, values are mean (DS), or median (25e - 75e percentile).

P 1

Late B lymphocyte action in dysfunctional tissue repair following kidney injury and transplantation

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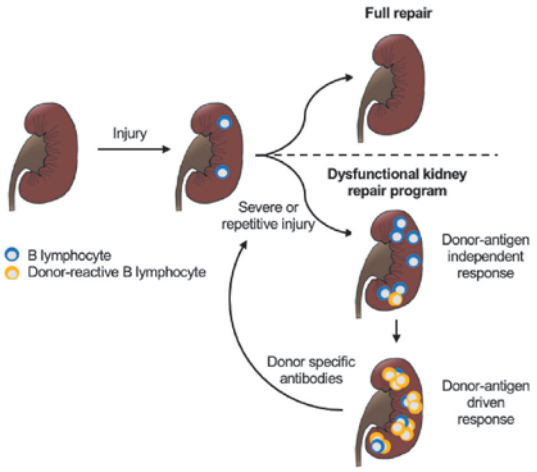
Background: Immune-mediated injury contributes to unsatisfactory long-term outcomes after kidney transplantation, but the mechanisms initiating late immunoreactivity are poorly understood.
Methods: In this translational study, we combined transcriptional profiling of serial protocol biopsies after kidney transplantation in humans (RNAseq analysis from 163 protocol biopsies) with the extensive characterization of immunological processes up to 18 months after ischemia/reperfusion injury (IRI) in mice (RNAseq, immunofluorescence, B cell receptor analysis and autoantibody detection).
Results: In human kidney allografts, a transcriptional B cell signature correlated with fibrosis and reduced graft function. The presence of a B cell signature at 1 year was associated with an injury/repair response earlier after transplantation, not primarily related to episodes of allograft rejection. In the mouse model, we identified a sustained immune response in the absence of foreign antigens in conjunction with the transition to chronic kidney disease. The late intrarenal response after IRI was characterized by the appearance of ectopic lymphoid structures hosting the proliferation and maturation of B lymphocytes into antibody secreting cells. The B cell receptor analysis was consistent with a process of clonal expansion and affinity maturation of B lymphocytes in the damaged kidney. In the absence of foreign antigens this process resulted in the production of systemically detectable broadly-reacting antibodies.
Conclusions: These findings highlight stage specific immunological responses to kidney injury shared between the mouse and human kidney and suggest a new disease model for chronic forms of injury and rejection after transplantation with dysfunctional kidney repair as the primum movens of late B cell mediated immunity.



New model to understand late alloreactivity after kidney transplantation. Severe or repetitive kidney injury induces a dysfunctional repair program leading to a sustained immune response in the kidney. Over time, the local immune response leads to the recruitment and activation of donor reactive B cell clones, which differentiate to plasma cells and produce donor specific antibodies, further contributing to tissue injury in a deleterious feedback mechanism.

P 2

Regulation of Klotho by proteinuria in Chronic Kidney Disease

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Background: Albuminuria, caused by lesions in the glomerular filtration barrier, promotes tubular inflammation, apoptosis and fibrosis in Chronic Kidney Disease (CKD). Previously, it was shown that albuminuria is associated with lower Klotho levels. Our aim is to further investigate how albuminuria regulates Klotho expression.
Methods: Transgenic mice with inducible podocyte apoptosis (POD-ATTAC) were used, as well an Alport mouse model, either wild type or deficient in albumin. For the *in vitro* experiments, HEK cells overexpressing the human transmembrane form of Klotho and HK-2 cells were used.
Results: *In vivo* in POD-ATTAC mice, 3 and 7 days after podocyte loss both Klotho mRNA and protein levels were downregulated without modifications of ADAMs activities and expression. *In vitro*, upon albumin treatment, the total and membrane fractions of the Klotho protein were decreased while Klotho protein half-life was also significantly reduced. Cleaved Klotho as measured in the supernatant was decreased proportionally, arguing against enhanced cleavage. Likewise, a reduction of Klotho mRNA and protein levels was observed in HK-2 cells. In the Alport mouse model, Klotho expression was decreased as measured by qPCR and Western blot. However, this was not the case in the albumin deficient Alport mice, implying some specificity of the regulation by albuminuria itself and not only by the primary renal disease. Similarly, there was no Klotho downregulation upon exposure to immunoglobulins *in vitro*. *In vivo* and *in vitro*, albuminuria induced some features of ER stress, mainly an early and persistent elevation of ATF4 and ATF3 transcription factors. Inhibition of ER stress increased Klotho protein levels *in vitro and in vivo*, suggesting that this mechanism may participate to the enhanced Klotho degradation by albuminuria.
Conclusions: In conclusion, albuminuria has a specific role on Klotho downregulation *in vitro* and *in vivo* that seems to depend on ER stress induction.

P 3

Tissue proteome profiling of hypoxic fetal kidneys reveals pathological changes associated with inflammation and aging

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Background: Intrauterine growth retardation (IUGR), resulting in low birth weight (LBW – <2.5 kg), increases the risk of adulthood diseases (hypertension, diabetes mellitus and/or chronic kidney diseases). An often underestimated risk factor for the development of IUGR is high altitude (>2400 m above sea level) and the concomitant exposure to chronic hypoxic conditions, which affects more than 140 million people. Kidneys of LBW patients are characterized by nephron under-endowment. In the long term, this imposes an extra work load on the remaining nephrons, making them vulnerable for further injury, which leads to a potentially deleterious cycle of accelerated functional decline. Prolonged hypoxia has been shown to promote inflammation and fibrotic remodeling of renal parenchyma in the adult. However, it is unclear, whether such mechanisms are already at play during kidney development.
Methods: We mimicked fetal oxygen deprivation by exposing gravid mice to chronic hypoxic conditions (10% O_2). Freshly isolated embryonic 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.
Results: A total of 6307 proteins were identified, of which 436 were significantly differentially regulated in normoxic vs. hypoxic samples. Functional annotation of these proteins showed altered lysosomal activity, enhanced glycolysis and reduced protein synthesis (down-regulated ribosomal proteins). Furthermore, neutrophil-derived proteins were significantly enriched in hypoxic kidney and staining for the neutrophil marker MPO confirmed an infiltration by these innate immune cells, clustering in the cortical region of hypoxic fetal kidneys. Increased MPO activity is also associated with aging and interestingly, several other proteins involved in aging were found to be regulated in hypoxic fetal kidneys.

Conclusions: Chronic hypoxia during kidney development leads to local inflammation in the proximity of newly forming nephrons and modulation of proteins associated with aging, which provides an explanation for the nephron under-endowment found in LBW kidney patients.

P 4

Mice deleted for cystathionine-gamma-lyase are protected from calcium oxalate nephropathy

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Background: Hydrogen sulfide (H2S), a gazotransmitter, was showed to mediate inflammation. Cystathionine-gamma-lyase (CSE), along with two other enzymes (cystathionine-beta-synthase (CBS) and 3-mercaptopyruvate sulfurtransferase (3-MPST)), contribute to the local production of H2S. CSE was reported to be expressed in the renal cortex and in the outer stripe of the outer medulla. Recent studies using pharmacological inhibition of CSE or CSE deficient mice have suggested a pro-inflammatory role of CSE in a mouse model of pancreatitis and in a model of cecal ligation and puncture-induced sepsis. However, administration of H2S donor also aggravated inflammation. We explore the role of CSE in the mouse model of renal calcium oxalate crystallopathy.
Methods: CSE-deficient *(Cse-/-)* mice were obtained from Dr. Ishii (Showa Pharmaceutical University, Tokyo, Japan). Eightweek old *Cse+/+* and *Cse-/-* male mice were allocated to 1.5% calcium plus 1.5% hydroxyproline (HP) enriched diet or to control diet for 3 weeks. Indirect methylene blue method was used to measure H2S producing capacity in renal tissue. Mice were kept in metabolic cage for collection of 24h urine before being sacrificed at the end of 3 weeks. Inflammatory parameters were evaluated by immunohistochemistry, western blot and qPCR.
Results: *Cse-/-* mice have similar mRNA expression of *Cbs* and *3-Mpst* in kidney tissue compared to WT littermates, indicating that no compensation mechanism are taking place for H2S production. Furthermore, *Cse-/-* mice display a strong decrease in renal H2S producing capacity compared to WT littermates by the indirect methylene blue method. After 3 weeks of the calcium-oxalate enriched diet, serum creatinine and blood urea nitrogen levels were significantly higher in WT mice compared to KO littermates. Concordantly, *Cse+/+* mice had significantly higher fibrosis quantified by Masson's trichrome staining in kidney tissue than their *Cse-/-* KO littermates.
Conclusions: Inhibition of CSE in mice decreases renal H2S production and protects against renal calcium oxalate crystallopathy.

P 5

Glucocorticoids affect steroid metabolome and concentration of galactose deficient IgA in patients with IgA nephropathy

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Background: Patients with IgA nephropathy (IgAN) have IgA1 with galactose (Gal)-deficient O-glycans which are recognized by anti-glycan antibodies, resulting in formation of circulating immune complexes (CIC) that deposit in glomeruli and trigger glomerular injury. In patients with active disease nonresponding to ACE inhibitors or AT II blockers, corticosteroids (CS) are recommended. CS therapy is associated with dysregulation of hypothalamicpituitary-adrenal axis and suppression of gonadal functioning.
Methods: The relationship between the corticosteroid therapy and serum levels of IgA, aberrantly O-glycosylated IgA1, IgA-containing immune complexes, and their mesangioproliferative activity was analyzed as well as the feedback-loop effects on steroid metabolome in the circulation of IgAN patients and disease and healthy controls. Steroids were quantified by GC-MS.
Results: Prednisone therapy significantly reduced proteinuria and levels of serum IgA, galactose-deficient IgA1, and IgA-IgG immune complexes in IgAN patients and thus reduced differences between IgAN patients and control groups. Not significant reduction of mesangioproliferative potential of IgA-IgG immune complexes and IgA sialylation was detected. Before initiation of prednisone therapy, IgAN patients exhibited significantly reduced activity of adrenal zona reticularis (ZR) androgens and lack of adrenal androgens and the low androgen levels were further suppressed by CS therapy.
Conclusions: The prednisone therapy reduces overall aberrancy in IgA1 O-glycosylation in IgA nephropathy patients. On the other hand, it further reduces overall androgen deficiency including the most efficient immunoprotective Δ5 steroids 7α, 7β, and 16α-hydroxy-metabolites. Appropriate combination of corticoid treatment with supplementation of Δ5 steroids or their 7α, 7β, and 16α-hydroxy-metabolites is potential solution for antibodies-mediated autoimmune diseases including IgAN.

P 6

Mechanism of sodium retention in a genetic mouse model of nephrotic syndrome (NCCR project)

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Background: Idiopathic nephrotic syndrome (NS) is the most frequent renal disease in children and is also commonly observed in adults. It is characterized by heavy proteinuria, hypoalbuminemia, and edema. NS combines a defect of the glomerular filtration barrier leading to proteinuria with increased tubular reabsorption of sodium generating edema. We dissected the mechanism of sodium retention in a new genetic mouse model which display an inducible podocyte-specific apoptosis generating massive proteinuria and ascites.
Methods: We use POD-ATTAC trangenic mice that display inducible podocyte specific apoptosis after chemically-induced dimerization of a FKB/caspase 8 fusion protein under control of the podocin promoter. Food and fluid intake recording as well as urine collections were performed for the 5 days following intraperitoneal infusion of the dimerizer. Mice were sacrificed either 3 or 5 days after induction of podocyte apoptosis and kidney were harvested for Western blotting and immunohistochemical analysis.
Results: Sodium retention and proteinuria occurred simultaneously and were maximal at day 3. Western blot analysis of kidney tubule transporters revealed an increase in cleaved g-ENaC abundance maximal at day 3 and sustained at least until day 5 after the onset of glomerular injury. This increase in abundance of cleaved g-ENaC was associated with decreased abundance of non-cleaved g-ENaC protein andg-ENaC mRNA levels. Imaging by immunohistochemistry showed increased apical localization of ENaC subunits and functional diuretic testing confirmed ENaC hyperactivity in POD-ATTAC mice. In parallel we observed decreased NCC abundance and phosphorylation associated with decreased natriuresis in response to thiazides. Both claudin-4 and claudin-10 protein levels were increased in POD-ATTAC mice, suggesting that paracelllar chloride and cation permeabilities were enhanced along the collecting system and the thick ascending limb, respectively.
Conclusions: Our results confirm that sodium retention occurs primarily via ENaC activation and demonstrate increased paracellular permeability to both cations and anions in nephrotic syndrome.

P 7

Coupling between paracellular and transcellular ion transport in renal collecting duct

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Background: The transport through epithelia can occur via the transcellular or paracellular pathway. Kidney tubule regulates hydroelectrolytic homeostasis. The aldosterone-sensitive renal collecting duct (CD) is the place of a precise and tight regulation of sodium and is mainly regulated by aldosterone. Tight junctions play a key role in mediating paracellular ion transport in the kidney. Claudin-8 is one of the main tight junctions proteins expressed in the CD. Coupling between transcellular sodium reabsorption and paracellular permeability may prevent the backflux of reabsorbed solutes and may promote paracellular Cl- reabsorption. We hypothesize that aldosterone controls both transcellular and paracellular permeability in a coordinated manner.
Methods: Male mice were fed for 7 days with either low (0.01% wt/wt), normal (0.18% wt/wt) or high sodium (1.25% wt/wt). One group of mice fed a low sodium diet received 0.35 mg/100g body wt/day of spironolactone for 7 days.
Results: We show here that low salt diet stimulates aldosterone secretion and increases claudin-8 abundance in mouse kidney. Reciprocally, claudin-8 abundance is decreased in kidneys of the mice fed with a high salt diet that blunted aldosterone secretion. In agreement, mice treated with spironolactone, a mineralocorticoid receptor (MR) antagonist, and mice with kidney tubulespecific MR deletion displayed a strong down-regulation of claudin-8. In cultured CD principal cells, aldosterone increased claudin-8 and enhanced transepithelial resistance but did not alter ZO-1 expression.
Conclusions: Taking altogether, our data reveal the coupling between transcellular sodium transport and claudin-8 expression levels that could prevent the backleak of reabsorbed sodium to the tubular lumen.

P 8

Molecular pathways of Calcineurin inhibitor toxicity in the kidney

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Background: Long-term treatment with Calcineurin inhibitor inhibitors (CNI) (Cyclosporine A or Tacrolimus) is associated with chronic kidney disease due to tubular atrophy, interstitial fibrosis and arteriohyalonosis of the kidneys. Calcineurin Inhibitor Nephrotoxicity (CNT) clinically affects 30–40% of non-renal solid organ recipients with increased morbidity and mortality. To date the mechanisms behind CNT are barely understood and specific treatment options are not available. We recently reported that CNI specifically act on structural cells of the kidneys, including epithelial cells to induce inflammatory and fibrotic responses. the molecular mechanisms of CNT in tubular epithelial cells remains unclear.
Methods: Using in vitro, ex vivo and in vivo approaches, we aim to decipher the molecular requirements for CNT in vitro and in vivo.
Results: We here present experimental data, that CNT is independent on NFAT-signalling in tubular epithelial cells, yet mediated by interaction with MAPK pathways, notably PI3K/Akt and p38 kinase. Ttreatment of tubular epithelial cells with cell-permeable or transfection with plasmid-encoded NFAT-inhibitors elicit features of CNT, including Fn14 induction. Inhibitors of MAPK pathways phenocopied the effect of CsA in vitro.
Conclusions: We present first experimental data, that CNT is independent of NFAT-inhibition in tubular epithelial cells. Possibly, the immunoinhibitory and profibrotic activities of CNI employ non-redundant pathways and could therefore be therapeutically dissected. This would allow efficient immunosuppression without nephrotoxic side effects.

P 9

The effect of dietary amino acids on chronic Kidney Disease Progression in rats (NCCR project)

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Background: The mechanisms by which ingested proteins/amino acids lead to an increase in the Glomerular Filtration Rate(GFR) and kidney function deterioration associated with CKD are not well understood. Our study aims to unravel the differential impact that specific dietary amino acids or groups of amino acids might have on the progression of Chronic Kidney Disease.
Methods: 5/6th Nephrectomised animals were randomly divided into groups receiving either the control diet (18% protein as casein) or one of different diets, in each case containing 8% protein supplemented with 10% of a mix of free amino acids (AAs): Essential (EAAs), Non-Essential (NEAAs), Branched Chain (BCAAs), Aromatic (AAAs), or all AAs in the same proportion as in casein (8+10). Additionally, we also had a group that was fed a diet containing 18% protein supplemented with 1.82% L-arginine. Both GFR (using transcutaneous FITC sinistrin) and RPF (using radiolabelled para-aminohippurate (PAH)) were measured in free moving animals.
Results: The pace of RPF and GFR alteration after nephrectomy was diet-dependent. Animals receiving AAAs and EAAs showed the slowest progression, whereas the most dramatic reduction was observed in animals on BCAA diet. The different diets had no effect on kidney function in sham-operated animals. The kidneys of the BCAAsreceiving nephrectomised rats also showed the strongest increase in smooth muscle actin and collagen mRNA expression, as expected for a higher level of inflammation and fibrosis. Towards deciphering the mechanisms underlying these differential effects on CKD progression, we are testing the activity of various signalling pathways, specifically measuring potential changes in phospho- and total Stat3, Akt and S6k.
Conclusions: Our results show that different amino acid diets exert no impact on healthy kidneys, but they show that in CKD, high levels of dietary BCAAs exert a detrimental effect on progression, whereas high levels of AAAs surprisingly display a protective effect.

P 10

A mouse model of renal calcium oxalate crystallopathy

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Background: Systemic crystal-producing diseases as well as in situ precipitation of drugs, proteins, immunoglobulins or various salts along the renal tubules induce renal crystallopathies. One of the most severe form of renal crystallopathies is primary hyperoxaluria, characterized by deposits of calcium oxalate salts and irreversible kidney failure.
Methods: After induction with doxycycline (1 mg/ml in 2% sucrose), *NCX1flox/flox*/Pax8-rTA/LC1 mice developed hypercalciuria, due to kidney-specific inactivation of the distal convoluted tubule-expressed sodium calcium exchanger (NCX1). Sixteen age- and sex-matched *NCX1flox/flox*/Pax8-rTA/LC1 WT and KO mice were induced by

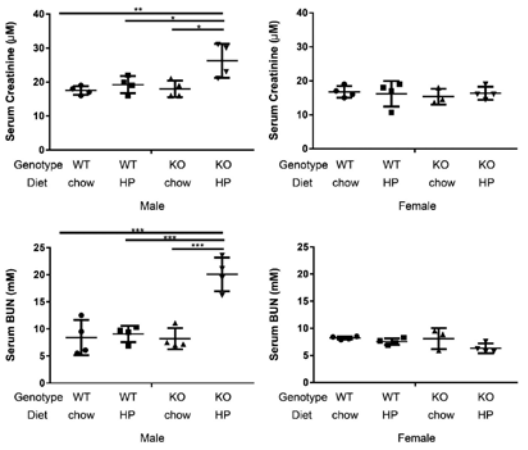

Figure 1. Serum creatinine and BUN of males and females *NCX1*$^{flox/flox}$/Pax8-rTA/LC1 KO and control mice under regular chow or HP diets after three weeks of treatment. *showed significant difference between males KO under HP diet versus KO and control mice under chow or HP diets (* p < 0.05; ** p < 0.01; *** p < 0.001); one serum of female KO mice under chow diet was excluded due to apparent hemolysis.

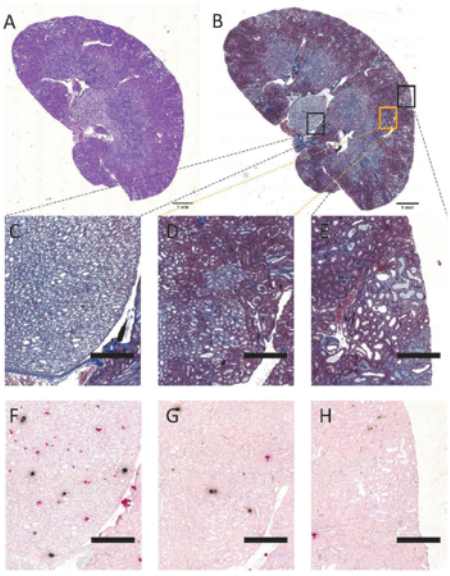

Figure 2. Histology of kidneys of males *NCX1*$^{flox/flox}$/Pax8-rTA/LC1 KO fed 2% HP for 3 weeks

A. Hematoxylin-eosin staining; B. Masson's trichrome staining; C. Masson's trichrome staining of inner medulla; D. Masson's trichrome staining of the cortico-medulla junction; E. Masson's trichrome staining of the cortex; F-H, corresponding Pizzolato's staining (scale bar = 1 mm in A and B; scale bar = 0.5 mm in C-H)

doxycycline at age of four weeks. Male and female mice were randomly allocated to chow diet or 2% hydroxyproline-enriched (HP) diet for 3 weeks.
Results: All KO mice presented significantly higher levels of calciuria compared to WT littermates under control and HP diet. Serum creatinine and BUN levels were significantly increased in male KO mice under HP-enriched diet compared to WT. Masson's trichrome staining of kidneys from male KO mice under HP diet showed patchy pattern of dilated tubules and interstitial fibrosis in the cortex. Pizzolato's staining identified deposits of calcium oxalate crystals in the cortex, the cortico-medulla junction and the inner medulla. Female KO mice under HP diet had similar levels of serum creatinine and BUN as controls.
Conclusions: *NCX1flox/flox*/Pax8-rTA/LC1 KO male mice have successfully developed calcium oxalate crystallopathy at the end of 3 weeks under 2% HP-enriched diet. Females seem to be resistant to crystal-induced nephropathy in this model. Both hypercalciuria and hyperoxaluria are required to develop a nephropathy in males. This model is providing a useful tool for interventional studies in primary hyperoxaluria.

P 11

Proregenerative role of long non-coding RNA H19 in ischemic acute kidney injury

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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 12

Effects of various thiol derivatives on a calcium oxalate crystallopathy mouse model

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Background: Sodium thiosulfate (STS) has been shown to reduce the number of prevalent calcium-containing kidney stones in uncontrolled trials in humans and calcium phosphate nephrolithiasis in a hypercalciuric rat model. STS was also shown to decrease aortic calcifications in a rat model of renal failure and is used for the treatment of calciphylaxis in humans. However, the mechanisms by which STS acts on tissue calcifications and whether it is effective to prevent calcium oxalate crystals is unknown.
Methods: We tested various thiol derivatives, namely STS, potassium thiosulfate (KTS) and sodium hydrogen sulfide (NaHS) as secondary prevention in a model of calcium oxalate renal nephropathy. Male mice *NCX1flox/flox*/Pax8-rTA/LC1 were rendered hypercalciuric by exposing them during 14 days to doxycycline and were then fed a 2% hydroxyproline-enriched diet for 3 weeks to generate calcium-oxalate crystallopathy. Then, 10 mice/group were started under the different interventional diets for 5 weeks. Renal function, fibrosis and crystal deposits were assessed at the end of the intervention.
Results: Mice under HP diet only had higher levels of serum creatinine and BUN compared to that under chow diet. We observed no difference of kidney function between groups under HP, HP+STS, HP+KTS, and HP+NaHS. Mice under HP+STS had significantly higher urine sodium excretion and those under HP+KTS had significantly higher urine potassium excretion. Mice under HP diet had numerous calcium oxalate deposits in the kidneys as shown by Pizzolato's staining. Quantitative analyses of the crystal deposits in Pizzolato's staining, as well as that of fibrosis assessed on Masson's trichrome staining were similar between groups under HP, HP+STS, HP+KTS, and HP+NaHS.
Conclusions: Adding STS, KTS, or NaHS to the food of mice with advanced calcium oxalate nephropathy did not ameliorate renal function, number of crystal deposits or improve fibrosis. Earlier intervention might be more successful and needs to be tested.

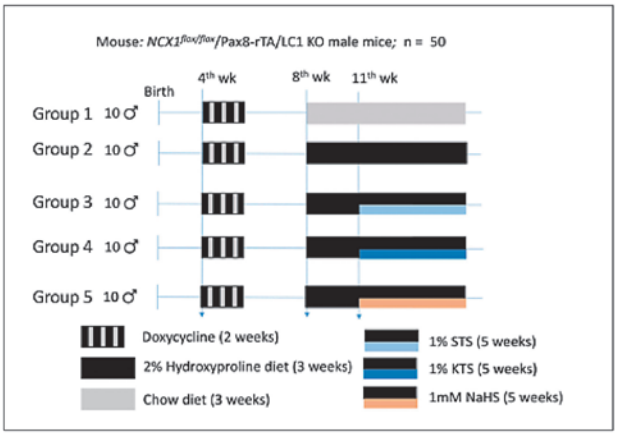

Figure 1. Scheme of the overall experiment: hypercalciuric *NCX1*$^{flox/flox}$/Pax8-rTA/LC1 KO male mice were fed a 2% HP-enriched diet for 3 weeks followed by 5 weeks of different treatment with thiol derivatives (1% Sodium thiosulfate (STS), 1% potassium thiosulfate (KTS), and 1mM NaHS).

P 13

A patient with very large Nuclei

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Background: We report the case of a 60 year old man with stage G4A1 chronic kidney disease (CKD).
Methods: The patient has no special comorbidities except a notion of hepatitis, familial history was negative and blood pressure was normal. The patient presented recurrent airways infections and elevated liver enzymes. A kidney ultrasound showed small bilateral kidneys. A kidney needle biopsy revealed interstitial fibrosis and hyperchromatic, irregular largenuclei of the tubular epithelial cells. The diagnosis of Karyomegalic Interstitial Nephritis was retained. Compound heterozygote mutations of FAN1 were confirmed by exome sequencing.
Results: Worsening of renal function resulted in peritoneal dialysis initiation two years later. Tolerance was initially bad due to acute pain, caused by an inflammatory peritonitis, diagnosed on surgical exploration. The patient was maintained on peritoneal dialysis with symptoms improvement, and has been placed on the kidney transplantation list. Biopsies of the liver, interstine and prostate were performed and did not show caryomegaly.
Conclusions: Karyomegalic nephrtis is a rare nephropathy first discovered and published in the late seventies, caused by a mutation of the fanconi anemia-associated nuclease 1 (Fan1) gene, resulting in an impairment of the DNA reparation activity leading to karyomegaly and renal fibrosis. Only few publications of this diagnosis are found and no experience in peritoneal dialysis or transplantation is reported. Biopsies in organs other than the kidney are usually not reported and we discuss the absence of large nuclei in other organs than the kidney despite a systemic mutation.

P 14

Fabry disease: incidence of pathogenic GLA mutations estimated by newborn screening studies

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Background: Fabry disease (FD), an X-linked lysosomal storage disorder, results from α-galactosidase A gene (GLA)mutations causing deficient α-galactosidase A (α-GalA) activity. There are two major subtypes: early-onset Type 1 "Classic" and Type 2 "Later-Onset" phenotypes. Type 1 males have essentially no α-GalA activity, marked microvascular endothelial globotriaosylceramide (Gb3) accumulation, and childhood/adolescent onset characterized by acroparesthesias, angiokeratoma, corneal opacities, and hypohidrosis. With age, progressive Gb3 deposition in microvascular endothelial cells, renal podocytes, and cardiomyocytes, leads to renal insufficiency/failure, cardiomyopathy, and cerebrovascular disease. Type 2 males have residual α-GalA activity, no microvascular Gb3 accumulation, lack Type 1 early manifestations, and present in adulthood with progressive cardiac and/or renal disease. Previously, FD prevalence was estimated at ~1 in 40,000–119,000 males. However, the incidence is unknown; it is best estimated by newborn screening (NBS) of male newborns, as enzyme screening does not reliability identify female heterozygotes.
Methods: Online databases were searched for FD NBS studies; those with *GLA* sequencing were reanalyzed for pathogenic mutations and phenotype.
Results: In 15 NBS studies reporting mutations, 1,566,931 newborns were screened (fig. 1). Of the seven studies that reported 247,286 males, 0.0546% had pathogenic mutations (Figure 2). Among these studies, the incidence of Caucasian and Asian males was ~1:4,000 and ~1:1,400, respectively, with Types 1 to 2 phenotype ratios of 1:20 and 1:13, respectively (table 1).
Conclusions: The estimated FD male incidence was markedly more frequent than the previously estimated prevalence, primarily since Type 2 males were previously under-diagnosed. In X-linked diseases, expected heterozygotes number twice the newborn males. For Type 1 males, NBS facilitates early treatment. For Type 2 males, NBS presents ethical issues, since manifestations develop in adulthood. Screening Types 1 and 2 at-risk family members will identify older previously undiagnosed affected family members for medical management including enzyme replacement or pharmacologic chaperone therapy.

Table 1. The estimated Incidence of Fabry Disease among male newborns*

	Worldwide*	Caucasians	Asians
FD overall	0.0546% 1:1 831	0.0237% 1:4 225	0.0719% 1:1 379
FD Classic Phenotype	0.0040% 1:24 729	0.0011% 1: 88 720	0.0050% 1:19 821
FD Later-Onset Phenotype	0.0509% 1:1 832	0.0225% 1:4 436	0.0668% 1:1 496
Relationship Classic/ Later-Onset Phenotype	**1/13**	**1/20**	**1/13**
Pathogenic mutations/ screened males	135/247 286	20/88 720	114/158 566
Publications	All	Spada et al., 2006 Colon et al., 2017 Navarrete-Martínez et al., 2017 Wasserstein et al., 2018	Lin et al., 2009 Hwu et al., 2009 Inoue et al., 2013

* Included only studies containing the mutations and the number of screened male newborns

Table 1: The estimated incidence of fabry disease among male newborns.

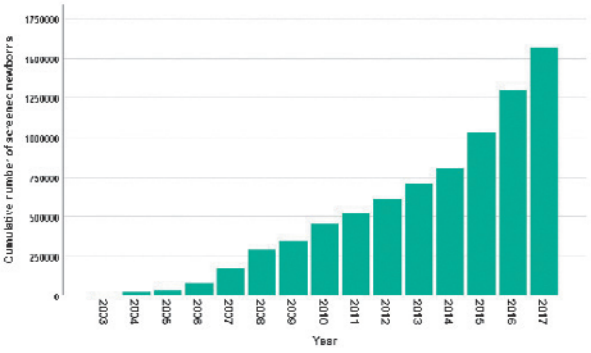

Figure 1: Cumulative number of newborns screened for fabry disease worldwide.

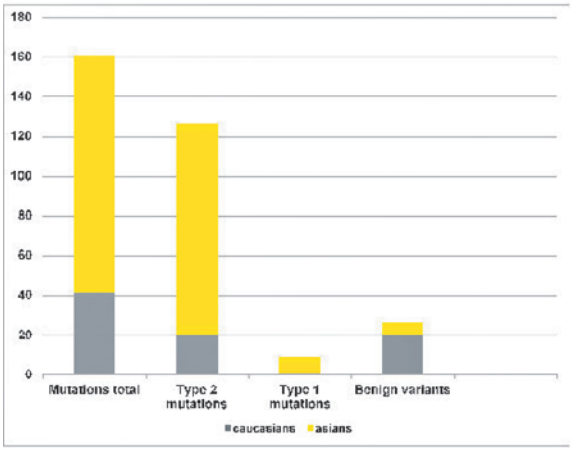

Figure 2: Number of male newborns with mutations.

P 15

Preformed donor-reactive T-cells that persist after ABO desensitization independently predict severe acute cellular rejection after living donor kidney transplantation

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Background: Donor-reactive T-cells impact allograft outcome due to a higher incidence of acute rejection early after transplantation. These donor-reactive T-cells rapidly acquire effector functions and are relatively resistant to standard immunosuppression.
Methods: We analyzed 150 first living-donor KTRs (KTRs) between 2008 to 2016, 92 ABO-compatible (ABOc) and 58 ABOincompatible (ABOi) KTRs. Samples were collected at 6 timepoints, before rituximab, before immunoadsorption, before transplantation, at +1, +2, and +3 months posttransplantation, and donor-reactive T-cells were measured using an interferon-γ Elispot assay.
Results: Among 150 KTRs, 32 KTRs (21%) showed detectable donor-reactive T-cells pretransplantation, whereas 118 KTR (79%) didn't. Risk factors that were independently associated with the presence of preformed donor-reactive T-cells included number of HLA-B- andHLA-DR-mismatches (p <0.05). 8/20 ABOc-KTRs (40%) with preformed donor-reactive T-cells showed acute cellular rejection within the first posttransplant year,whereas 17/72 ABOc-KTRs (24%) without preformed donor-reactive T-cells developed acute cellular rejection (p = 0.163). 7/12 ABOi-KTRs (57%) with preformed donor-reactive T-cells showed acute cellular rejection within the firstposttransplant year, whereas only 3/46 ABOi-KTRs (7%) without preformed donor-reactive T-cells developed acute cellular rejection (p = 0.001). Interestingly, 6/7 ABOi-KTRs (86%) with preformed donor-reactive T-cells that persist after ABO desensitization developed acute cellular rejection, whereas only 1/5 ABOi-KTRs (20%) with preformed donor-reactive T-cells that disappeared during ABO desensitization showed acute cellular rejection (p = 0.072). Among 118 KTRs without preformed donor-reactive T-cells, 10/72 ABOc-KTRs (14%), but 0/46 ABOi-KTRs (0%) showed development of de-novo donor-reactive T-cells (p = 0.006).
Conclusions: The presence of preformed donor-reactive T-cells puts KTRs at an increased risk of acute cellular rejection. Strategies to provide a better risk stratification within this high-risk group, however, don't exist. Here, preformed donor-reactive T-cells that persist despite initiation of CNI-based maintenance immunosuppression identifies KTRs at highest risk of acute cellular rejection. Less de-novo donor-reactive T-cells after ABO desensitization may account for less acute cellular rejection among ABOi-KTRs.

P 16

Kidney re-transplantation after graft failure: a single center experience

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Background: There is an increasing demand for kidney re-transplantation. To date most studies report inferior outcome compared to primary transplantation, consequently feeding an ethical dilemma in the context of chronic organ shortage. In addition, criteria favoring re-transplantation remain unknown.
Methods: We retrospectively analyzed all patient transplanted at our center between 2000 and 2016 with follow up until12/2017. Survival was estimated with Kaplan-Meier method, chance of re-transplantation with Cox regression, using time to transplantation as dependent variable.
Results: Over all 1376 primary transplants and 192 (12%) first re-transplants were performed. 10-year graft survival was comparable for primary transplantation and first re-transplantation (67% vs. 64%, log-rank p = 0.08). Among all 341 patients who lost their graft and went on dialysis, a consecutive 223 (65%) individuals received a new kidney (192 second, 28 third, 2 fourth re- transplantation). Multivariate Cox regression revealed, that candidates were significantly more likely to have re-transplantation if age at graft loss was < 65 years (likelihood ratio LR2.7; 95%CI 1.3–5.5), initially ≤1 light comorbidityin the Charlson-Deyo-Index (LR 1.5; 95%CI 1.0–2.4), BMI <30 kg/m^2 (LR 2.1;95%CI 1.0–4.8), former graft survival >5 years, initial duration of dialysis <3 years (LR 1.7; 95%CI 1.2–2.4), initial use of peritonealdialysis (LR 1.5; 95%CI 1.1–2.2), and a minimized number of previous re-transplants(LR 1.4; 95%CI 1.0–2.0).
Conclusions: Our data demonstrate comparable graft survival for primary- and re-transplant within the first 10years. Eligible patients should have readily access to re-transplantation. Further studies are needed to demonstrate, which of our current likelihood factors are truly legitimate in optimizing candidate selection for re-transplantation.

P 17

Revisiting cytomegalovirus sero-status and infection as risk factors in the current era of renal transplantation

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Background: Cytomegalovirus (CMV) sero-status and occurrence of CMV-infection are considered as risk factors for inferior outcomes after renal transplantation. We aimed to investigate whether this still holds true in the current era of antiviral prophylaxis and sensitive monitoring for CMV-replication.
Methods: We investigated 599 consecutive kidney transplantations from 2005–2015, who had a standardized CMV prevention protocol consisting of either prophylaxis (D+/R- and R+ with ATG induction) or monitoring with pre-emptive treatment (R+ without ATG induction). Patients were grouped according to CMV sero-status (high risk [D+/R-]: n = 122); intermediate risk [R+]: n = 306; low risk [D-/R-]: n = 171) and occurrence/severity of CMV-infection (no CMV-infection: n = 419; asymptomatic active CMV-infection: n = 110; CMV-syndrome: n = 39; tissue-invasive CMVdisease: n = 31).
Results: Median follow-up time was 6.5 years. Graft and patient survival were not different between the three CMV sero-status groups as well as the four CMV-infection groups (p ≥0.44). Forty-nine of 599 patients (8%) suffered from complicated CMV-infection (need for intravenous ganciclovir therapy and/or hospitalization and/or ≥2 relapses and/or relapsing CMV-viremia in need for antiviral treatment). These patients had a reduced graft survival (p = 0.008) and a trend towards a reduced patient survival (p = 0.06). Independent risk factors for complicated CMV-infection were the maximal CMV-viral load (OR3.24 (1.88–5.56); p <0.0001) and occurrence of tissueinvasive CMV-disease (OR 4.63 (1.54–13.92); p = 0.006). A maximal CMV-viral load ≥10'000 IU/ml was strongly associated with complicated CMV-infection (sensitivity 78%; specificity 74%; AUC = 0.82; p <0.0001).
Conclusions: In the current era, only complicated CMV-infection is associated with inferior outcomes and is best characterized by a maximal CMV-viral load ≥10'000 IU/ml.

P 18

Serum bicarbonate levels are associated with graft survival and mortality in kidney transplant recipients in Switzerland

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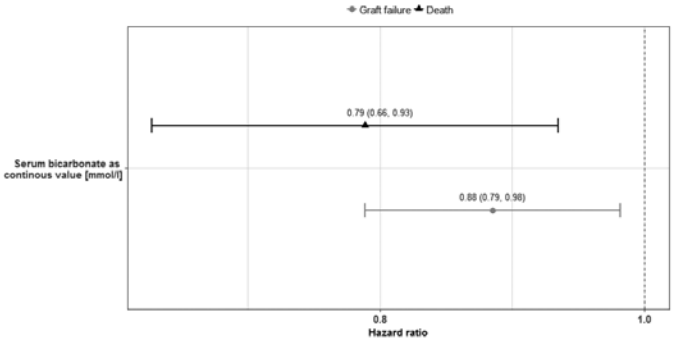
Background: Metabolic acidosis (MA) is a frequent complication of chronic kidney disease (CKD) and an independent risk factor for kidney disease progression and mortality. MA is also highly prevalent after kidney transplantation. Thus, we wanted to investigate if serum bicarbonate is associated with graft outcome and mortality in kidney transplant recipients (KTRs) in Switzerland.
Methods: We performed a single-center retrospective study including adult (≥18 years) patients that have been subjected to *de novo* kidney transplantation between 1999 and 2015. Cox proportional hazard model was used to analyze a possible association between time-dependent serum bicarbonate measurements and graft loss (defined as re-entry to dialysis or second kidney transplantation) or death.



Results: 430 KTRs were included in the analysis with a mean age of 50.9 ± 13.4 years. Mean observation time was 4.7 ± 2.8 years. 284 (66%) were male and 318 (74%) had received a deceased donor kidney transplant. Mean bicarbonate and eGFR levels at baseline were 22.7 ± 3.1 mmol/l and 61 ± 26 ml/min, respectively. Prevalence of MA (defined as serum bicarbonate <22 mmol/L) was 51.2% after transplantation and decreased to 30.8% one year post-transplant. 14 (3%) patients died and 31 (7%) suffered from graft failure. Higher bicarbonate levels were associated with significantly lower hazards for graft failure (HR = 0.88; 95% CI, 0.79–0.98; p = 0.022) and mortality (HR = 0.79; 95% CI, 0.66–0.93; p = 0.006) after adjusting for potential confounders such as age, type of donor and time-varying eGFR (fig. 1).
Conclusions: Our analysis showed that higher serum bicarbonate levels are associated with long-term graft and patient survival in KTRs in Switzerland. Thus, serum bicarbonate may serve as a predictor for graft and patient outcome after kidney transplantation as has been previously shown for patients with CKD.

P 19

Effect of denosumab on trabecular bone score in de novo kidney transplant recipients

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Background: Kidney transplant recipients (KTR) are at risk to lose bone mass. The trabecular bone score (TBS) represents a recently developed parameter of lumbar spine trabecular bone texture that correlates with the occurrence of fractures.
Methods: We analyzed the 1-year changes in TBS in 44 de novo KTR that were randomized 1:1 to denosumab or no treatment. TBS were derived from dual energy X-ray absorptiometry (DXA) and were correlated with 1-year areal bone mineral density (aBMD) changes at the lumbar spine and total hip. Correlations were also performed with parameters of peripheral bone microarchitecture and bone strength at the distal tibia and distal radius, as assessed by high-resolution peripheral quantitative computed tomography (HRpQCT) and micro-finite element analysis (mFEA).
Results: The baseline TBS in KTR amounted to 1.312 ± 0.101 which is lower than the TBS of an age-matched normal control population (range 1.364 to 1.471). The TBS correlated positively with aBMD at the lumbar spine (Spearman's r = 0.56; p <0.001) and total hip (r = 0.33; p <0.05). The baseline TBS also correlated with HRpQCT-derived total (r = 0.49; p <0.05) and trabecular volumetric BMD (r = 0.57; p <0.01) and trabecular separation (r = –0.46; p <0.05) at the tibia. Denosumab treatment led to an increase in TBS, paralleling the BMD changes at the lumbar spine.
Conclusions: The TBS is a useful additional score of bone health, which may help to better define fracture risk. Treatment with denosumab led to improved trabecular bone texture in de novo KTR in addition to its beneficial effect on BMD.

P 20

Follow-up of bone mineral density changes in de novo kidney transplant recipients treated with two doses of the RANKL inhibitor denosumab

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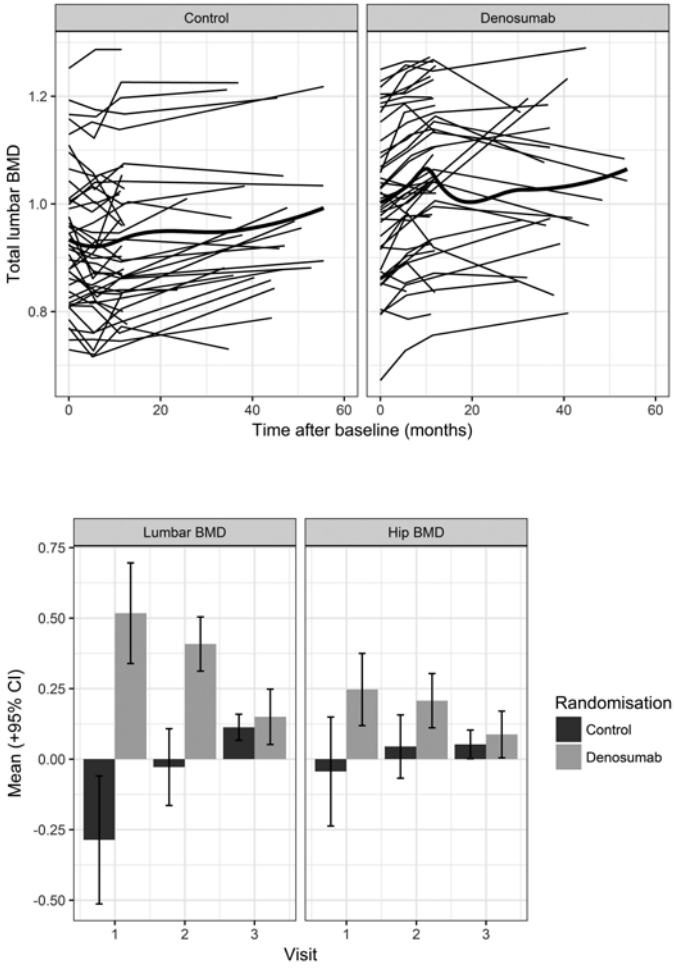
Background: Recently, several studies in women with post-menopausal osteoporosis have shown that discontinuation of treatment with denosumab leads to an increased risk of vertebral fractures due to enhanced bone turnover and rapid loss of bone mineral density (BMD).
Methods: In a retrospective analysis of the POSTOP study we analyzed follow-up DXA after denosumab withdrawal in 54 de novo kidney transplant recipients which had been treated for 1 year with either two 6-month doses of denosumab on top of standard treatment (daily calcium and vitamin D) (n = 25) or with standard treatment alone (n = 29). Follow-up visits took place between 2 and 6.5 years after baseline visit. The percentage change of BMD at the lumbar spine and the hip was divided by months after baseline visit or 12 months visit and compared between the treatment groups with a Wilcoxon rank sum test.
Results: The study population had a mean age of 51 ± 13 years; 57.4% were male; mean baseline eGFR was 55.4 ± 16.0 ml/min/1.73 m^2. The BMD at the lumbar spine declined after discontinuation of treatment with denosumab but increased thereafter (fig. 1). The average monthly percentage change in lumbar spine BMD from baseline was similar in the control and denosumab group (0.11% vs 0.14%, p = 0.592) (fig. 2). However, the average monthly percentage change in lumbar spine BMD from month 12 onward was 0.15% in the control group and 0.01% in the denosumab group (p = 0.021).



Conclusions: In de novo kidney transplant recipients treated with two doses of denosumab we detect a drop in lumbar and hip BMD when denosumab is discontinued. To prevent the decline in BMD after denosumab discontinuation, bisphosphonate treatment might be considered to antagonize the enhanced bone turnover.

P 21

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 prevention of progressive loss in renal allograft recipients. Given the expanding number of CKD patients – including former kidney transplant recipients – an alkali treatment study in kidney transplant patients is of prime importance and has the potential to show that such treatment may slow or reduce the progression towards graft failure and decrease the rate of ESRD.
Methods: This study is a multi-center, prospective, randomized, single-blinded, placebo-controlled interventional trial to test the superiority of alkali treatment compared to placebo for preservation of kidney function in 300 kidney transplant recipients. The duration of the study is 2 years for each individual participant. Patients are randomized into 2 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: The Preserve-Transplant Study has received all required approvals by the end of March 2017. Patient recruitment has started on June 12th, 2017 in Zurich. Both study sites in Berne and Geneva have been operative since July 12th 2017. As of September 8th 2018, 158 patients have been enrolled. By now treatment has been tolerated very well by study participants.
Conclusions: The study has been launched successfully. High recruitment rates are essential to achieve the planned number of 300 patients by the end of the recruitment period in June 2019.

P 22

Two decades of kidney transplantation in the elderly: the gender gap in mortality impacts patient survival after kidney transplantation

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Background: Previous reports suggest favorable short-term patient and kidney allograft outcomes and increased life expectancy of kidney transplant recipients (KTRs) in the elderly population. However, long-term outcomes are urgently needed to improve selection criteria, allocation policies and the use of marginal donors.
Methods: We analyzed patient and kidney allograft outcomes of 244 KTRs between 1999 and 2018 within the Eurotransplant Senior Program (ESP) and assessed quality of living compared to 82 ESP-waitlisted dialysis patients using the standardized shortfrom-8 questionnaire (SF-8).
Results: We observed 1-, 5-, and 10-year patient survival of 91.7%, 66.3%, and 38.0% among ESP-KTRs. Independent mortality risk factors included male gender ($p = 0.006$) and acute cellular rejection ($p < 0.001$). Median Patient survival of male ESP-KTRs was 80 vs. 131 months for female ESP-KTRs ($p = 0.006$). 1-,5-, and 10-year deathcensored allograft survival was 93.3%, 82.6%, and 70.4%.I ndependent risk factors included high BMI ($p < 0.001$) and acute cellular rejection ($p < 0.001$). After re-initiation of dialysis median patient Survival was 58 months. Change of eGFR showed a mean decline of 2.3 and 6.8 mL/min at 5- and 10-years. Median physical and mental component scores of ESP-KTRs were 40.2 and 48.3, significantly higher compared to dialysis patients ($p < 0.05$). 97.5% of ESP-KTRs who underwent transplantation would again do so.
Conclusions: Long-term outcomes of ESP-KTRs over 2 decades ultimately support the effectiveness of the ESP allocation system for the use of elderly organ donors with respect to patient survival, allograft survival, and quality of living. The presence of the gender gap in mortality suggests sex differences as an important factor for treating CKD patients in the elderly, to improve gender-specific care, to assess gender-specific outcomes, and to equalize access to renal replacement therapy.

P 23

Ethical evaluation before living kidney donation: a monocentric pilot study

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Background: Many transplantation teams have focused their programs on encouraging living kidney donation. An independent living donor advocate team is strongly encouraged but not always possible in the organization of transplant centers. In April 2016, Geneva University Hospitals' medical direction commissioned the Clinical Ethics Committee (CEC) to evaluate all potential living kidney donors.
Methods: From July 2016 until February 2018, on monthly dates pre-booked for the year, 29 potential living donors (women 65%) have been evaluated by 2 members of the CEC at the end of their assessment and in the absence of medical, surgical and psychiatric contra-indications for donation. One woman could not follow this path because of organizational difficulties. Conclusions of the CEC concerning the eligibility or not of the potential living donor were sent within 24 hours to the transplant team.
Results: 27 potential living donors had been deemed eligible for donation. The 2 unfavourable opinions delivered, in connection with a lack of information on the surgical plan and regarding financial support, respectively, lead to a second evaluation between 1 and 2.5 months, that was positive this time. Following the 29 ethical evaluations, 24 renal transplantations were performed, 3 are in the process of organization and 2 were cancelled after the recipient underwent a deceased donor transplantation. No delay in the organization of transplantations was attributed to the ethical evaluation. The transplant and donor's teams were reassured in their care and were able to improve their information to potential living donors, thanks to the expertise and feedback of the CEC.
Conclusions: To best of our knowledge, we report the first systematic ethical evaluation of kidney living donors in Switzerland. As complex ethical issues relate to all kind of living donation, with kidney donors making up 95% of all worldwide, we suggest to provide each potential living donor with an ethical evaluation.

P 24

Severe West-Nile meningoencephalitis in a recent renal transplant recipient: a case report

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Background: West-Nile infection is a life-threatening disease in immunosupressed patients. In Romania, from May to August 2018, 117 meningoencephalitis were diagnosed, leading to 13 deaths, in patients with old age, diabetes, or cancer.
Methods: A 49-year-old female underwent a first, living donor kidney transplantation, on June 1st 2018 for IgA nephropathy. Immunosuppression consisted of basiliximab, methylprednisolone, tacrolimus and mycophenolate acid (MPA) . Renal function went immediately well with a creatine of 1.1 mg/dl at discharge at day 6. Anti-infectious prophylaxis consisted of Trimetoprim/sulfamethoxazole, Valacyclovir and Isoniazide (latent tuberculosis which could not be taken in charge before transplantation).
Results: On day 62 , the patient was admitted in emergency for fever, headaches, diplopia, vertigo, and myalgia. Meningoencephalitis was diagnosed with rapidly deterioration of consciousness, Glasgow Coma Scale of 8. At day 8, blood and cerebrospinal fluid PCR came back positive for West-Nile virus, leading to stop tacrolimus and MPA, with methyprednisolone as only immunosuppressive drug. Facing low CD4 78/mm^3 and IgG 3g/l, intraveinous immunoglobulins (IVIg) (0.5 g/kg every other day for a total of 1.5 g/kg) and Ribavirine 1000 mg/day

for 7 days were administered. On day 13, the patient's state of consciousness began to improve slowly. West Nile viremia turned negative on day 21, allowing tacrolimus reintroduction. The patient was discharged at day 27 in stable clinical condition, and a functional graft.
Conclusions: To our knowledge, we report hereby the first West Nile infection in a renal transplant recipient in Romania, a country endemic for this infection, where preventable general and individual measures should be of high importance (yard disinfection, appropriate clothes, use of repellent substances, avoidance of evening walks). Reduction of immunosuppression is the cornerstone of the care, but could lead to rejection when performed early after transplantation. Use of IVIg and ribavirine could help in the therapeutic management of the virus.

P 25

Allograft dysfunction in patients with progressive atherosclerotic disease of the common iliac artery: a case series

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Background: Deterioration of perfusion in kidney transplants may occur immediately after transplantation or during followup. Stenosis of the renal transplant artery is the most common long-term vascular complication. However, due to progressive atherosclerotic disease of iliac vessels, allograft dysfunction in some patients can be observed.
Methods: –
Results: We describe 3 cases of kidney transplanted patients who developed allograft dysfunction during long-term follow up due to progressive atherosclerotic disease of the common iliac artey (CIA). A 46-year-old woman experienced a constantly rise of her blood pressure and an increase of serum creatinine eight years after living kidney transplantation (LKT). Duplex sonography showed an occlusion of the right CIA and a significant stenosis of the left CIA, with retrograde perfusion of the allograft on the right side. Therefore, an angioplasty of the left CIA, as well as an iliac-femoral crossover bypass to the right side was performed. A 62-year-old patient complained about symptoms of claudication and an increase in his blood pressure eight years after transplantation. Duplex sonography revealed a stenosis of the right CIA. Angioplasty and stenting of the right CIA via brachial access were conducted. A 78-year-old right sided transplanted patient complained about symptoms of claudication, and an increase of serum creatinine was noticed eight years after LKT. Duplex sonography showed an occlusion of the right CIA, with retrograde perfusion of the allograft. Cross-over recanalization and stenting via left femoral access was successfully performed.
Conclusions: In patients with claudication, new onset or worsening of hypertension and rise of serum creatinine during long-term follow-up after kidney transplantation, stenosis or occlusion of the CIA should be ruled out. Interdisciplinary approach in diagnosis and treatment are of immense importance to preserve renal transplants function.

P 26

Prediction of allocation date in deceased donor transplantation. A retrospective single center experience

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Background: Deceased donor kidney transplantation (DDT) is an effective treatment for patients with end stage renal disease. Due to shortage of donor organs, waiting time of potential recipients for a suitable organ is substantial and can be several years, depending on blood group and anti-HLA immunisation. Recent studies in general surgery highlight the importance of physical and psychological prehabilitation. It is likely, that prehabilitation is beneficial in organ transplantation, yet currently such programs are scarce due to unpredictability of allocation. It was the goal of this work to predict allocation date based on individual allocation history and donor-derived determinants, including blood group and anti-HLA immunisation.
Methods: We analyzed a cohort of 97 consecutive DDT from a single tertiary University hospital for waiting time, waiting time prediction and outcome. Allocation date was predicted based on the individual allocation history and compared with the actual date of transplantation.
Results: Median waiting time was 3.03 years (range: 0.35 years–10.98 years) for the whole cohort. Waiting time for the was 4.29, 2.43, 2.42, and 2.4 years for blood groups 0, A, B and AB respectively. 10% of patients were transplanted within 30 days (e.g. 15 days before to 15 days after), 25% patients within 90 days, 47% patients within 180 days and 63% patients within 360 days of projection. Patients where prediction was inacurate, were more likely to have cPRA >25%, non-A/B Blood Group or CIT-Status at the time of prediction.
Conclusions: Prediction of allocation seems feasible within 6 months for unimmunized blood group O and A recipients. These patients should be informed enrolled in prehabilitation programs. Larger cohorts are needed to validate the results and prospective studies to demonstrate the feasibility and effectiveness of prehabilitation before DDT. Furthermore, DQ alloimmunisation and policy adaptations of Swiss transplantation allocation need to be included in future studies.

P 27

Preliminary results of the STCS renal allograft twin study

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Background: We study all available pairs of renal allograft recipients enrolled in the Swiss Transplant Cohort Study (STCS) where each of the two recipients has received its allograft from the same deceased donor ("renal allograft twins").
Methods: We analyzed concordance of delayed-graft function and allograft failure in all consenting pairs of renal allograft recipients that received their transplant from the same deceased donor. The analysis period is between 2008 and end of 2017.
Results: We analyzed 1370 kidney recipients building 685 pairs. Overall, 247 (18%) recipients experience DGF and 116 (8.5%) lost their kidney transplant. In 47 pairs (6.9%) both recipients experienced DGF, in 485 pairs (70.8%) none of the recipients experienced DGF and in 153 pairs (22.3%) only one of the recipients had a DGF. If all 247 DGF would have occurred in discordant pairs, 36% of pairs would have been discordant. If all 247 failures would have occurred in concordant pairs, then 18% (123 pairs) of kidney pairs would have been concordant. The *adjusted proportion* of 38.5% (7%/18%) of all possible concordant pairs were observed to be concordant whereas 62% (22%/36%) of all possible discordant pairs were observed to be discordant. For Graft failure, concordance of failure in 14 pairs (2%), concordance of non-failure in 583 pairs (85.1%) and discordance of graft failure in 88 pairs (12.8%). The observed results show that 23.5% (2% out of 8.5%) occurred in concordant pairs and 75% (12.8 out of 17%) occurred in discordant.
Conclusions: For DGF and allograft failure, the adjusted proportion of discordant failures is clearly higher than the adjusted proportion of concordant failures. We conclude that the impact of recipient risk factor are more important the onor risk factors for DGF and allograft failure.

P 28

Renal arteriovenous fistula in a renal transplant recipient: a case report and literature review

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Background: Renal arteriovenous fistula (AVF) is a rare complication after total nephrectomy, with only 72 cases reported in the last literature review published in 1997 and none concerning a renal transplant recipient. The potential consequences of hemodetournement on the graft function are therefore unknown.
Methods: We hereby report the case of renal AVF occurring in a renal transplant recipient and analysed all cases of post nephrectomy renal AVF described from 1997 to 2017.
Results: A 75-year-old woman with autosomal hepatorenal polycystic disease underwent right nephrectomy (900 g) and kidney transplantation in right iliac fossa 16 years earlier. While she presented to the emergency department for viral gastroenteritis, the clinical exam revealed a loud continuous murmur in right flank and back. When asking, she noticed an exercise dyspnea progressively appearing for a year and an easy-fatigability. Her serum creatinine was slightly raised, but returned to normal value with hydratation. Echocardiography showed a moderate to severe dilatation of the left ventricle, with decreased ejection fraction 50%. An injected thoracoabdominal CT scanner demonstrated a communication between the stump of the right renal artery and inferior vena cava (fig. 1). An endovascular

approach was decided, and arteriography confirmed a high-flow renal AVF (fig. 2). A successful embolization was performed with Amplatzer plug and coils placed in the distal renal stump, just upstream of fistula. Total occlusion of the fistula was obtained (fig. 3). Symptoms of exercise dyspnea disappeared with regression of left ventricular dilatation at 6-month echocardiography follow up.
Conclusions: To our knowledge, we hereby described the first case of post-nephrectomy AVF in a renal transplant recipient. Graft function was not altered and successful AVF occlusion by endovascular procedure allowed resolution of cardiac symptomatology. Heart failure in a post-nephrectomy renal transplant recipient must raise suspicion for AVF, in the absence of usual heart failure causes.

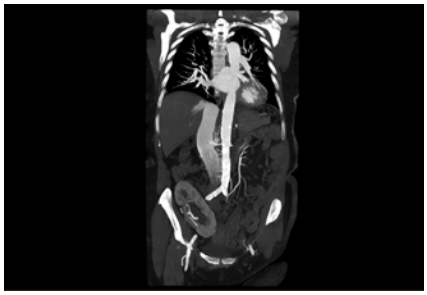

Figure 1

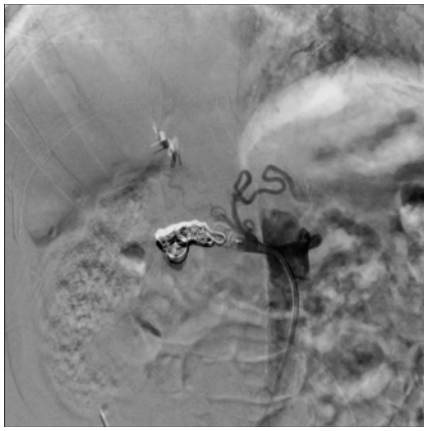

Figure 2

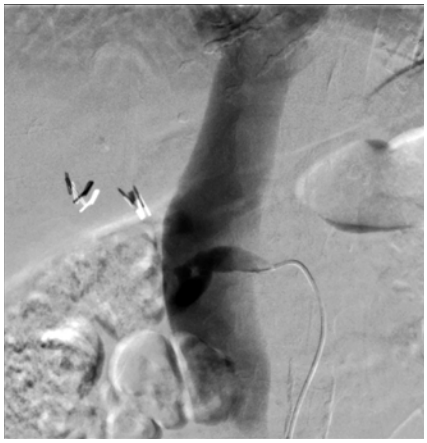

Figure 3

P 29

Current state of renal transplant patients in a southern area of Algeria

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Background: Renal transplantation (RT) is the best treatment for end stage renal diseases (ESRD). The aim of this study, is to examine the clinical situation of transplant patients in Ghardaia.
Methods: In this observational descriptive study, we included all kidney transplant patients for over a year living in Ghardaia we examined the patients and consulted the medical files.
Results: Twenty-two patients included, the average age is 35 (22–53), sex ratio is 0.4, average duration in dialysis was 5 years, two preemptive grafts, all the patients were in hemodialysis. The kidney donor was, in 36% a siblings, 32% a parent, 22% a spouse, 2 cases of unrelated donor, the average donor age was 42; the average duration of the transplant is 7.5 years. The estimated GFR by CKD EPI is 68 ml / min / 1.73 m^2 (20–102), 68% of patients are hypertensive, dyslipidemia in 23% and overweight in 45% of cases, no case of diabetes. Infectious complications are frequent: urinary 40%, pneumocystis and brucellosis 13% each, one case of cryptococcal disease.
Surgical complications are rare, 03 cases of ureteral stenosis; immunosuppressive therapy is: ciclosporin 40%, tacrolimus 45%, two patients on sirolimus and five patients without corticosteroids.
A case of PTLD (Kaposi's tumor) in a young patient of 32 years old and a case of breast neoplasia in a 42 years old woman no renal biopsy was performed.
Conclusions: Despite the young age of the patients, short duration of transplantation and an adequate immunosuppressive treatment, the function of the graft is weak. The infectious risk to unusual germs is important, it is probably due to rural living and climatic conditions high heat and drought. Non-collaboration between the transplanting centers and local nephrologists, absence of systematic biopsies of the grafts, and the scarcity of performing laboratories, are not insignificant factors.

P 30

Protective effect of magnesium supplementation against kidney fibrosis (NCCR Kidney.CH project)

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Background: Recent epidemiological studies have shown that low levels of magnesium (Mg) were independently associated with chronic kidney disease and end-stage renal disease. Furthermore, low levels of Mg are associated with hypertension, vascular calcification and also with an increased risk for cardiovascular disease. However, the mechanisms involved in the putative protective effect of Mg remain unclear. We therefore used unilateral ureteric obstruction (UUO), a well-established model to study renal fibrosis, to address this question.
Methods: We performed UUO on C57BL6J mice. During the 2 weeks following UUO, mice received either a control diet containing 0.2% Mg or a diet supplemented with Mg carbonate leading to 0.8% Mg. After this period, urine and blood were collected, mice were sacrificed and the obstructed and contralateral control kidneys were collected for analysis.
Results: After 16 days, urinary Mg concentration was higher in mice receiving 0.8% Mg diet, with an increase of the Mg to creatinine ratio. Mg supplementation during 16 days led to a significantly decreased expression of fibrosis markers in the kidney. Alpha smooth muscle actin and fibronectin mRNA expression decreased by 31% and 50% respectively, in comparison to the mice that received the control diet. The mRNA expression levels of collagens were also decreased with the Mg supplementation: collagen 3a1 by 83%, collagen 1a1 by 78% and collagen 6a1 by 42%.
Conclusions: Further experiments are presently being carried out to address the mechanisms underlying the reno-protective effect of Mg in fibrosis.

P 31

Familial anti-GBM disease associated with a deletion in the COL4A3 gene: a potential clue to etiology

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Background: Anti-glomerular-basement-membrane (GBM) disease is characterized by crescentic glomerulonephritis (cGN) and/or alveolar hemorrhage. It is caused by antibodies that bind the non-collagenous domain (NC1) of the collagen IV α345 network in the glomerular and alveolar basement membranes. Antibodies bind to α3 and α5 NC1 monomers but not the native α345NC1 hexamer, indicating that a perturbation of the quaternary structure of the hexamer is required for eliciting an autoimmune response.
Methods: We describe a case of familial anti-GBM disease that is associated with a novel structural alteration in the α345NC1 domain. The index-patient was affected at the age of 45y by alveolar hemorrhage and renal failure due to cGN with anti-GBM antibodies. Her son developed the same clinical phenotype at the age of 24y.
Results: We discovered a heterozygous 18 bp deletion in both subjects in the region of the COL4A3-gene coding for the NC1 domain. The deletion leads to an elongated collagen α3NC1 domain, which substitutes eight additional amino acids (AA) for the very last C-terminal AA. Mutations in the COL4A3-gene typically cause autosomal dominant/recessive Alport's or thin basement membrane disease, however there was no evidence for this in our patients. GBM-antibodies of our patient behaved like in classical anti-GBM cases. Analysis of the 3D model of the α345 hexamer revealed that the mutant extension might lead to conformational changes that impact epitope presentation. The epitope structure may be altered to include residues of the extension or rendered accessible by the antibody.
Conclusions: This is the first report of a COL4A3 mutation associated with anti-GBM disease. The occurrence of this mutation in two family members, with autoantibodies against the α3NC1 autoantigen, indicates that the mutation plays a key-role in disease etiology. The association of this mutation with disease may be a clue to the etiology of familial and sporadic cases of anti-GBM disease.

P 32

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. Efficacy of thiazides for kidney stone prevention was tested in 11 trials in the past. However, all these trials had major methodological deficiencies. Nowadays, thiazides are widely used in the treatment of recurrent nephrolithiasis and arterial hypertension, but at significantly lower doses. In the case of recurrent nephrolithiasis, however, this practice is not supported by randomized evidence. Thus, evidence for benefits and harms of thiazides in the prevention of kidney stones remains unclear.
Methods: NOSTONE 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 hydrochlorothiazide (placebo, 12.5 mg, 25.0 mg, 50.0 mg) in kidney stone prevention. The primary outcome is incidence of stone recurrence (a composite of symptomatic or radiologic recurrence) at 3 years, a low-dose CT will be performed at the beginning and the end of the trial. A total of 416 patients from 12 hospitals throughout Switzerland will be included in the study.
Results: NOSTONE received all necessary approvals by the end of February 2017. Recruitment started in Bern on the 9th of March 2017, all study sites are operative since June 30th 2017. As of September 6th 2018, 249 patients were randomized in the trial (regular updates: www.nostone.ch).
Conclusions: The NOSTONE study is currently in the second recruitment year. A continued effort is needed to reach the minimum inclusion goal of 416 patients until the end of the recruitment period in May 2019.

P 33

The association between zinc and blood pressure – Preliminary data from a population based study

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Background: A status of zinc deficiency has been found to increase dietary sodium intake through a low salt taste acuity and/or a high salt preference in young female and also in patients on hemodialysis. Zinc deficiency may thereby increase blood pressure. However, both, decreased and increased blood and urine zinc levels have been reported to be associated with hypertension in the past.
Methods: We examined in a large, population-based study with 1128 participants the associations of plasma and urine zinc levels with parameters of blood pressure and the renin-angiotensin-aldosterone (RAA) system.
Results: The median plasma zinc concentration was 784 µg/l and the median 24-hour urine zinc excretion was 329 µg. In multivariable analysis adjusting for sex, age, BMI, kidney function, plasma and urinary sodium and potassium and plasma aldosterone and renin activity, the plasma zinc levels were positively associated with mean nighttime ambulatory systolic and diastolic blood pressure only in men. By contrast, plasma zinc levels were positively associated with systolic nighttime blood pressure dipping only in women.
Conclusions: These preliminary data support a sex-specific relationship between the zinc metabolism and blood pressure regulation. If parameters of the RAA system contribute to this association remains to be examined in further analysis within this study.

P 34

Effect of bariatric surgery-induced weight loss on blood pressure, renal function, electrolytes urinary excretion and hormones: a single center 12 months follow-up

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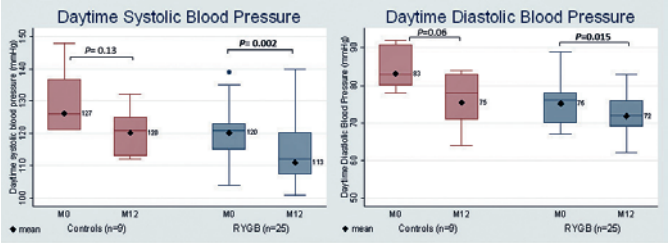
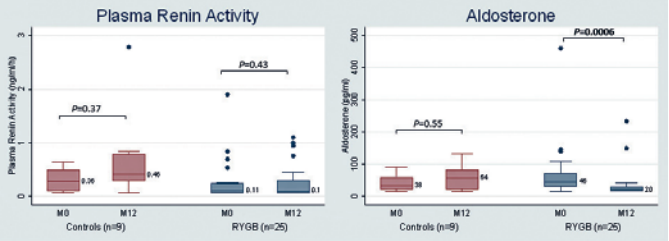
Background: Obesity is strongly associated with the development of hypertension. Weight loss interventions have been shown to be effective in blood pressure reduction. However, the mechanisms linking weight reduction to a decrease in blood pressure are incompletely explored in humans. The objective of this study was to evaluate the effect of weight loss after Roux-en-Y gastric bypass (RYGB) on blood pressure, sodium and potassium renal handling, renal function and hormones before and at 12 months after surgery.
Methods: This was a case-controlled prospective study including 25 obese patients referred for RYBG and 9 obese controls who were receiving nutritional advice by obesity specialists for one year. Anthropometric, daytime ambulatory blood pressure, creatinine clearance, inulin clearance, electrolytes excretion, plasma renin activity, aldosterone, adiponectin and leptin were measured at M0 and M12.

	Controls (n=9)			RYBG (n=25)		
	T0	T= 12 months	*P-value*	T0	T= 12 months	*P-value*
Weight (kg)	123.8	116	0.09	121	78	0.0001
BMI (kg/m²)	43	44	NS	42	31	0.02
Daytime SBP (mmHg)	126	121	NS	120	113	0.03
Daytime DBP (mmHg)	81	75	NS	75.8	72	0.01
Heart frequence (bpm)	85	80	NS	80	74	0.003
Urinary Sodium (mmol/24h)	197	163	0.009	179	129	0.01
Urinary Potassium (mmol/24h)	62	55	NS	59	46	0.008
24h measured creatinine clearance (ml/min)	149	136	NS	137	106	0.0025
24h measured inulin clearance (ml/min)	105	89	0.027	106	67	0.0001
Adiponectine (mcg/l)	9842	11676	NS	11448	21687	0.0001
Leptin (mcg/l)	52.6	43	NS	49	17	0.0001
Plasma renin activity (ng/ml/h)	0.82	0.93	NS	0.27	0.28	NS
Aldosterone (pg/ml)	45	57	NS	70	36	0.03
Aldosterone-to-renin ratio (ARR)	200	132	NS	608	258	(NS)





Results: 37 patients were included in the study, data were available for 34 patients after 12 months (9 controls, 25 patients with RYBG). Compared to controls, patients with RYBG had a significant decrease in weight, BMI, daytime SBP, daytime DBP and HR. Sodium and potassium urinary excretion were lower at 12 months in the RYBG but remains the same in the control group. Mean measured creatinine and inulin clearance decreased significantly at 12 months only in the RYBG group. Twelve months after RYBG, leptin decreased and adiponectin increased significantly. Aldosterone decreased but renin showed no significant variation.
Conclusions: The weight loss induced by RYBG was higher compared to specialized follow-up only. This weight reduction had a major impact on sodium excretion, systolic BP, diastolic BP and measured GFR. Interestingly, a decrease in plasma aldosterone without any change in PRA was observed despite a decrease in sodium excretion. This observation suggests that a drastic bariatric surgery-induced weight loss has a renin-independent effect on aldosterone secretion, which could contribute to the BP lowering effect of RYBG.

P 35

Renal handling of Zinc in a cohort of chronic kidney disease patients as compared to normo-and hypertensive controls with preserved renal function

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Background: Zinc deficiency is commonly encountered in Chronic Kidney Disease (CKD) for incompletely understood reasons. The aims of this study were to assess whether Zinc deficiency was related to increased renal excretion of Zinc, and whether Zinc deficiency plays a role in the progression of CKD.
Methods: Plasma and 24-hour urinary Zinc levels were measured together with urinary electrolytes and uromodulin in a cohort of 108 CKD patients and 81 individuals without CKD (39 patients with arterial hypertension and 42 healthy controls). Serum creatinine values were collected for three years to calculate the yearly change in estimated glomerular filtration rate (eGFR), and multivariable regression analysis was performed to assess the association between baseline Zinc levels and yearly change in eGFR.
Results: CKD patients had lower circulating Zinc levels (figure 1) and a higher 24h-urinary Zinc excretion than non CKD participants (612.4 ± 425.9 vs 479.2 ± 293.0 µg/day, p = 0.02). The fractional excretion (FE) of Zinc was also higher, and significantly increased at more

advanced CKD stages (figure 2). The FE of Zinc correlated negatively with 24h-urinary uromodulin excretion (r = –0.29, p <0.01). Lower baseline plasma Zinc levels were associated with a faster yearly decline of renal function in age, gender, diabetes and hypertension adjusted models, but this relationship was no longer significant when baseline eGFR or proteinuria was included in the model.
Conclusions: Zinc levels are lower in CKD, and not compensated by reduced renal Zinc excretion. The inverse association between urinary Zinc excretion and uromodulin possibly points to an impaired tubular activity, which could partly account for the Zinc imbalance in CKD. Zinc status might be important to the evolution of kidney disease, but further studies elucidating the underlying mechanisms and the potential role of Zinc supplements in CKD are needed.

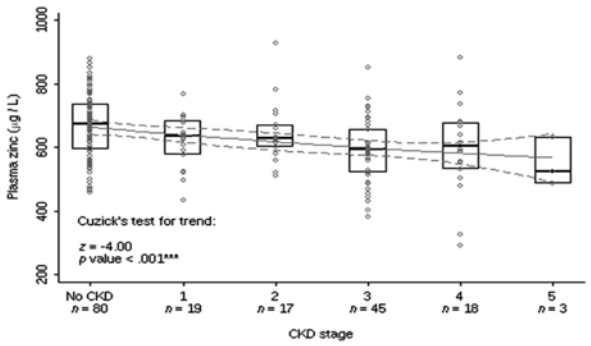

Figure 1. Relationship between plasma Zinc and CKD stage. The line with a 95% confidence interval results from the prediction of a linear regression, and illustrates the trend.

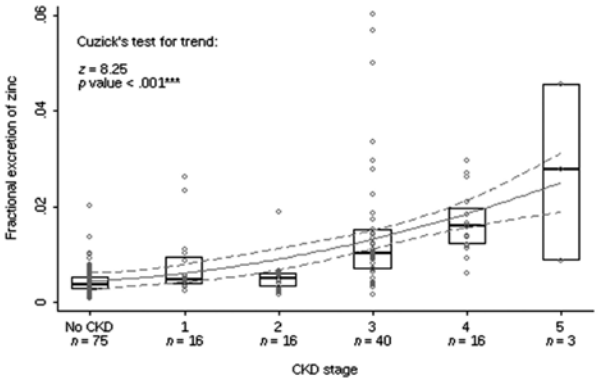

Figure 2: Relationship between urinary fractional excretion of Zinc and CKD stage. The curve (with a 95% confidence interval) represents the prediction of a quadratic regression.

P 36

Renal tuberculosis wake-up call: a case report

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Background: Tuberculosis (TB) is a global burden with more than 2 Billion people estimated to be infected and with the highest rates in sub-Saharan Africa. Renal TB is the third most common form of extrapulmonary TB. The classical presentation is via hematogenous spread. There are no early specific symptoms and sterile pyuria may be an incidental finding. Frequency, dysuria, and low back pain appear with advanced disease.
Methods
Case-Report: We report a case of a 34 year old Kurdish woman with no H/O renal disease, who presented with intermittent suprapubic pains irradiating to the right flank. The symptoms appeared 18 months after the birth of the third child. Repeated urine specimens were negative for bacterial growth. Gynaecological infections were ruled out and the medical history was otherwise unremarkable.
Results: The clinical examination showed an apyretic patient with normal breast sounds, no enlarged lymph nodes, but a right flank tenderness. Initial laboratory data showed a normal renal function and normal LFT's. The urinary spot was characterized by the presence of microematuria and massive leucocyturia, with negative urine culture. A Quantiferon determination was then performed, which resulted positive (TB1-Ag 7.3, IU/ml, TB2-Ag 10.1 IU/ml, N <0.35). Abdominal CT-scan showed the presence of multiple caliectasis and strictures throughout the right collecting system consistent with renal tuberculosis. The diagnosis of renal TB was confirmed by the detection of Mycobacterium tuberculosis complex in repeated early-morning urine cultures. A standard anti-TB therapy was started combined with a 3 wks steroid treatment to reduce uretherocaliceal strictures risks. A pigtail was inserted to minimize persistent pains and hydronephrosis.
Conclusion: Our report show that in presence of persistent pyuria with repeated negative urinary culture, renal TB should be suspected. Because of the recent global migration phenomenon, it is mandatory to include renal TB in the differential diagnosis of urinary disturbances.

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The Bern ADPKD registry

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Background: ADPKD is the most common inherited disorder of the kidney. Translational research in recent years has yielded a wealth of novel information with respect to diagnosis, evaluation and treatment of ADPKD patients. The Bern ADPKD registry was launched to harmonize patient care, promote efficient integration and monitoring of novel therapies and build a local platform for education, research and collaboration in the area of ADPKD.
Methods: The Bern ADPKD registry is a prospective observational cohort study. Inclusion criteria are age ≥18y, clinical diagnosis of ADPKD, informed consent. The main exclusion criterion is need for renal replacement therapy. Assessments include yearly collection of demographic, anthropometric, imaging, laboratory and clinical data, quality-of-life questionnaires and biobank samples.
Results: Between October 2015 and August 2018, 110 ADPKD patients (51 men, 59 women) were recruited from internal and external sources. Baseline median age was 46 y, median HtTKV was 717 ml/m and median eGFR was 62 ml/min. At baseline, arterial hypertension (treated or office BP ≥140/90 mm Hg) was present in 79 patients (72 %) and 74 patients (67%) already received antihypertensive treatment. Overall, only 3.3% of patients met the currently recommended blood pressure target at baseline (office BP ≤110/75 mmHg if aged 18–50 y and GFR >60 ml/min, otherwise ≤130/85 mmHg). A treatment indication for Tolvaptan was identified in 42 patients (38%) and treatment has thus far been initiated in 37 patients (34%).
Conclusions: The launch of the ADPKD registry caused a standardization of patient care at our clinic, enabled efficient introduction of a novel disease-modifying pharmacological therapy and allows continued surveillance of therapy and assessment of compliance with guideline-defined treatment goals. Our data reveal a high prevalence of arterial hypertension in Swiss ADPKD patients and suggest that a large fraction of patients does not meet currently recommended blood pressure targets.

P 38

Systemic lupus erythematosus in male patients

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Background: Systemic lupus erythematosus (SLE) in males is rare and whether it differs from SLE in females is still a matter of debate. We set out to identify differences between genders regarding clinical manifestation as well as renal and cardiovascular outcome of SLE.
Methods: Data from patients included in the Swiss SLE Cohort Study (SSCS) were used. Cardiovascular events and damage accrual were recorded within the Systemic Lupus International Collaborating Clinics/ American College of Rheumatology Damage Index (SLICC-SDI). Risk differences were calculated with multiple regression models.
Results: We analysed 93 men and 529 women with a mean follow up time of 2.8 years. Men were significantly older at diagnosis (44.3 versus 36.5 years, p <0.001). Men had significantly less arthritis (57.0% vs. 74.1%, p <0.001), psychosis (1.1% versus 6.4%, p <0.05) and dermatological disorders (61.3% versus 76.2%, p <0.003). Kaplan Meier curve for renal failure was similar between genders. Kaplan Meier curve for progression to a lower chronic kidney (CKD) stage were significantly worse in men (p <0.02), showing an estimated cumulative renal survival after 3 years of 71.6% in males versus 79.5% in females. SLICC-SDI was in both groups comparable (men 1.6, women 1.3, p <0.07). Men had significantly higher rates of coronary arterial disease (16.9% versus 4.2%, p <0.001) and myocardial infarction (9.6% versus 2.3%, p <0.001). After adjusting for age, ethnic background and disease duration, the odds ratio for coronary arterial disease was 5.6 (p <0.001) and for myocardial infarction 3.9 (p <0.03) for men compared to women.
Conclusions: This study indicates that gender differences in SLE exist. The reasons for the worse outcomes in males are still not quite clear. Whether hormonal factors or other gender-specific behaviour play a role, needs further investigation. However, male gender is possibly a risk factor for cardiovascular events and renal function worsening in SLE.

SLE manifestations

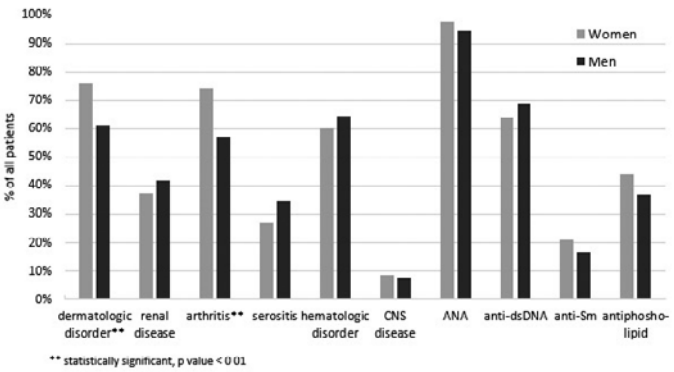

Figure 1: Clinical and immunological manifestations of SLE prior inclusion

Renal function survival

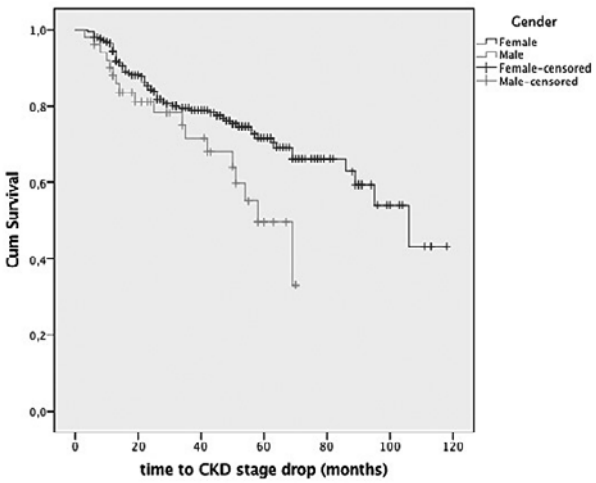

Figure 2: Renal function survival time in males and females until a decrease to a lower CKD stage.

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Primary Hyperoxaluria (PH): Type 1, 2, 3 or none?

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Background: Children with urolithiasis and/or nephrocalcinosis need careful metabolic investigation. In particular, hyperoxaluria has to be kept in mind.
Methods: • Case 1: 7 month-old girl with first febrile urinary tract infection. Ultrasound (US) showed medullary nephrocalcinosis. Urinary analysis revealed increased excretion of oxalate and glycerate. Genetic analysis showed a heterozygous mutation in the AGXT gene, consistent with PH type 1.
• Case 2a: 3 year-old boy with first episode of nephrolithiasis (stone analysis: 100% Calcium-oxalatemonohydrate). US was normal, but urinary analysis revealed increased excretion of oxalate and glycerate. Genetic analysis showed a homozygous mutation in the GRHPR gene, confirming PH type 2.
• Case 2b: His identical twin brother is asymptomatic.
• Case 3: 21 month-old boy with bladder stone (analysis: Calcium-oxalate-mono/dihydrate); one year later further episode of nephrolithiasis. US was normal, but urinary analysis revealed persistent hyperoxaluria and minimally elevated glycerate. Genetic analysis showed a homozygous mutation in the HOGA1 gene, confirming PH type 3.
• Case 4: 3 year-old boy with acute right flank pain and microhaematuria, suggesting nephrolithiasis. US was normal, but urinary analysis showed persistent hyperoxaluria. Genetic analysis for PH type 1/2/3 did not show any mutation.
• All patients have normal renal function and avoid dietary oxalate excess. Cases 1 to 3 are on long-term oral Citrate.
Conclusions: Children with urolithiasis and/or nephrocalcinosis need careful investigation including urinary oxalate. If hyperoxaluria persists, genetic analysis is required to confirm primary hyperoxaluria. There are at least 3 types of PH with great genotypic/phenotypic variability: Whereas PH type 1 often leads to end-stage renal failure with subsequent combined kidney-liver transplantation, PH type 2 and 3 have a more favourable course. Lifelong medication with oral citrate to inhibit calcium-oxalate crystallization may both prevent urolithiasis and maintain renal function.

P 40

Atypical Hemolytic-Uremic Syndrome (aHUS) in Armenian children: cluster of DEAP HUS?

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Background: Multiple genetic abnormalities may predispose to aHUS. Deficiency or absence of complement factor H (CFH) – related proteins 1 and 3 due to deletion of coding genes and CFH autoantibody – positive HUS (DEAP-HUS) is a rare subtype comprising only about 6% of all cases of aHUS.
Methods: We report on 4 children (age 4–10 y/o, 2 females) from Armenia presenting with aHUS. Detailed complement profiles (in 3) and genetic analysis (in all) were done in Germany and Hungary.
Results: Patients were admitted at the Arabkir hospital between November 2015 and January 2018 with non-bloody diarrhea, vomiting, microangiopathic hemolytic anemia, thrombocytopenia and AKI followed by repeated episodes of TMA with extrarenal involvement such as myocarditis (1), dilated cardiomyopathy (1), hepatitis (1) and CNS complications (3). All were hemodialysis dependent from the beginning and had low C3 level. Further examination revealed homozygous deletions in CFHR1/CFHR3 genes (in all), and autoantibodies against CFH (3 examined). The treatment was started empirically. All patients received methylprednisolone pulses followed by oral prednisolone and plasma exchanges (PEX) (# 3-14). In addition, 2 patients received eculizumab.One patient received only 3 PEX, which were discontinued because of heart failure and followed by cyclophosphamide pulses and mycophenolic acid. TMA stopped and dialysis was discontinued in all after 1.2–9.5 months. There were no severe renal sequelae, eGFR at follow-up of 7–33 months was 47–148 ml/min/1.73 m^2.

Conclusions: Notably all 4 children diagnosed with aHUS admitted within 2 year period had DEAP-HUS, which may suggest a possible cluster of deletion of CFHR1/CFHR3 genes. However, this number is close to the true incidence of the disease, and may reflect increased awareness in recent years. Early diagnosis and immunosuppressive treatment and/or PEX in DEAP-HUS are important for the prognosis.

P 41

Characteristics and outcome of IgA nephropathy in Switzerland-a single center perspective

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Background: Immunoglobulin A nephropathy (IgAN) is the most common primary glomerulonephritis worldwide. 40% of affected patients progress to end-stage renal disease (ESRD) by ten years. Geographic differences in clinical course and response to treatment may partly result from different disease entities. The purpose of this retrospective cohort analysis was to study all cases of IgAN of a single center with respect to clinical and histological characteristics, treatment practices and outcome.
Methods: This retrospective cohort analysis identified 158 cases of adult biopsy-proven IgAN diagnosed between 1980 and 2017 by chart review. Detailed phenotypisation including clinical, paraclinical, histological, treatment and outcome parameters was performed. Remission status was defined as described previously (Reich 2007). Statistical analysis was performed using Excel and SPSS software and included standard descriptive methods and simple and multiple regression analysis.
Results: Subjects were majorly male and of Caucasian descent (table 1). Mean estimated glomerular filtration rate at diagnosis was 55.4 ml/min/1.73 m^2, mean proteinuria was 2.3 g/d. 70.3% of the patients were hypertensive at presentation. 28.5% of initial biopsies showed moderate or severe tubular atrophy and interstitial fibrosis, 38% of initial biopsies included crescents, 1.9% included >50% crescents. 89% of the patients were treated by reninangiotensin-aldosteron-blocking medications, 44.3% received immunosuppressive therapy including steroids in 43% and other immunosuppressive medications in 28.7% with the most common being azathioprin. Overall outcome included 25.3% complete, 22.1% partial remissions.

Variable	Value
Gender (% male)	73.4
Age (yr; mean ± SD)	53.5 ± 14.7
Ethnicity (%)	
Caucasian	84.2
African	3.2
Asian	10.1
Hispanic	2.5
Tonsillectomy (% performed)	11.4
BMI (kg/m^2, mean ± SD)	26.6 ± 5.9
Clinical presentation	
Hypertension (% subjects)	70.3
Edema (% subjects)	19.0
Flank pain (% subjects)	9.5
Macrohematuria (% subjects)	28.5
Purpura (% subjects)	1.9
Arthritis (% subjects)	0.6
Systolic blood pressure (mmHg; mean ± SD)	138.1 ± 21.7
Diastolic blood pressure (mmHg; mean ± SD)	83.9 ± 14.1
Chronic kidney disease (% subjects)	88.0
Acute kidney injury (% subjects)	10.8
Proteinuria 24 h (g/d, mean ± SD)	2.3 ± 2.0
No proteinuria/microalbuminuria (% subjects)	1.9
Microalbuminuria (% subjects)	3.8
Proteinuria < 1g/d (% subjects)	27.2
Subnephrotic proteinuria (% subjects)	27.8
Nephrotic proteinuria (% subjects)	22.8
Nephrotic Syndrome (% subjects)	9.5
Renal histology (% subjects)	
Presence of crescents	36.1
Presence of ≥ moderate tubular atrophy or interstitial fibrosis	28.5
Treatment (% subjects)	
Renin-angiotensin-aldosteron-blocking medication	88.9
Immunosuppressive therapy	44.3
Steroids	43.0
Other immunosuppressive therapies	28.7
Overall outcome (% subjects)	
Complete remission	25.3
Partial remission	22.1
Relapse after partial or complete remission	29.3
Progression to end-stage renal disease	42.4
Recurrence after transplantation	16.3
Last follow-up	
Systolic blood pressure (mmHg; mean ± SD)	129.5 ± 14.9
Diastolic blood pressure (mmHg; mean ± SD)	79.2 ± 11.4
Patients receiving antihypertensive therapy (% subjects)	83.5
1 antihypertensive drug (% subjects)	41.8
2 antihypertensive drugs (% subjects)	24.1
3 antihypertensive drugs (% subjects)	13.9
No proteinuria/microalbuminuria (% subjects)	19.0
Microalbuminuria (% subjects)	12.7
Proteinuria <1g/d (% subjects)	36.7
Subnephrotic proteinuria (% subjects)	13.9
Nephrotic proteinuria (% subjects)	4.4
Nephrotic syndrome (% subjects)	1.3

Table 1. Baseline characteristics and outcome of 158 patients with immunoglobulin A nephropathy

29.3% of patients experienced at least one relapse. Progression to ESRD was noted in 42.4%. Recurrence rate after transplantation was 16.3%.
Conclusions: This analysis gives insight into the characteristics and treatment practices of a Swiss single center cohort of IgAN patients from 1980–2017. Clinical profile and outcome of the cohort largely correspond to reported values in the literature.

P 42

Red blood cell volume may not always be decreased in anemic chronic kidney disease patients

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Background: Anemia is defined according to decreased blood hemoglobin concentration ([Hb]), which isconsidered a marker of low total red blood cell volume (RBCV). Alterations of plasma volume (PV) may also modify [Hb] without concomitant changes in RBCV. Since anemia and fluid retention are frequent complications of chronic kidney disease(CKD), we hypothesized that anemia during CKD may in part be related to expanded PV without a simultaneous decrease in RBCV. This has never been considered in studies aiming at normalizing [Hb] in CKD patients.
Methods: We quantified hemoglobin mass, RBCV, PV and total blood volume (BV) using an automated carbon monoxide device in 0 consecutive stage 3–5 CKD patients not on dialysis and in 7 healthy male controls of the same age range. These were compared within and to predicted volumes according to Nadler's formula. Arterial stiffness and NT-proBNP were measured.
Results: RBCV was similar to predicted values range in anemic CKD patients 2073(1818–2704) versus, 2061(1725–2473) ml, p>0.05. In contrast, PV was largely increased in anemic CKD patients (3881(3212-4352) versus 2916 (2851–3201), p = 0.01. Out of 26 anemic patients, only 6 had a >20% decrease in RBCV as the cause for their anemia, whereas 14 had a >20% increase of PV as a cause for their anemia. NT-pro BNP correlated with eGFR but neither with PV nor BV, whereas arterial stiffness was not correlated to blood volumes.
Conclusions: Anemia in predialysis CKD as diagnosed by low [Hb] is not necessarily associated to low RBCV but may reflect only increased PV. This finding has implications for the treatment of CKD patients and may refrain from normalizing [Hb] levels in all CKD patients. It may also explain some of the increased CV events associated to [Hb] normalization in CKD.

P 43

Chronic kidney disease and therapeutic patient education program

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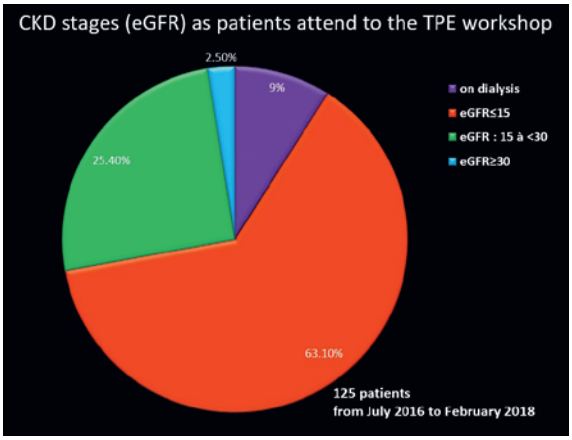
Background: Therapeutic patient education (TPE) is necessary in the field of nephrology, because it promotes the acquisition of self-care skills and adaptation to the disease. Chronic kidney disease (CKD) patients have specificities in their need in TPE given along asymptomatic phase and a very demanding treatment. Since more than ten years, we offer an education session to help patients choosing the best renal replacement therapy. We here describe the referred population and our observations to propose a better adapted offer in TPE
Methods: We retrospectively analyzed the patients referred to a TPE session during 15 months. We analyzed the CKD stages at time of referral as well as demographic data. We report the results of a focus group in dialysis CKD patients to better understand their needs on health literacy to promote their empowerment and satisfaction.
Results: As shown on the pie-chart as experienced in our practice, the 125 patients who attend to the workshop (between July 2016 and February 2018), were mainly in advanced stages of CKD (72.1% stage 5 of CKD). Many patients were on dialysis or symptomatic. From our focus group, many hemodialysis patients were disappointed by the absence of choice in their dialysis method because of a late referral and felt less satisfied with the medical care, than peritoneal dialysis patients. From our different observations, we propose to set up different workshop adapted to patient's needs, which differs according to CKD stages.



Conclusions: TPE has to be part of the care of CKD patients, even at early stages of the disease. TPE allows to prepare the patients, favoring autonomy and shared decision making. We propose to adapt an education program in nephrology in 3 workshops dedicated to different stages of CKD, including from early to end stage of renal disease.

P 44

Attitudes and practices among swiss nephrologists regarding end-of-life care: is there a change in the past 12 years? A national survey

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Background: End-of-life care for dialysis patients is an important issue. However little is known regarding attitudes and practice of nephrologists and needs for education. AIM: To survey attitudes and practices among Swiss nephrologists regarding End-of-life care, to evaluate a change in the past decade and identifying and educational needs.
Methods: In 2005 and 2017 active members of the Swiss Society of Nephrology (SGN-SSN) were invited to participate in a survey. It consisted of 118 questions, covering 8 categories: a) education and training, b) current practise, c) perceived barriers, d) decision making e) vignettes f) individual experience g) role of the Swiss Society of Nephrology and h) demographic data.
Results: The survey was completed by 77 Swiss nephrologists (2005: 45, 2017: 32). They reported a high reliance on trial and error in learning to care for terminally-ill patients, significantly less in 2017 (67% vs 44%, p <0.045). A lack of formal training was identified (no training 2005: 47%, 2017: 25%). Nephrologists rated their competencies in pain control, communicating with patients/ families and discussing withdrawing or not-initiate dialysis to be high with a tendency to increase 2017 (2005 >80%, 2017 >90%). Family conflicts followed by unrealistic expectations of patients/ families were found to be most challenging. Lack of Pain-service or Palliative-Care-Team was identified as a barrier, accessibility increased in 2017 (Pain-Service 2005: 48%/ 2017: 83%, Palliative-Care-Team 2005: 24%/ 2017: 59%). More programs at the annual meeting of SGN-SSN were considered to be the most helpful initiative improving skills in End-of-life Care.
Conclusions: Swiss nephrologists are integrating symptom-control and decision-making in their routine End-of-life care, although barriers exist making comprehensive care a challenge. Over the past decade significantly more nephrologists were formally trained, there is a tendency to feel more competent in symptom-control, decision-making suggesting a development in clinical attitude. More programs are considered being helpful.

P 45

Systemic primary Sjögren's syndrome with multi-organ involvement – a rare case

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Background: Sjögren's syndrome is an autoimmune disease of the exocrine glands. Systemic complications can occur but renal involvement is rare, affecting <10% of patients. The most common renal manifestation is tubulointerstitial nephritis. Membranoproliferative glomerulonephritis secondary to cryoglobulinemia is less frequent.
Methods
Case report
Results: A 40-year-old male with a previously diagnosed, but untreated primary Sjögren's Syndrome presented with multi-organ manifestation and newly identified acute kidney injury. The creatinine level was 319 umol/l with a predominant tubular proteinuria of 970 mg/d (urine protein/creatinine 97mg/mmol, urine albumin/creatinine 8.6 mg/mmol, urine a1mikroglobulin/creatinine 25 mg/mmol). The urine sediment revealed signs of a tubular damage, however there were no laboratory signs of tubular dysfunction. Kidney biopsy identified an ongoing tubulointerstital nephritis with transition to interstitial fibrosis and atrophy in 30% of the specimen. No glomerular involvement was detectable, although a mixed hypocomplementemic cryoglobulinemia was identified beforehand. Moreover, a monoclonal gammopathy, without evidence of a lymphoma, was diagnosed 8 months before presentation. Immediately after presentation a therapy with high-dose corticosteroids was initiated. Nevertheless, the renal function deteriorated within 9 days and renal replacement therapy was required. Simultaneously the patient experienced multiple epileptic seizures owing to a cerebellitis with upward herniation which required a craniotomy and insertion of an external ventricular drain. Although the histopathological findings of the brain were not conclusive, a cryoglobulinemic vasculitis secondary to Sjögren's syndrome was postulated. Therefore, the therapeutic regime was extended by plasmapheresis and rituximab. Subsequently, the renal function recovered and the intermittent haemodialysis was successfully stopped after 7 weeks. To date, the kidney function stabilised with a creatinine of 180 umol/l and a proteinuria below 0.5 g/d, although systemic signs of disease activity and high cryoglobulinemia persisted.
Conclusions: We present a rare case of fulminant Sjögren'ssyndrome with renal involvement preceding cryoglobulinemic vasculitis of the cerebellum.

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Using the CKD-EPI formula for drug dose adjustments in patients with impaired kidney function – a graphical analysis

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Background: Many drugs require dosage adjustments in patients with impaired kidney function. It is a common clinical practice to use the CKD-EPI equation for this purpose, which estimates GFR in ml/min normalized to a body surface area of 1.73 m^2. Dosing recommendations for prescriptions on the contrary are usually based on estimates of creatinine clearance (e.g. Cockcroft-Gault) or absolute values of GFR. Discordant results between these equations are common, but the clinical importance of these differences remains a matter of debate. Here we present a systematic comparison of the CKD-EPI equation (in ml/min/1.73 m^2) to Cockcroft-Gault and the denormalized CKD-EPI equation (both in ml/min) respectively.
Methods: Our analysis is based entirely on calculations made with published formulas. Mathematica 11.3.0.0 was used for computations. In different graphics we display absolute and relative differences between CKD-EPI and Cockcroft-Gault/denormalized CKD-EPI across weight and height ranges provided by NHANES and an age spectrum of 18–90y. Areas where these discrepancies result in assignments to differing GFR or clearance categories typically used for dose adjustement recommendations are also delineated.
Results: The CKD-EPI estimation provides substantially lower results than Cockcroft-Gault at lower ages and higher weights. The inverse is true at higher ages and lower weights. Significant misclassifications of GFR/clearance reduction occur within common age and weight ranges. Although the differences between CKD-EPI and its denormalized form are generally smaller than with Cockcroft-Gault they nevertheless lead to a substantial portion of misclassifications. This is especially true for male patients, where only a minority will have BSA values close to 1.73 m^2.

Conclusions: Using the CKD-EPI equation where recommendations for dose adjustements are given on the basis of creatinine clearance or denormalized CKD-EPI equation can result in significant discrepancies in dose adjustments in patients with impaired kidney function.

P 47

Liquid intake in the Swiss Kidney stone cohort

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Background: Kidney stone is one of the most frequent diseases of the uro-nephrological axis and is associated with disorders of food and fluid intake or with renal tubular dysfunction. Food and fluid intake is difficult to assess in real life and several tools have been developed. We report here on a unique database which consists in data gathered by multiple Swiss nephrological clinics on stone formers and on the assessement of liquid intake by 24h recall interviews and the software Globodiet® by trained dieticians.
Methods: Adult patients were recruited from the five Swiss University Clinics of Nephrology (Basel, Bern, Geneva, Lausanne and Zurich) and Kantonspital Aarau if they were recurrent stone formers or had a single episode with pre-determined risk factors. Work-ups are standardized between the centers and include 2×24h urine collection, food and activity questionnaires and structured 24h recall interviews of food intake by trained dieticians with the help of the software Globodiet®. Samples of urine, blood and DNA are stored in a biobank. All lab analysis are centralized. Follow-up visits are organized at 3 months and annually.
Results: More than 624 patients have been included as of July 2018 and 819 Globodiet-interviews have been conducted by trained dieticians. Liquid intake of stone formers was compared with urine output and the correlation was poor. Quantitative analysis of liquid intake shows that water is the main liquid ingested (61%), followed by coffee (10%), soft drinks (8%), herbal tea (5%), milk (4%), and fruit juice (3%). Of note, milk is drunk by only 39% of the patients. In addition, we observed strong regional differences in the amount of liquid intake.
Conclusions: We propose a first analysis of the quantitative and qualitative liquid intake of stone formers in Switzerland.

P 48

A young woman with primary membranous nephritis complicated by aHUS: is there a link?

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Background: Membranous nephropathy (MN) and atypical hemolytic uremic syndrome (aHUS) are rare diseases affecting the kidney. Methods: A 17-year-old woman presented to our outpatient clinic with nephrotic syndrome several weeks after a viral infection of the respiratory tract. Phospholipase A2 receptor antibodies (PLA2RAb) were positive and kidney biopsy confirmed MN. Initially, renal function remained normal and symptoms were well controlled with diuretics and ACE-inhibitors but in the course, proteinuria rose to >10 g per day and PLA2RAb titer persisted. Six months after diagnosis she presented with severe acute renal failure and thrombotic microangiopathy (TMA). ADAMTS 13 was normal whereas Coombs-Test, ANA, antiphospholipid antibodies and shiga-toxin were negative. aHUS was diagnosed and she received plasmapheresis and hemodialysis. After three sessions of plasmapheresis anti-C5-antibody (eculizumab) therapy was commenced. Kidney biopsy showed TMA, MN and acute tubular injury. In the complement factor H gene (CFH) we detected a heterozygous mutation of unknown significance which had been previously described in aHUS. Furthermore, we detected several aHUS risk polymorphisms in other complement genes (CFH, MCP, CFHR1). After initiating eculizumab, the patient rapidly regained renal function and TMA parameters normalized. Because nephrotic proteinuria persisted 3 months later, we treated the patient with rituximab and PLA2RAb disappeared.
Results: One year after initiating eculizumab and 6 months post rituximab, renal function is normal and proteinuria has decreased to 0.48 g per day.
Conclusions: We present the first case of MN associated with aHUS that was successfully treated with eculizumab and rituximab. The co-occurrence of these rare diseases suggest a pathophysiological link. Proteinuria might have triggered aHUS by disturbing the equilibrium of activating and inhibiting complement factors in this patient with predisposing genetic alterations in complement genes. Nephrologists need to be aware of this complication and initiate urgent therapy when TMA appears in the context of nephrotic Syndrome.

P 49

Lower belly pain, flu-like symptoms and nephrotic syndrome

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Background: Nephrotic syndrome (NS) which is characterized by proteinuria >3–3,5 g/d, hypoalbuminemia, hyperlipidaemia and oedema is found with an incidence of 3/100.000. In adulthood membranous glomerulonephritis (MGN) and focal-segmental glomerulosclerosis (FSGS) are the most common causes of the NS. Depending on medical history, laboratory testings and histological findings the MGN and FSGS are classified into primary and secondary forms. These secondary forms can be caused by e.g. infections, malignant diseases, drug induced, systemic diseases and others. Usually a kidney biopsy is necessary in order to get a diagnosis.
Methods
Case report
Results: In this case we report on a 21-year old caucasian man with flu-like symptoms and pain in the lower belly, who was sent to hospital because of high proteinuria. He described also an unwanted gain in weight about 7 kg in the last weeks. We found a NS with a proteinuria of 9 g/diem, a hyperlipidaemia, a severe hypoalbuminemia (15 g/l) and eyelid oedema. The ultrasound showed no pathological findings on the kidneys but small amounts of pleural effusion and ascites. A kidney biopsy was performed with the histologic finding of a (most likely secondary) membranous glomerulonephritis with nearly complete loss of podocyte foot processes, but also reticular aggregates in the endothelial cells consistent with a HIV-infection or a SLE. The laboratory testing showed an infection with HIV as well as lues. We initiated a supportive treatment (ACE-inhibitor, diuretics, statines) and a single shot of benzathinepenicillin was given. The short-term follow-up showed a rapid complete resolution of the nephrotic Syndrome.
Conclusions: HIV and lues are both known as a rare cause of NS and the combination of both is remarkable. The relevance of these two infections in the presented case will be discussed.

P 50

Too much of a good thing: three cases of vitamin D intoxication due to lifestyle use

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Background: Vitamin D supplementation has become increasingly popular over the past two decades due to increasing awareness of vitamin D deficiency and the putative benefits of supplementation beyond bone health. At the same time, there is an increasing trend to using high doses of over-the counter or internet purchased vitamin D for various doubtful indications or simply as a “lifestyle” drug.
Methods: Within 6 months at this center alone, we observed three cases of severe hypercalcemia and renal failure due to self-medication with high doses of vitamin D:
Results: The main toxicity of vitamin D is from absorptive hypercalcemia. Initial treatment therefore is directed at reestablishing

normocalcemia. Since native Vitamin D has a very long half life of 15–69 days, we also tried to promote inactivation by inducing CYP24S1 (24-hydroxylase) with low dose phenytoin. Estimated half-lives of serum 25-OH D3 nevertheless were approximately 50 days. Although none of the three patients had permanent kidney failure, time to recovery (defined as return to baseline serum creatinine) was long (43-65 days). All three patients had extended exposure to high doses of vitamin, yet hypercalcemia developed only after several months. The risk factors for developing hypercalcemia with vitamin D overdoses are not well defined.

	Daily Vitamin D dose (IE)	Exposure months	Peak S-calcium (mmol/l)	Peak S-creatinine (umol/l)	Peak 25-OH vitamin D (nmol/l)	Days to renal recovery
Patient 1	50.000-100.000	12	3.19	367	1750	65
Patient 2	300.000	6	3.50	303	1526	43
Patient 3	10.000-40.000	24	3.03	168	600	54

Conclusions: Hypercalcemia due to self medication with high doses of vitamin D appears to be on the rise. It should be discouraged in pharmacies and in the public.

P 51

Successful management of pembrulizumab-induced acute interstitial nephritis without discontinuation of the oncologic drug in a patient with disseminated melanoma

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Background: The development of renal toxic effects from novel anticancer drugs represents a serious problem for oncologists, nephrologists and patients, because it often leads to discontinuation of treatment or dose reduction with loss of efficacy of potentially life-prolonging treatments. We report a case of a patient with disseminated melanoma with pembrolizumab-induced acute interstitial nephritis that was successfully treated with steroids without pembrolizumab discontinuation. Pembrolizumab, an anti-PD-1 antibody, is a new treatment for metastatic melanoma. The anti PD-1 receptor antibodies present an high risk for development of organ specific immune-related adverse events and they could possibly induce an immuno-related form of kidney injury like acute or delayed interstitial nephritis.
Methods
Case report
Results: A 69-year-old woman affected by recurrence of cutaneous melanoma with metastatic disease in the mediastinum and lungs was treated with pembrolizumab from August 2017. After 21 days of treatment the eGFR decreased from 60 ml/min/1.73 m^2 to 40 ml/min/1.73 m^2. After 2 months the eGFR dropped further to 15 ml/min/1.73 m^2 and a renal biopsy was performed. The biopsy showed a severe tubulointerstitial nephritis. After multidisciplinary discussion between oncologists and nephrologists, the patient was treated with corticosteroids but pembrolizumab was not interrupted because of the severity of the metastatic disease without any other effective treatment available. After 2 weeks of steroids, the renal function improved considerably (eGFR from 15 ml/min/1.73 m^2 to 40 ml/min/1.73 m^2) and remained then stable for the next 12 months.
Conclusions: This case highlights that anti-PD-1 immunotherapy can be continued in case of acute interstitial nephritis with adequate steroid treatment. This knowledge could prevent unnecessary discontinuation of an oncologic therapy that could be the last option in many cases. A close interaction between oncologists and nephrologists is essential to manage these cases in order to provide the best care for the patients.

P 52

Acute renal failure in a patient with Rivaroxaban-Induced hypersensitivity syndrome: a case report and review of the literature

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Background: As the use of the new oral anticoagulants (NOACs) increases, the reporting of adverse drug reactions to these new molecules also increases. Still, underreporting is suspected as recent literature recognizes an increased risk of nephropathy induced by anticoagulants. The renal injury induced by the NOACs has been described either as an immune-allergic reaction or as due to tubular obstruction by red blood cell casts (also called anticoagulantrelated nephropathy). A recent meta-analysis also reported that rivaroxaban had a greater risk of creatinine increase in comparison to the other NOACs.
Methods: We report a case of acute kidney failure in a patient with a rivaroxaban-induced hypersensitivity syndrome and we compare it to the other cases reported in the literature of acute renal failure (ARF) associated to rivaroxaban.
Results: Case report: 2–3 days after the prescription of 20 mg/day of rivaroxaban, an 82-year-old female patient began to develop an edema and petechiae of the lower limbs associated to a hepatic dysfunction and acute renal failure (creatinine 215 µmol/l, non-nephrotic proteinuria, leucocyturia and no hematuria). After stopping the medication, these signs and symptoms improved spontaneously and the patient recovered a normal renal function one week later. For this reason a renal biopsy was not performed.
Conclusions: In our review of the literature we found 4 full-published case reports of rivaroxaban-associated nephropathy. However, more cases have been reported in pharmacovigilance registres, for instance the World Health Organisation reported in 2017, 20 cases of tubulointerstitial nephritis. The data of the 4 case reports we found are summarized in table 1. In these cases ARF developed within 2 to 60 days of rivaroxaban therapy and in 2 of them renal function improved with low dose corticotherapy. Therefore, medical doctors should be aware that rivaroxaban can induce ARF. The elderly and those with cardiovascular diseases seem to be the most at risk.

P 53

Plasma angiotensins in hypertensive patients screened for aldosteronism

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Background: Plasma aldosterone (aldo)-to-renin ratio (ARR) is the recommended laboratory parameter to screen for primary aldosteronism in patients with hypertension. Instead of renin, plasma angiotensin (Ang) I and its metabolites may be quantitated by mass spectrometry but their relationship with ARR and other parameters in routine patients is still unclear.
Methods: Ten plasma angiotensins were determined by liquid chromatography-tandem mass-spectrometry (LCMS/MS) supine, and ARR was measured supine and upright in 23 hypertensive patients routinely evaluated for secondary hypertension (44% female). Urinary excretion of Na, K, creatinine (creat) and TH-aldosterone was quantitated in concomitant 24h urine (u) collections. Circulating (native) plasma and equilibrium angiotensin concentrations (conditioned plasma) were measured using LC-MS/MS-based protocols. All medication incompatible with the tests had been stopped beforehand. Pearson's r was calculated (*p <0.01).

Results: ARR was abnormal in 2 patients using guideline cut-off >105 pmol/ng (upright). Circulating plasma Ang concentrations were mostly below detection level. In equilibrium plasma analyis, correlation coefficients for supine Ang II (median 38 pM) with supine Ang I, renin and aldo were r = 0.98*, 0.94*, –0.05; with upright renin and aldo 0.93* and –0.07 and with uTH-aldo and uTH-aldo/ucreat <0.2. Ang metabolites were not significant. Correlation of aldo/Ang II with supine ARR was r = 0.61*. uTH-aldo and uTH-aldo/ucreat correlated strongly with supine (r ≤0.7*) and upright plasma aldo (r >0.7*) but not with ARRs, Ang II or aldo/Ang II (r <0.45, p >0.01). Plasma Na and K and urinary Na/creat or K/creat were not or only weakly correlated the other parameters (r <0.5, p >0.01).
Conclusions: Aldo/Ang II may be a valid and useful alternative to ARR. Future investigations will need to determine the performance of aldo/Ang II compared to ARR for the detection of aldosteronism.

P 54

Rhabdomyolysis-induced acute renal injury following concomitant use of Genvoya® (evg/cobi/etc/taf) and simvastatine: a case report

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Background: Genvoya® (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide) is a single regimen for HIV treatment. Predicting drug interactions is difficult, especially when associated with HMG-CoA reductase inhibitors. We describe a case of severe rhabdomyolysis-induced AKI following treatment with genvoya and simvastatin.
Methods: A 54-year-old man with HIV had been treated with lamivudine, stavudine and indinavir since 1997. He had dyslipidaemia treated with simvastatin for many years. He consulted his primary care physician (PCP) with a 10-day history of asthenia, myalgia and jaundice. Liver enzymes were elevated but kidney function was preserved. He was newly diagnosed with acute hepatitis A and hepatitis C genotype 1a. A second visit to his PCP 6 days later showed improved liver enzymes. As stavudine had been withdrawn from the Swiss market, his HIV therapy was switched to Genvoya® at that time. Ten days later he presented with worsening myalgia, asthenia and oliguria. On evaluation in our emergency department, he had jaundice, hepatomegaly and diminished muscle strength.
Results: Laboratory evaluation revealed elevated creatinine kinase 185190 U/l, creatinine: 553 µmol/l, phosphate: 3.03 mmol/l, potassium: 7.2 mmol/l, ASAT: 7017 U/l, ALAT: 2881 U/l, GGT: 198 U/l, and total bilirubin: 130 µmol/l. Arterial blood gas showed primary metabolic acidosis with a positive anion gap and appropriate respiratory compensation. Abdominal ultrasound revealed homogeneous hepatomegaly without biliary or urinary tract obstruction. A diagnosis of severe rhabdomyolysis-induced AKI was made. Antiretroviral and lipid lowering therapy were discontinued. He was initially treated with intravenous fluids . Because of refractory hyperkalaemia with ECG changes, he was initiated on haemodialysis in a tertiary care setting. The cobicistat-simvastatin combination played pivotal role in causing rhabdomyolysis since cobicistat increases plasma concentration of simvastatin by P450 cytochrome inhibition.
Conclusions: This case reveals the complexity in treating HIV-positive patients who are at risk for potential drug interactions. Heightened vigilance is essential and multidisciplinary collaboration is advised.

P 55

Evaluation of sFlt-1/PlGF Ratio for predicting and Improving clinical management of pre-eclampsia in lupus nephritis: a single case experience in CHUV

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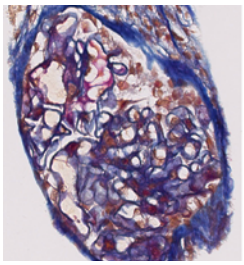
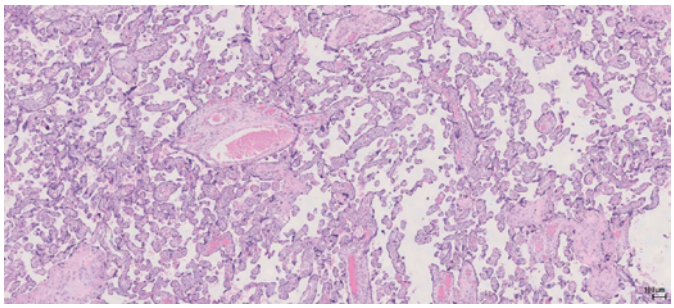
Background: Tyrosine kinase/placental growth factor ratio (sFlt-1:PlGF) >38 is highly predictive for pre-eclampsia, its application for lupus nephritis is uncertain.
Methods: A 37-year-old women developed a nephrotic syndrome at the 14th week of gestation. Biopsy showed a class V lupus nephritis. Evolution was favorable under antihypertensive agents, Tacrolimus and Corticosteroids. At 24 weeks of gestation, the patient developed edemas, hypertension and weight gain of 3 kg in 2 weeks. Laboratory: creatinine 122 umol/l, albumin 25 g/l, proteins 56 g/l, C3 1.16 g/l, C4 0.26 g/l, anti-dsDNA 155 U/ml, anticardiolipin antibodies negative, Flt-1:PlGF ratio 27. The evolution was rapidly worsening with increasing hypertension (TA 200/95 mmHg), AKI (creatinine 243 umol/l), oligo-anuria, thrombocytopenia without schistocytes (PLT 65 g/l), proteinuria 11 g/d. A caesarean was performed in emergency at 25 weeks of gestation. The Placenta's microscopic analysis has not highlighted of vascular lesions specific for LN or MAT. The evolution was quickly favorable except for severe and prolonged hypertension.
Results: Several hypotheses could be discussed: – Evolution towards a diffuse lupus nephritis: low probability with a normal complement/dsDNA value and the favorable clinical course after placental delivery; – primary or secondary MAT (tacrolimus): unlikely because of normal haptoglobine levels and the absence of schistocytes even if tacrolimus-endothelial toxicity may have contributed to hypertension; – Hypertension and fluid-retention secondary to nephrotic syndrome Pre-eclampsia could remain the first hypothesis despite a sFlt-1:PlGF ratio <38.
Conclusions: In complex situations, determination of risk of pre-eclampsia by sFlt-1:PlGF ratio remains to be validated and requires further studies.





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Devastating cefepime-induced nephrotoxicity

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Background: We present the unique case of direct Cefepime-induced tubular toxicity.
Methods: We report a case of Cefepime-induced nephrotoxicity based on clinical findings, laboratory data and kidney biopsy.
Results: A 75-year-old woman was admitted to the emergency room because of severe shortness of breath and impaired consciousness. She was intubated and antiepileptic drugs were administered intravenously after tonic-clonic seizure. Twenty days before this admission, antibiotic treatment with Cefepime was prescribed because of a foreign body associated infection due to Enterobacter cloacae following osteosynthesis of a femoral neck fracture. On admission, the creatinine level was 517 µmol/l, and eosinophilia was present. Given the recent exposure to antibiotics, a diagnosis of acute allergic interstitial nephritis was made and, immunosuppressive therapy with systemic steroids was started. Furthermore, Cefepime-induced neurotoxicity was confirmed by very high Cefepime plasma levels (160 mg/l). Daily hemodialysis was installed with rapid decline in Cefepime plasma levels and neurologic improvement. Kidney biopsy showed acute tubular injury with minimal interstitial infiltration of inflammatory cells. Since no acute interstitial nephritis was diagnosed, treatment with steroids was stopped.

Conclusions: So far, neurological toxicity induced by Cefepime is well known. However, with the exception of Cefepimeinduced nephrotoxicity reported in rats, this is the second case report describing Cefepime-induced nephrotoxicity in humans. Awareness of this newly recognized side effect should prompt physicians to perform kidney biopsy in a timely manner.

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A case of crystal nephropathy after amoxicillin administration

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Background: Amoxicillin is a widely used antibiotic. We report a case of Amoxicillin-induced crystal nephropathy (AICN).
Methods: A 75-year-old patient was hospitalized because of left ventricular assist device thrombosis. The patient was known for a dilatative cardiomyopathy, a vascular and cardiorenal chronic renal failure G3b and a gout. His medication included phenprocoumon, acetylsalicylic acid, esomeprazole, amiodarone, bisoprolol, ramipril, tamsulosin, allopurinol and colchicine. The thrombosis was successfully treated with alteplase. On the 10th day of hospitalization a urinary tract infection from Enterococcus faecalis was diagnosed and he was treated with piperacillin/tazobactam (day 10–12) followed by Amoxicillin 2 g four times daily (after day 12). On day 16 there was an increase of the serum creatinine from 150–160 µmol/l to 199 µmol/l and on day 18 he developed anuria. The patient was 7 kg above his ideal weight without respiratory distress. His blood tests revealed a creatinine of 446 µmol/l, a metabolic acidosis (bicarbonate 15mmol/l), a hyperkalemia (potassium 5.8 mmol/l) and a hyponatremia (sodium 120 mmol/l). A postrenal cause or perfusion deficit were ruled out by sonographic imaging. The urinary sediment microscopy confirmed a nonglomerular microhematuria with needle-shaped crystals indicating an AICN. Amoxicillin was immediately stopped. Fluids were administered restrictively. The patient developed diuresis within the next days, the electrolyte changes and kidney function gradually returned to baseline.
Results: AICN is characterized by a sudden oliguria and nonglomerular haematuria in patients under high dose amoxicillin. Risk factors include high dose of amoxicillin, preexisting renal failure, low urinary pH and low urinary output. Diagnosis relies in urine sediment microscopy which shows needle-shaped birefringent crystals. Stopping the offending agent leads frequently to a recovery of the renal function.
Conclusions: In patients under high dose amoxicillin who develop abrupt oliguria and hematuria, an amoxicillin induced crystal nephropathy needs to be ruled out.

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Angioplasty with stenting in acute coronary syndromes with very low contrast volume (<30 ml) using 6F Cordis diagnostic catheters and improved cardiovascular and renal outcomes

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Background: To safely perform angioplasties in acute coronary syndromes with low contrast volume using 6F Cordis diagnostic catheters. Contrast-induced nephropathy is a common clinical problem, and it could be prevented by using low contrast volume.
Methods: In 574 patients (687 lesions/ 746 stents) with acute coronary syndromes angioplasty was performed with Cordis 6F diagnostic catheters. Primary angioplasty was performed in 151 cases. In 74% of cases, Iodixanol was used. All contrast injections were given by hand. Regular follow-up of the patients was performed at 30 days. The procedures were performed through femoral route only. Tirofiban was used in 99% of cases with adjusted dosages based on the creatinine values. Pre-dilatation with balloons was performed in 181 cases. The mean contrast volume used per patient was 28 ml (±7 ml). 30 patients had creatinine more than 2 mg/dl before the procedures. 23 patients had cardiogenic shock at presentation. 78% of the cases had diabetes. A variety of coronary stents from various companies were used in the procedures. Buddy wires were used in 16 cases.
Results: Mild reversible contrast-induced nephropathy was observed in three patients. One another patient with creatinine 5.6 mg/dl at presentation developed acute renal failure, and he was started on regular hemodialysis. After 1 m, he was started on medical management only. Five mortality was observed in this series, and of these five patients four had cardiogenic shock, and one patient expired one week after discharge due to possible acute stent thrombosis. Mild cardiac failures were seen in 14 cases which were treated with diuretics injections/infusions. Two patients required the ventilator for congestive heart failure therapy.
Conclusions: Angioplasty and stenting could be performed safely in patients with acute coronary syndromes using Cordis diagnostic catheters using a low volume of contrast. Low contrast volume usage would result in lower incidence of contrast-induced nephropathy and cardiac failures.

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Prevalence of cardio renal risk factors in population-baseline data of a selected rural community in Bangladesh (BAN Ca-Re study)

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Background: The incidence of hypertension, diabetes and kidney disease is increasing affecting mostly developing countries. There are almost no systematic data investigating simultaneously the prevalence of these cardio renal risk factors in rural population of Bangladesh.
Methods: In this survey a rural area with defined geographical boundary (a union) was selected. Listing of all households in the selected union and the number of residing duelers were listed. For participant selection and sample collection field enumerators, visitors (FV), attendants, local and central coordinator (CO) were recruited and trained. Baseline data of all were collected by a short questionnaire via face-to-face interview. The ultimate sampling units are randomly selected one adult individual residing within the selected household. This study is being conducted by a multi specialty-national kidney disease research group (KDRG).
Results: In 22354 subjects 14091 were adults with 48:52 ratios of male and female. Age was between 18–24 (21%), 25–54 (61%), 55–64 (10%) and >65 yrs (8%). Among them 26% were tobacco user and 88% took added salt with food. Diagnosed cases of HTN was 10%, DM 6%, IHD 4%, CVA 2% and nephropathy in 1% subjects. Comparison between male and female showed female were over all less educated and under employed (P <0.001); less smoker (25% vs., 1%, p <0.001) but more oral tobacco user (10% vs. 14%. P <0.001); more hypertensive (8% vs. 12%, p <0.001) and more diabetic (5% vs. 7%, p <0.001).
Conclusions: Cardio-renal behavioral risk factors like tobacco use and extra dietary salt intake is alarmingly high in rural population. The diagnosed disease burden of diabetes and hypertension indicates a much higher percentage of undetected proportion that needs to be investigated urgently. Women are more affected probably due to their lower education and economic status.

P 60

Outpatient post-dialysis Daptomycin prescription in an anephric hemodialysis (HD) patient: how much?

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Background: In chronic HD patients, post-dialysis intravenous Daptomycin allows to manage severe infections on an outpatient basis. This lipopetide antibiotic has bactericidal activity against Gram positive organisms and can be used for Staphylococcus Aureus (SA) bacteremias or complicated soft tissues infections. Its elimination is mainly renal. It can be prescribed post-dialysis thrice-weekly, but contradictory data are reported concerning the dose adjustment in HD patients.
Methods: We report the data of therapeutic drug monitoring (TDM) in a anephric HD patient treated with post-dialysis daptomycin.
Results: A 37-years anephric HD patient developed a severe SA bacteremia after a 2 weeks holidays. A vascular access infection was suspected without signs of endocarditis. After 2 weeks of in-hospital flucloxacilline, she received post-dialysis daptomycin thrice-weekly for 4 further weeks as outpatient. The initial doses ranged from 9 to 12 mg/kg and resulted in very high pre-dialysis daptomycin concentrations, associated with a 6-folds increase of CK. The post-dialysis dose was progressively diminished according to the TDM approach, down to 4 mg/kg. Even after a 72 hours interval this dose resulted in pre-dialysis serum concentrations higher than the recommended therapeutic range of 12–20 mg/l. During a 4-hour high-flux HD (with a BF of 300 ml/min) the daptomycin concentrations decreased by 50%.
Conclusions: For HD, the recommended post-dialysis Daptomycin doses range from 4 to 9 mg/kg every 48 or 72 hours. However most studies did not consider the potential role of the residual renal function, when present. In our anephric patient, even the doses in the lower recommended range resulted in pre-dialysis concentrations higher than the therapeutic range and even above the toxicity limit of >24.3 mg/l. In conclusion our data suggest that in patients with no residual renal function the post-dialysis doses of daptomycin should be lower than the ones presently recommended.

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Creation of the Renal Access Dialysis Registry (RADY): difficulties and initial results

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Background: In 2016, our vascular access (VA) survey showed that 73% of patients of the four teaching hospitals of Ticino started hemodialysis with a central venous catheter (CVC). 13% of these patients were late referral, while 14% had unsuitable surgical condition for a functioning arteriovenous fistula (AVF). CVC-starting patients had an increased risk of surgical intervention to maintain VA-patency compared to AVF-starting patients (1 intervention every 8.2 vs 1 every 14.4 month/patient). These data, far from the international guidelines recommendations, highlighted the need of a registry to analyze data in real-time and to detect inadequate outcomes.
Methods: The Renal Access Dialysis Registry (RADY) was developed between 1.1.2018 and 30.6.2018. All fields related to patient's characteristics and VA-history data were selected according to international definitions. RADY compilation started on 01.08.18, data derived from the Vascular Surgery Registry (Swissvasc) and from the Swiss Renal Registry (SRRQAP) were completed by autofill-mode.
Results: We collected data from 247 incident patients on dialysis from 1.1.2013 to 31.12.2017. The autofill-mode completed 40/61 fields (73% of the compulsory ones) for each patient. All the fields were completely filled for 66 patients (26.7%). In 73.3% of the patients, at least one of the VA-related data could not be collected or properly defined. The main difficulties we encountered in completing the RADY were related to missing, incomplete or wrong VA-procedure description, incomplete patients data, unclear complications or treatments.
Conclusions: The RADY is an innovative, usefull and user-friendly tool. In the future, the number of data available with autofill-mode will increase thanks to registers crosstalk improvement. Moreover, the most urgent challenge is to unify clinical practice and definitions to the international standards in order to significantly decrease human intervention to complete the RADY. In our opinion, this goal is achievable only by creating discussion groups and active cooperation between healthcare professionals.

P 62

T50 and fetuin modification by dialysis initiation

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Background: Cardiovascular events are observed in the first three months of dialysis initiation. The net effect of HD or PD initiation on the serum propensity to inhibit calcification, on fetuin level and pulse wave velocity (PWV) remain unknown.
Methods: We measured the evolution of the T50 test and of its main determinants including fetuin as well as arterial rigidity by pulse wave velocity (PWV) before dialysis initiation and monthly during three months in Hemodialysis (HD) or peritoneal dialysis (PD) in Geneva and Lausanne.
Results: 58 patients were included. 46 initiated HD and 12 PD. Among the 58 patients, there were 45 men (77.6%); median age was 67 years (25th–75th: 54–77). Most patients were caucasians (n = 40, 70.2%) and suffered from hypertension (n = 51, 87.9%), 28 had diabetes (48.3%) and 17 known ischemic cardiopathy (29.3%) at baseline. During the 3 months after dialysis initiation 2 patients died, 2 stopped dialysis, 3 moved away and 1 was transplanted, leaving 38 HD patients with a complete follow-up. Among those, 3 patients developed acute cardiovascular events. There were no dialysis modality change. When analyzing all patients , T50 significantly increased between M0 (before dialysis initation) and M3 (3 months after dialysis initiation) from 183 (120–266) to 245.5 (175–330) minutes, p <0.001. Fetuin increased between M0 and M3 (p <0.001). Phosphate, Magnesium and calcium also changed but not albumin or bicarbonates. Taking into account the time, factors associated with change in T50 were changes in fetuin, phosphate and magnesium (p <0.001). Calcium, albumin and CRP were not associated. Fetuin changes were associated with inflammation related factors (albumin, crp) but not to phosphocalcic parameters. Arterial stiffness, as assessed by pulse wave velocity, was not significantly modified between M0 and M3.
Conclusions: T50 and fetuin are modified by dialysis initiation. A low t50 and fetuin may argue for dialysis initiation in some patients.

P 63

The performance of saliva uric acid reduction ratio as a measure of dialysis efficiency in maintenance hemodialysis

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Background: Current methods of assessing dialysis efficiency require monthly laboratory blood assays. This may be challenging in low-income economies where medical care is hugely self-funded. Furthermore blood sampling may worsen renal anemia in a context of limited access to erythropoietin. Cheaper and safer alternatives are therefore needed.We aimed to evaluate the performance of saliva uric acid reduction ratio as a measure of dialysis adequacy in patients undergoing maintenance hemodialysis.
Methods: We conducted a cross-sectional study in patients on maintenance hemodialysis at the Yaounde General Hospital, Cameroon. We included stable patients who could provide unstimulated saliva.Patients with inflammatory oral pathologies were excluded. After at least a 15 minutes fast, 2 ml of unstimulated saliva and 2 ml of blood were collected simultaneously before and after the second dialysis session of the week for saliva uric acid, serum creatinine, blood urea and uric acid assays. Saliva uric acid was determined semi-quantitatively using saliva uric acid dipsticks (SAUA strips, IBT Inc, USA). Urea reduction ratio (URR), blood uric acid

reduction ratio (BUARR) and saliva uric acid reduction ratio (SUARR) were calculated from pre and post dialysis values. Efficient dialysis was defined as a blood URR >60%.
Results: We included a total of 70 patients (58% males), with a median (25th–75th percentile) age of 51(38-60.25) years. The median reduction ratio(table 1) for URR was 66.05% and 46(66%)of 70 participants met criteria for efficient dialysis. The BAURR was 73.85%, SAURR: 69.6%. Correlation between blood UARR and SUARR (r = 0.444, p <0.001). The diagnostic performance of SUARR in identifying efficient HD sessions was good (AUC (CI 95%): 0.713, sensitivity = 66.7%, specificity = 64.0%, p= 0.003, cut-off = 55%).
Conclusions: Saliva uric acid reduction ratio maybe a cheap, simple and safe alternative to blood-based assays in assessing HD efficiency. More studies are required to validate the tool.

Table 1: Laboratory parameters of study participants N= 70

Variables	Pre-dialysis	Post-dialysis	P-value	Reduction ratio
Serum creatinine (mg/dl)	13.8(9.5-16)	3.9(2-6.2)	<0.001	66.05(57.73-77.88)
Blood uric acid (mg/dl)	7.5(6.2-8.4)	1.8(1-2.6)	<0.001	73.85(64.6-82.73)
Blood urea(mg/dl)	155(119.5-196.8)	44(19-713)	<0.001	69.6(60.65-80.6)
Saliva uric acid (mg/dl)	2(1-5)	1(0.5-1)	<0.001	60(50-75)
Saliva pH	6.8(6.4-7.2)	6.4(4-6.4)	0.007	6.25(5.56-35.04)

P 64

A retrospective case series of vascular graft materials for hemodialysis

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Background: Grafts, which allow early cannulation have been increasingly used to avoid starting dialysis via tunneled hemodialysis catheters. As we noted failures in patients with early cannulation grafts, we reviewed the outcome in a case series and compared it to ePTFE vascular grafts.
Methods: We retrospectively analyzed time to first intervention, primary and secondary patency rates as well as the number of interventions needed to maintain patency in patients who received an early cannulation graft (GORE® ACUSEAL, acuseal) or an ePTFE (GORE-TEX®) vascular graft between January 2016 and November 2017 in our medical center.
Results: 13 patients who had received an acuseal vascular graft were compared with the same number of patients with an ePTFE vascular graft. The mean time to first intervention was similar in both groups (141 days in the acuseal and 131 days in the ePTFE group). On average 0.45 interventions per graft were needed per month to maintain patency in the acuseal group, and 0.08 in the ePTFE group (p = 0.011). The primary patency rate did not differ significantly between the groups. The secondary patency rate at the end of the observation period was significantly worse in the acuseal group. Four grafts were lost after a mean of 202 days, whereas none of the ePTFE grafts was lost.
Conclusions: Our data are consistent with our clinical impression of an increased number of interventions and lower longevity of the acuseal vascular graft. These data need conformation in a larger cohort.

P 65

The role of intraoperative continuous renal replacement therapy in severe acidosis – a single center experience

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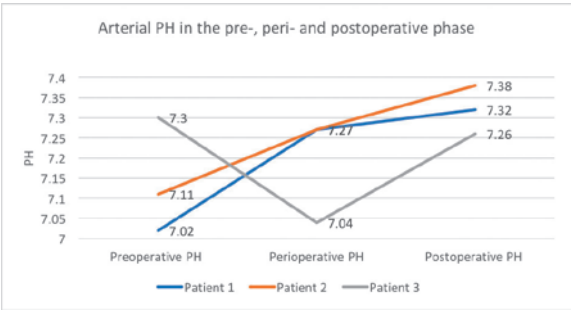
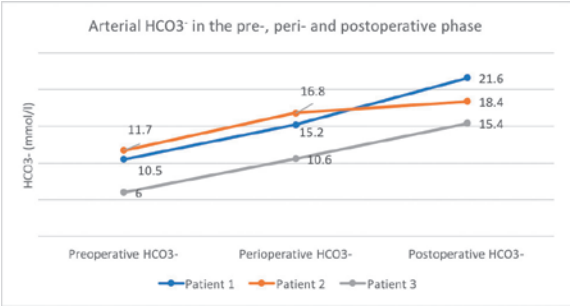
Background: Patients on continuous renal replacement therapy (CRRT) with severe metabolic or electrolytic disorders requiring surgery may benefit from intraoperative continuation of treatment. While there is growing body of evidence about intraoperative CRRT in patients undergoing liver transplantation, there are very few data on which other patients may benefit from this treatment.
Methods: We performed a retrospective review of patients receiving intraoperative CRRT at the intensive care unit of the Ospedale Regionale di Lugano between January 1, 2013 and June 31, 2018.
Results: During the observation period of 4.5 years, of the 166 patients supported with CRRT, 97 (58.4%) underwent surgery and three (1.8%) received intraoperative CRRT. Demographics, baseline characteristics, laboratory parameters before CRRT, intraoperative details and technical data of intraoperative CRRT are shown in table 1.

Demographics, baseline characteristics and laboratory parameters before CRRT start	Patient 1	Patient 2	Patient 3
Age (y)	42	76	78
Sex	m	f	f
Comorbidities			
Diabetes mellitus	yes	no	yes
Coronary heart disease	no	yes	yes
Chronic kidney disease	no	yes	no
Liver cirrhosis	yes	no	no
SAPS II score	24	70	51
S creatinine (mcmol/l)	120	237	105
S urea (mmol/l)	5.8	18.3	13.7
eGFRmml/min/1.73m2 (MDRD)	58	18	44
S potassium (mmol/l)	4.4.	5.3	4.4.
Vasoactive agents	yes	yes	yes
Mechanical ventilation	no	yes	yes
Bicarbonate therapy	no	yes	yes
Intraoperative details			
Surgical time (min)	120	100	120
Summary of CRRT characteristics			
RRT type	CVVHD	CVVHD	CVVHDF
Blood flow (ml/min)	180	110	150
RRT time before surgery (min)	320	975	60
Total RRT time (min)	2860	3420	1900
Number of filters	1	1	1
Anticoagulation	citrate	citrate	heparine
Net delivered dose (ml/h)	3600	2000	4000

Pre-, peri- and postoperative arterial pH- and HCO3--values are reported in Figures 1 and 2. Patient 1 was affected by septic shock due to mesenteric ischemia and underwent ileal resection. Patient 2 had a septic shock with multi organ failure (MOF) secondary to necrotizing fasciitis of the arm, which was treated sequentially with fasciectomy, disarticulation and resection of the clavicula, scapula and shoulder muscles. Patient 3 was affected by MOF secondary to acute ischemia of the limbs. She underwent embolectomy and fasciotomy. In patient 1 and 3, CRRT was started because of severe lactic acidosis, whereas in patient 2, the indication was oliguric renal failure with hyperchloremic metabolic acidosis. Patient 1 survived and renal function was normal at five years. Unfortunately, both patients 2 and 3 died two days after surgery.
Conclusions: In our cohort, intraoperative CRRT was feasible, although requiring complex organization. It was used in a small number of severe ill patients to stabilize the metabolic situation. Mortality was very high in this small subgroup of patients.





P 66

Survival on dialysis: Switzerland in comparison with other countries

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Background: Survival in dialysis patients is highly diminished compared to the general population. However, some evidence suggests that mortality rates among incident dialysis patients have decreased over the last few years. With the present analysis, we would like to compare the survival of Swiss dialysis patients with other countries.
Methods: Incident dialysis patients (hemo- or peritoneal dialysis; N = 3567) from the Swiss dialysis registry were followed up from 2014 on until December 31, 2017 (mean follow up days = 591). Deaths occurring during this time (N = 670) were recorded and survival was examined using the Kaplan Meier method, with transplantation as censored observation. To categorize the causes of death, all deaths between 2013 and 2017 were analyzed.
Results: Characteristics of the dialysis population stratified according to survival status are provided in Table 1. Dialysis patients in Switzerland have an 8% and 14% higher survival in the first and second year, respectively, compared to other European countries (Annual ERA-EDTA Report 2015). The main cause of death is cardiac arrest / sudden death with 12.6%, followed by patient refusing further dialysis with 10.2% and unknown cause of death with 9.7%. Our hemodialysis patients aged from 45 to 74.9 years die in 30% due to cardiovascular disease, compared to 42% in other European countries (DOPPS). Also, in the oldest age group (≥75 years), there is a difference of 10% in favor of Switzerland versus other countries. One of five patients in Switzerland aged older than 75 years is dying because dialysis was stopped, compared to only 3.5% in other European countries.

Characteristics (given as mean±SD or percentage) in incident dialysis patient according to their diabetic status

	Non-Survivors, n= 671	Survivors, n= 2898	p-value
Age, years	73.4 ± 12.4	64.7 ± 16.1	0.000
Male gender, %	66.5	65.1	0.506
Body mass index, kg/m²	24.8 ± 6.1	28.1 ± 5.6	0.294
Dialysis vintage, days	495 ± 343	1460 ± 613	0.000
Dialysis duration per week (h)	11.2 ± 1.5	11.5 ± 1.4	0.000
Kt/V	1.49 ± 0.41	1.64 ± 0.48	0.000
Hemoglobin, g/dL	10.5 ± 1.8	11.2 ± 1.4	0.000
Ferritin, ng/mL	560 ± 666	438 ± 371	0.000
Calcium, mmol/L	2.22 ± 0.22	2.21 ± 0.19	0.001
Phosphat, mmol/L	1.52 ± 0.49	1.61 ± 0.47	0.009
PTH, ng/L	295 ± 360	364 ± 294	0.292
Iron substitution, %	73.1	76.5	0.102
EPO substitution, %	81.2	81.7	0.782
Comorbidities, n	3.5 ± 2.1	2.2 ± 1.9	0.000
CCI*	6.0 ± 2.7	4.1 ± 2.1	0.000

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

		1 year	2 year	3 year
0-19 yrs	(N=36)	94.4	94.4	94.4
20-44 yrs	(N=326)	97.9	95.1	94.8
45-64 yrs	(N=1036)	93.9	90.9	89.7
65-74 yrs	(N=973)	91.8	84.8	81.2
75+ yrs	(N=1198)	88.8	79.5	73.8
Men	(N=2333)	91.9	85.5	82.2
Women	(N=1236)	92.1	86.5	83.2
Diabetes	(N=712)	92.6	85.5	82.7
Renal vascular disease	(N=790)	91.4	82.8	79.7
Glomerulonephritis	(N=541)	95.2	93.3	90.6
Other causes	(N=1528)	90.9	84.9	81.1
All	(N=3589)	92.0	85.8	82.5

Conclusions: Swiss dialysis patients have a markedly better survival than dialysis patients in other European countries. Also, causes of death vary widely among European countries.

P 67

Zinc serum concentration in hemodialysis patients with and without zinc supplementation

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Background: Currently literature data points towards a zinc deficiency among dialysis patients. Zinc is an essential trace element required for a plethora of biological processes. Among our patients, some receive a postdialysis zinc supplementation as a standard chronic wounds treatment. The aim of our study was to measure zinc concentration in all our patients, in order to: a) evaluate if there is a difference in serum concentrations between naïve and supplemented patients and b) investigate whether there is an association between zinc concentrations and other clinical or biological parameters.
Methods: Predialysis zinc levels were measured by atomic absorption spectroscopy in fifty-one patients (mean age 65 ± 12 years). Among them 10 (19.6%) received zinc supplement thrice-weekly (50mg zinc, given as 220 mg zinc sulfate). Zinc concentrations were compared between those with and without supplementation. We completed patient assessment by statistical analysis correlating zinc concentrations to other biological parameters.
Results: Results are summarized in table 1. Mean serum zinc concentration is 13.8 ± 2.3 µmol/l and is significantly higher in patients receiving zinc supplementation (15.5 ± 2.7 vs 13.4 ± 2.1 µmol/l, p <0.05). Only 1 patient (1.9%) had zinc levels lower than normal and 3 slightly higher (5.9%, 1 supplemented). We found no association between serum zinc concentrations and the other biological parameters considered, except a significant direct positive correlation between zinc levels and responsiveness to EPO treatment.

Parameter	Range	Total N=51	No supplement N=41 (80.4%)	With supplement N=10 (19.6%)
Age	years	64.7 ±12.0	64.4±12.8	66.4±7.9
Sex	Female/male	F:23 (45%) M:28 (55%)	F:20 (49%) M:21 (51%)	F:3 (30%) M:7 (70%)
Diabetes	n (%)	20 (39%)	16 (39%)	4 (40%)
Zinc	9.2-18.4 µmol/l	13.8 ±2.3	13.4 ±2.1	15.5±2.7*
- zinc < 9.2 µmol/l	n	1	1	0
- zinc >18.4 µmol/l	n	3	2	1
Albumin	37-51 g/l	39.2±4.9	39.1±5.2	39.6±3.3
Transferrin sat.	15-50%	27.6±12	28.7±12.9	23.2±6.2
Ferritin	30-300 µg/l	616.6±725.4	614.1 ±809.4	626.9±107
Vitamin D	>75 nmol/l	77.0±29.3	77.6 ±28.3	74.6±34.8
PTH	15-65 ng/l	250±201	245±184	268±269
Weekly EPO	U/week	8216±7344	8171±7116	8400±8631

*p<0.05, compared with no supplemented patients.

Conclusions: In contrast to the data of the literature suggesting low zinc levels in HD patients, almost all our patients (98%) have zinc sufficiency. A supplement of 3 weekly postdialysis oral doses of 50 mg of zinc-element was well tolerated and was associated with significantly higher zinc levels, without clinical sign of toxicity. We also find that zinc is a good biomarker candidate to predict EPO responsiveness. If zinc supplementation can improve EPO responsiveness remains open and a randomized study is required.

P 68

Survival in Swiss diabetic patients on dialysis: a follow-up

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Background: Unlike for many other countries, who have found diabetes to be a clear mortality risk factor in dialysis patients, this was not observed for Switzerland. To the contrary, diabetics in our country showed a tendency to slightly better survival, at least in the first two years after initiation of dialysis therapy. The aim of the present analysis was to further analyze these surprising results with an additional year of follow-up and a higher number of patients.
Methods: Incident dialysis patients (HD or PD; N = 3567) from the Swiss dialysis registry were followed-up from 2014 on until December 31, 2017 (mean follow-up days = 591). Deaths occurred during this time (N = 670) were recorded and mortality risk was assessed with Cox-proportional hazard models. Patients were stratified according to their status regarding systemic diabetes mellitus, both type 1 and 2, regardless of renal involvement with diabetic nephropathy.
Results: Characteristics of the dialysis population are provided in table 1. Cox regression analyses were adjusted for age, gender, BMI and coronary artery disease. Unlike the analyses performed with a

Characteristics (given as mean±SD or percentage) in incident dialysis patient according to their diabetic status

	With diabetes, n=1328	Without diabetes, n=2239	p-value
Age, years	69.9 ± 12.1	64.4 ± 17.4	0.000
Male gender, %	68.6	63.5	0.002
Body mass index, kg/m²	27.9 ± 6.0	25.0 ± 5.3	0.000
Dialysis vintage, days	618 ± 398	575 ± 398	0.959
Hemoglobin, g/dL	11.1 ± 1.5	11.0 ± 1.6	0.044
PTH, ng/L	336 ± 279	366 ± 319	0.000
Kt/V	1.5 ± 0.4	1.7 ± 0.5	0.000
CCI*	4.0 ± 2.0	3.7 ± 2.2	0.020

shorter follow up and less patients, no difference regarding survival in the first year after dialysis start can be shown. However, in the second and the third year after dialysis start, diabetic patients have an about 30% higher mortality risk (p = 0.004, respectively p = 0.005) than non-diabetic patients.
Conclusions: The slightly better survival shortly after initiation of dialysis therapy from our last year's analyses with diabetics was not sustained with longer follow-up analyzing a higher number of events. Again, we assume that patients with diabetes initiate dialysis therapy earlier, and, thus, no difference in survival can be shown in the first year after dialysis start compared to patients without diabetes. However, from the second year on, our results are in line with those of other countries with diabetic patients having a higher mortality risk.

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Effectiveness of thoracoscopy in treating pleural effusion in peritoneal dialysis

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Background: Incidence of pleural effusion due to pleuroperitoneal leak ranges from 1.6–10% in continuous ambulatory peritoneal dialysis (CAPD) patients. Its development is due to either congenital (more frequent in young females) or acquired diaphragmatic defects and is most frequently right–sided. It is often considered as an incurable complication and constitutes a major cause of PD drop-out and permanent transfer to haemodialysis.
Methods: We describe here the case of a 75-year-old women who was started on CAPD in June 2015. In April 2016 she presented with dyspnoea and shortness of breath. Right-sided hydrothorax was diagnosed and thoracentesis performed. Subsequent fluid analysis demonstrated a high pleural fluid-to-serum glucose gradient, highly suggestive of pleuroperitoneal leak. CAPD was temporarily interrupted (without need for interim haemodialysis thanks to good residual renal function) then resumed four weeks later with low-volume exchanges that were progressively increased. Two months later, right-sided hydrothorax recurred. As she firmly refused a permanent transfer to haemodialysis, we decided to perform a video-assisted thoracoscopy.
Results: No macroscopic diaphragmatic defect could be identified (fig. 1) and talc pleurodesis was performed (fig. 2) without surgical complications but with significant pain with breathing in the postoperative phase. After four weeks cessation, low-volume then full-volume CAPD was reinstated. The patient suffered in the next two years no recurrence and is up to now still on CAPD and most satisfied with her therapy.
Conclusions: Management of pleuroperitoneal effusion is still challenging in CAPD patients. First-line treatment remains temporary CAPD interruption for 2–6 weeks then retrial with low-volumes. Upon recurrence, our case report demonstrates effectiveness of thoracoscopy with talc pleurodesis. Before considering permanent transfer to haemodialysis, it could therefore be proposed as a therapeutic option to highly motivated patients with thorough information about risk of recurrence as well as pain in the postoperative period.

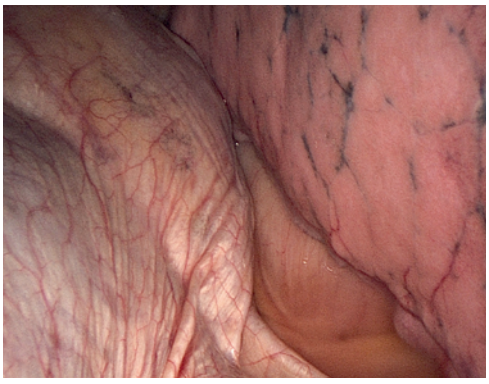

Figure 1

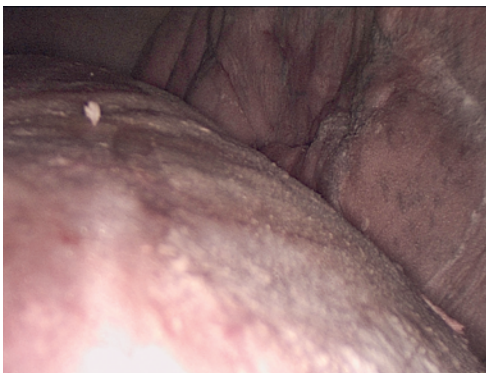

Figure 2

P 70

The Effects of regular physical exercise on nutrition and inflammation in patients on maintenance haemodialysis in Cameroon. A non-randomized single-arm clinical trial

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Background: Intra-dialytic physical exercises are associated with better patient outcomes. However most studies have involved the dialysis population in high-income countries which is much older than that in low-income countries. We aimed in this study to determine the effects of an 8 week regular physical exercise programme on nutrition and inflammation in patients on maintenance haemodialysis (MHD) in Cameroon
Methods: We conducted a non-randomised single-arm clinical trial from November 2017 to May 2018, involving physically inactive patients on MHD at the Yaounde General Hospital. Patients with acute illnesses, known cardiac disorders and physical disabilities were excluded. Patients were subjected to 8 weeks of aerobic cycling on stationary ergometers for 30mins before each HD session and prescribed 30 minutes of moderate-intensity exercise on non-dialysis days. Our primary outcomes were: a ≥2 g/L increase in serum albumin(SAlb) and a ≥50% decrease in high sensitive-CRP (hs-CRP) and the secondary outcomes were: improvement in physical function, muscle strength, health-related quality of life (HRQoL) and tolerance to physical exercise. Data was analysed using an intention-to-treat analysis.
Results: A total of 17 physically inactive participants were enrolled. Their mean age was 47 ± 14.85 years, and comorbid conditions, vital parameters and use of erythropoietin and L-carnitine did not vary

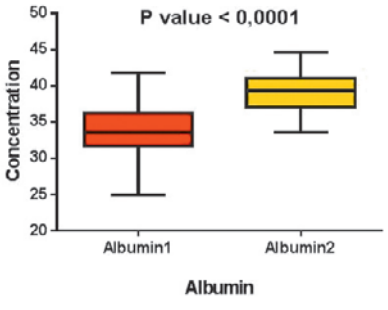

Figure 1: Evolution of serum albumin of patients on maintenance haemodialysis after 8 weeks of physical exercise, (N=17).

Table 1 physical function: Change in Physical function and Muscle Strength after 8 weeks of physical exercise in patients on maintenance hemodialysis (N=17)

Variable	Baseline N=17	After 8 weeks N=17	P value
30sec sit-to-stand test*	8.59 ±1.87	9.71 ±2.76	**0.006**
Muscle strength** (kg)	24.1 (20.65-33.45)	24.7 (21.5-32.6)	0.25

*mean ±SD, **median, IQR

Table 2: Change in health-related quality of life after 8 weeks of regular physical exercise (N=17)

Variable	Baseline N=17	After 8 weeks N=17	P value
Physical health			
Physical role	53.12 ±14.90	54,82 ±17.16	0.4028
Physical functioning	38.71 ±8.68	41,29 ±9.033	0.2
Body pains	61.79 ±11.91	64.68 ±13.67	0.31
Mental health			
General health	50.47 ±14.15	58.76 ±14.53	**0.0026**
Vitality	35.59 ±7.977	42.88 ±9.219	**0.0005**
Emotional role	52.65 ±20.38	58.29 ±18.69	0.25
Social function	51.85 ±17.23	53.65 ±17.23	0.375
Emotional well being	43.03 ±6.874	46.04 ±7.126	**0.0057**

during the study. The overall compliance to our intervention was good. Serum albumin (fig. 1)significantly increased (39 ± 2.97 g/l vs. 33.7 ± 4.12; p <0.0001), and a non-significant decrease in hs-CRP level. A total of 11 participants experienced a ≥2 g/l increase in SAlb, and 7 participants a ≥50% decrease in serum hs-CRP. There was a significant increase in physical function, muscle strength (table 1) and (table 2) HRQoL scores. No dropouts were recorded.
Conclusions: Our results confirm the beneficial effects of physical exercise in this patient population.

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End Stage Renal Disease in pediatric and adolescent population in a southern area of algeria

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Background: In Algeria, the number of children reaching ESRD increases annually. Epidemiological studies of the pediatric ESRD in Algeria are few, there is no operable national register. The objectives of this study are to determinate the epidemiological characteristics of dialyzed children.
Methods: We included all patients under the age of 19 years at the time of the ESRD, living in Ghardaïa, treated at least 03 months by hemodialysis (HD) or peritoneal dialysis (DP) during the period between 01/01/2005 to 12/31/2017. Information was collected from the medical files, interrogation of patients and their parents.
Results: Thirty (30) children under the age of 19 years have reached the ESRD. The average age was 12 years, sex ratio was 0.9 (14 M/16 F) Frequency was high for patients between 10 and 14 years of age (44%), no difference between the two sexes. Congenital abnormalities of kidneys and urinary tract (CAKUT), hereditary nephropathies were the first causes of ESRD (27% each) Followed by primary Glomerular nephropathy (23%), 23% of the cases,the etiology was indeterminated. Hemodialysis is the first treatment method for incident (76%) and prevalent (70%) patients.It was in most cases urgent (68%). A very high mortality rate (33%) mainly due to dialysis insufficiency.
A very low school enrollment (40%), significant retardation of growth (60%). The transplant rate is very low, only 1 patient has been transplanted, obstacles to kidney transplantation are numerous, mainly the absence of donor (58%).
Conclusions: In the end of this study, we were able to raise the following remarks: Very high incidence and prevalence of pESRD Delayed diagnosis of chronic kidney disease. Very limited access to specialized therapies (urological surgery, genetic tests). A comprehensive, planned and multidisciplinary care of the dialysis child is needed, it should ensure acceptable growth, good schooling and a better quality of life.

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Aerococcus sanguinicola – a rare cause of pd-related peritonitis

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Background: Peritonitis is an important complication in peritoneal dialysis (PD) and may involve unexpected organisms. Identifying the organism is crucial for a targeted Treatment.
Methods: We present the case of an 83-year-old male nursing home resident treated with assisted PD for two years. He was assigned to the emergency department because of nausea, vomiting and progressive abdominal pain. On admission the catheter exit site was clean, he was febrile (38.5 °C), hemodynamically stable with a tender abdomen. The peritoneal fluid was cloudy with a white blood cell count of 8200/ul (90% neutrophils). We administered an empiric intraperitoneal antibiotic therapy with 2 g of vancomycinand 1.5 g of ceftazidime. After 2 hours the patient developed a septic shock. Suspecting intestinal perforation we added piperacillin/tazobactam, but in accordance with the patient's advance directive we neither admitted him to the intensive care unit nor performed a CT scan. Within 24 hours his clinical condition improved rapidly and he could be discharged after 5 days.
Results: Microbial culture of peritoneal fluid showed growth of *Aerococcus sanguinicola* while cultures derived from blood and urine remained sterile. Treatment was reduced to Vancomycin intraperitoneally for 3 weeks. Followup cultures remained sterile without prior replacement of the PD catheter. The route of infection remains unclear.
Conclusions: To our best knowledge we present the first case of PD-related peritonitis due to *Aerococcus sanguinicola*, a grampositive bacterium found in air and dust, but also as a colonizer of the urinary tract or the oral cavity [1, 2]. It mainly causes infections in immunocompromised individuals and is susceptible to current empirical treatment regimens targeting Gram-positive organisms [3, 4].

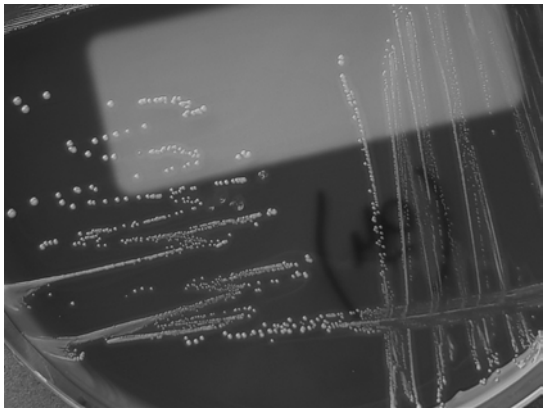
1 R. E. Williams et al. Journal of General Microbiology (1953).
2 P. A. Lawson et al, International Journal of Systematic and Evolutionary Microbiology, (2001).
3 E. Senneby et al, Diagnostic Microbiology and Infectious Disease, (2015).
4 M. Rasmussen et al, Clinical Microbiology and Infection (2016).

Material / Entnahmeort:Punktat, Blutkultur-Fl, Dialysat

Blutkultur aerob pos
Kultur aerobe Flasche
Aerococcus sanguinicola nachgewiesen Keim Nr. 1

Antibiogramm	Keim Nr.	1					1
Amoxicillin-Clavulansäure		e			Moxifloxacin		e
Ampicillin		e			Penicillin		e
Clarithromycin		e			Trimethoprim-Sulfamethoxazol		r
Clindamycin		r			Vancomycin		e
Doxycyclin		e					

e = empfindlich m = mässig empfindlich
r = resistent f = folgt



P 73

Low copeptin (CTproAVP) levels in patients with intradialytic hypotension

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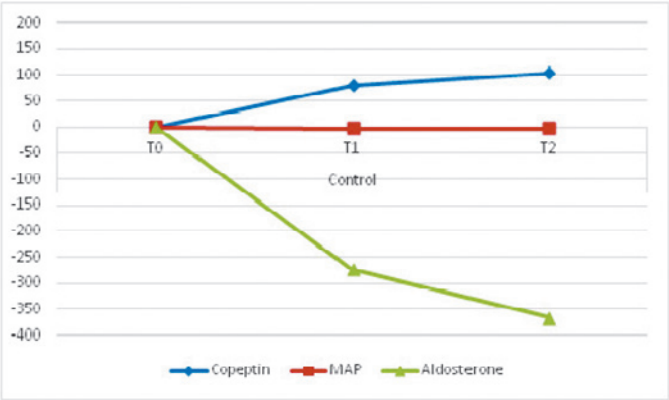
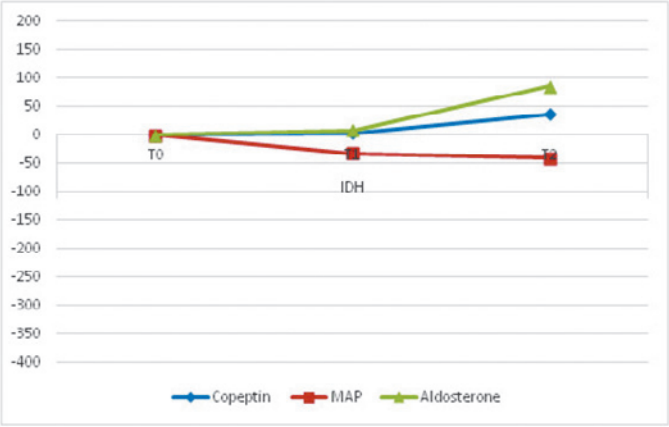
Background: Intradialytic hypotension (IDH) is related with high morbidity and mortality. There is evidence that argininevasopressin (AVP) responses could play a role. Copeptin is the reliable biomarker of AVP. In this study, copeptin, aldosterone, epinephrine, and norepinephrine levels in patients with IDH were evaluated throughout a hemodialysis (HD) session and compared with control group.
Methods: Study is composed of 15 patients that are normotensive during HD and 15 patients IDH with a minimum HD vintage of 1 year. Patients using any antihypertensive drugs, midodrine, and drugs effecting central or peripheral nervous systems were excluded. Other exclusion criteria were diabetes, infection, malignancy, anorexia, obesity, and hypo- or hyperthyroidism. Food intake was not permitted and dialysate sodium and calcium were adjusted as 140 and 1.5 mmol/l, respectively. Blood samples were collected before initiation of HD session (T0), in the mid-session for control group, 30 minutes after mean arterial pressure (MAP) drop for IDH patients (T1), and at the end of the session (T2).
Results: Groups had similar demographic features, interdialytic weight gains, and ultrafiltration amounts (table 1). IDH group had a MAP decline of 39,9 (±6,4) mm Hg. Copeptin levels of control group elevated averagely 79.9 (±97.5) pmol/l at T1and additionally 24.8 (±33.9) pmol/l at T2. In IDH group, copeptin level rise at T1 and T2 were 3.2 (±5.5) pmol/l and 34 (±44.6) pmol/l; respectively.Copeptin levels of IDH group were significantly lower at T1(p <0,001), and similar at T2 (p = 0,7); and significantly lower at T0-T2 than control group (p = 0,05). In control group, aldosterone levels distinctly decreased and, in IDH group, aldosterone levels elevated (p <0,001). Small changes were detected in epinephrine and norepinephrine levels for both groups and did not reach significance (p = 0,6 and p = 0,3; respectively) (Graphic 1 and 2).
Conclusions: Significantly lower copeptin levels suggest inadequate AVP responses in patients with IDH.

	Control group (n=15)	IDH group (n=15)	*p* value
Female/male (n)	7/8	9/6	*0,5*
Age median (SD)	51,0 (±16,8)	51,9 (±16,6)	*0,7*
BMI mean (SD)	22,5 (±2,8)	23,9 (±3,5)	*0,2*
BUN mean (mg/dl) (SD)	61,6 (±10,2)	60,3 (±12)	*0,2*
Cre mean (mg/dl) (SD)	8,4 (±3,1)	8,5 (±1,6)	*0,7*
Na mean (mEq/l) (SD)	139,5 (±2,3)	138,8 (±2,0)	*0,4*
K mean (mEq/l) (SD)	4,9 (±0,7)	4,7 (±0,6)	*0,3*
Hb mean (g/dl) (SD)	11,4 (±1,5)	11,3 (±1,1)	*0,7*
Alb mean (g/dl) (SD)	3,8 (±0,2)	3,7 (±0,2)	*0,07*
Ca mean (mg/dl) (SD)	8,9 (±0,6)	8,7 (±0,4)	*0,5*
iPTH (pg/ml)(min-max)	400 (±235)	361 (±314)	*0,3*
Kt/V mean (SD)	1,8 (±0,5)	1,8 (±0,4)	*0,9*
URR(%) (SD)	74,2 (±8,4)	77,3 (±5,9)	*0,2*
Urine output (n)	3/15	1/15	*0,3*
Dialysis vintage (months) (SD)	76,0 (±67)	71,1(±47,8)	*0,6*
MAP T_0 (mm Hg) (SD)	90,2 (±8,6)	79,3 (±7,4)	*0,002*
Copeptin T_0 (pmol/l) (SD)	116,5 (±83,7)	185,9 (±87,7)	***0,01***
Aldosterone T_0 (pg/ml) (SD)	706,5 (±416,7)	304,2 (±106,7)	***0,007***
Epinephrine T_0 (ng/ml) (SD)	143,8 (±92,2)	178,8 (±76,3)	*0,3*
Norepinephrine T_0 (ng/ml) (SD)	588 (±429,4)	701,9 (±345,4)	*0,2*
Int W Gain (%) (SD)	3,6 (±0,8)	3,7 (±0,6)	*0,5*
UF median (min-max)	2400 (500-3500)	2300 (1700-3000)	*0,08*





The numbers refer to the pages of this supplement.