Cross-talk between oxygen sensing and sodium handling in the collecting duct "NCCR project"

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Background: Regulation of sodium reabsorption by the collecting duct is crucial to maintain body sodium balance. Tubular handling of sodium is the major factor influencing renal oxygen consumption. We hypothesized that mismatching between oxygen supply and oxygen consumption in response to increased sodium transport may lead to activation of oxygen sensing mechanisms.

Methods and results: Using mpkCCDc4 cells, a model of collecting duct principal cells, we showed that sodium transport stimulation by aldosterone activates HIF signaling pathway revealed by HIF1α protein stabilization and increased HIF target genes expression. Activation of HIF signaling pathway by hypoxia or CoCl2 inhibited the transepithelial sodium transport by 60% and decreased expression of β and γ-ENaC subunits in mpkCCDc4 cells. HIF1α or HIF2α silencing using lentivirus encoding specific shRNAs results in a strong increase of sodium transport via increased β and γ-ENaC expression in mpkCCDc4 cells. In vivo, C57B16 mice exposed to hypoxia display a down-regulation of NCC and ENaC are up-regulated. To clearly discriminate the role of HIF1α and HIF2α, we started to investigate the consequences of HIF1α or/and 2α knock-out on renal sodium handling using Pax8-tTA/TRE- Hif1α or/and 2α f/f mice that we generated. The mice have been fed with low, normal and high sodium diet and the expression of the different channels in charge of sodium handling using PCR, Western blotting and immunohistochemistry. Preliminary results revealed a down-regulation of NKCC2 and NCC whereas β and γ-ENaC were up-regulated in HIF1α knock-out mice compared to control mice.

Conclusion: According to our results, HIF is a new player in sodium reabsorption along the renal tubule through a coordinated regulation of NKCC2, NCC and ENaC subunits.

Phenotype and disease severity reflected by serum lysoGb3 levels in patients with Fabry disease

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Background: Fabry disease (FD) is a rare X-linked lysosomal storage disease caused by mutations in the α-galactosidase A (GLA) gene leading to a deficiency of α-galactosidase A activity and resulting in a progressive sphingolipid accumulation, especially GB3, in all body liquid and tissue lysosomes. In this study, we asked whether plasma lysoGB3 (degradation product of the accumulating GB3) would reflect phenotype and disease severity in a large cohort of FD patients.

Methods: We included 61 consecutive adult patients (females: n = 36 [59%]) at the University Hospital Zurich, all with a GLA-mutation confirmed diagnosis, who presented for routine annual examinations at our FD center. Serum LysoGb3 levels were measured by high-sensitive electrospray ionization liquid chromatography tandem mass spectrometry (ESI LC-MS/MS).

Results: The serum levels of lysoGb3 were higher in Classical as compared to Later-Onset phenotype in males and females; in healthy controls, lysoGb3 levels were lower than in FD patients (fig. 1A and 1B). In a multivariate linear regression analysis, serum lysoGb3 levels were independently associated with Mainz Severity Score Index, estimated glomerular filtration rate, presence of cardiomyopathy and

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<th>Multivariate</th>
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</table>

Table 1

Figure 1A and B

Conclusion: LysoGb3 helps to distinguish between patients without FD and with the Classical FD phenotype. In males, it also discerns the Later-Onset phenotype. While in females, there is some overlap between Later-Onset phenotype and controls. LysoGb3 were associated with response to enzyme replacement treatment and to the disease severity in FD patients.
The effects of high phosphate intake on general health become clearer, almost nothing is known about underlying mechanisms. The aim of this study is to test if dietary phosphate has an impact on blood pressure and renal Na+ handling by the sodium chloride cotransporter (NCC) as a possible mechanism for phosphate related adverse outcomes.

Methods: This study is a prospective single-center observational cross-over trial testing the effects of low- or high-phosphate diet on blood pressure regulation in healthy males. All participants received fixed meals during the whole study period (19 days). Additionally, all probands were subjected to high- and low-phosphate diet in a cross-over design for 5 days including a washout period of 7 days in between. Low-phosphate diet consisted of oral supplementation of sevelamer hydrochloride and phosphate supplementation. Blood pressure values as well as blood and urinary samples were collected to analyze the effect of phosphate.

Results: Participants (n = 10, mean age 29 ± 3.2 years) showed during high-phosphate diet significantly higher plasma phosphate levels (0.13 mmol/l; 95%-CI 0.04–0.23; p = 0.011), increased FGF-23 levels (9.2 pg/l, 95%-CI 1.2–17.1; p = 0.029) and urinary phosphate excretion than during low-phosphate diet. Systolic blood pressure was higher on day 5 of high-phosphate intake (2.3 mm Hg; 95%-CI 0.35–4.26; p = 0.026) than on day 5 of low phosphate intake. NCC levels in urin exosomes were also higher during high-phosphate diet.

Conclusions: Healthy probands on high-phosphate diet have higher systolic blood pressure during day compared to low-phosphate diet, paralleled by increased expression and activation of NCC.
Renal arterial resistive index in patients with lupus nephritis: correlation with disease activity and biopsy parameters

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Background: Lupus nephritis (LN) affects up to 60% of patients with systemic lupus erythematosus (SLE). Moreover, LN has a negative impact on survival of SLE patients. The aim of this work was to evaluate the predictive value of renal resistance index (RRI), measured by Doppler Sonography in comparison with disease activity score, serologic and biopsy parameters in patients with LN.

Subjects and methods: This study was carried out on 40 SLE patients, they were categorized into two groups: Group I included thirty patients with lupus nephritis and Group II included ten patients without lupus nephritis and Group III included ten healthy subjects of matched age and sex as control group. All were subjected to history taking, clinical examination, assessment of disease activity by SLEDAI, laboratory investigations including FBG, blood urea, serum creatinine, serum albumin, CBC, ESR, CRP, complete urine analysis, UAC ratio, eGFR, serum ANA, anti ds-DNA titre, C3, C4. Renal biopsy was done for those with lupus nephritis. All subjects underwent renal Doppler with measurement of RRI.

Results: The mean value of RRI was statistically significantly higher in group I than that of group II and group III. Out of 33 cases of LN cases, 6 patients had RRI of 0.7 and above giving a percentage of 18.18%. LN patients with RRI higher than 0.7 had statistically significantly higher age, mean serum creatinine and blood urea levels and a lower eGFR, higher chronicity index of renal biopsy. No statistical significant difference was observed between renal biopsy classes and RRI.

Conclusion: RRI is of great clinical utility in predicting the chronicity index of renal biopsy which is a major determinant of renal outcome.

An in vitro model of idiopathic membranous nephropathy reveals PL2AR- and complement-dependent pathways of podocyte injury

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Background: Idiopathic membranous nephropathy (IMN) is an autoimmune kidney disease that usually manifests as nephrotic syndrome through damage of podocytes and leads to progressive renal failure in a significant proportion of patients. Recently, the target antigen of autoantibodies in the majority of patients with IMN has been identified as the phospholipase A2 receptor (PL2AR). The definitive proof for pathogenicity of PL2AR antibodies, however, is still lacking. Furthermore, mechanisms of podocyte injury remain elusive, although sublytic complement injury has been proposed. In this study, we aim to develop an in vitro model for IMN to determine downstream mechanisms of anti-PL2AR-antibody mediated injury to podocytes.

Methods: PL2AR expression levels in conditionally immortalized human podocytes were modulated by infection with a lentivirus vector carrying FLAG-tagged full length human PL2AR or by siRNA-mediated knock down. These cells were then pretreated with sera from PL2AR-positive IMN patients or control sera and subsequently, human complement was added. Cell lysates were collected and analyzed by qPCR, Western blot, and IF.

Results: Podocytes overexpressing PL2AR treated with a high-titer (1:1000) PL2AR antibody positive sera and complement in sublytic concentration resulted in inhibition of Akt and ERK phosphorylation. In addition, synaptopodin and NEPH1 expression was decreased with concentration resulted in inhibition of Akt and ERK phosphorylation. (1:1000) PLA2R antibody positive sera and complement in sublytic concentration resulted in inhibition of Akt and ERK phosphorylation. Podocytes overexpressing PLA2R treated with a high-titer (1:1000) PL2AR antibody positive sera and complement in sublytic concentration resulted in inhibition of Akt and ERK phosphorylation. Podocytes overexpressing PLA2R treated with a high-titer (1:1000) PL2AR antibody positive sera and complement in sublytic concentration resulted in inhibition of Akt and ERK phosphorylation. Podocytes overexpressing PLA2R treated with a high-titer (1:1000) PL2AR antibody positive sera and complement in sublytic concentration resulted in inhibition of Akt and ERK phosphorylation. Podocytes overexpressing PLA2R treated with a high-titer (1:1000) PL2AR antibody positive sera and complement in sublytic concentration resulted in inhibition of Akt and ERK phosphorylation. Podocytes overexpressing PLA2R treated with a high-titer (1:1000) PL2AR antibody positive sera and complement in sublytic concentration resulted in inhibition of Akt and ERK phosphorylation.

Conclusion: Podocyte injury by IMN serum and sublytic complement includes synaptopodin and NEPH1 degradation appeared to occur via two independent pathways that require cysteine and aspartate proteases, respectively.

Demography of the dialysis population in Switzerland

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

Methods: All medical establishments in Switzerland (N = 88) providing chronic treatment by either hemo- and/or peritoneal dialysis, had to provide relevant data for the year 2015. All individuals being on chronic dialytic therapy in the year 2015 were enrolled (N = 4452). For patients alive on December 31 2015, data were gathered from this date or closest to this date. For patients who died during 2015 or were being transplanted, data refer to time of event, or to a date closest to the event.

Results: Fifty percent of the patients were older than 70 years, and almost ¼ was beyond 80 years. No significant differences were found between female and male patients regarding mean age (88.1 vs. 67.9 years, respectively). However, women have been significantly longer on dialysis compared to men (51.5 vs. 45.5 months, respectively).

Conclusion: After almost two decades, Switzerland is again contributing data to the ERA-EDTA registry. With a coverage of almost 100% for both centers and patients, the data gathered can be considered highly representative. In Switzerland, the majority of
Familial nephrotic syndrome caused by COQ2 mutations, an inherited mitochondrialopathy

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Background: The majority of familial steroid-resistant nephrotic syndrome (SRSN) is genetically determined. Recessive coenzyme Q2 (COQ2) mutations leading to a mitochondrialopathy have recently been identified. Most affected individuals present with neurological and muscular symptoms, whereas nephrotic syndrome (NS) has been reported very rarely. We here present siblings with SRSN. Genetic analysis performed in one of them revealed pathogenic compound heterozygous COQ2 mutations.

Methods: Laboratory investigations were performed in Yerevan and Zurich, renal biopsy was evaluated in Zurich (Switzerland) and molecular genetics studied in Marburg and Ingelheim (Germany).

Results: A girl aged 17 months of Armenian origin was admitted with NS, severe proteinuria and preserved renal function. Leu340Val; paternally, COQ2 p.Arg173Leu). Spontaneous clinical and molecular genetics studied in Marburg and Ingelheim (Germany). (DE); 5University Children's Hospital, Zurich

The Effect of Dietary Amino Acids on Chronic Kidney Disease Progression (NCCR Project)

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Background: Chronic kidney disease (CKD) is a world-wide phenomenon affecting over 10% of the population (Troidle, 2014). In Switzerland, 18% of primary care patients are thought to suffer from CKD (Tomonaga et al., 2015). High intake of proteins as in Western-type diet is known to increase Renal Plasma Flow (RPF), induce hyperfiltration and increase acid load. In addition to these, the source of the protein i.e. animal or vegetal (Goraya and Wesson, 2016) and consequently its amino acid content might also play a role in the progression of the disease. The actual mechanisms by which these proteins / amino acids lead to increased Glomerular Filtration Rate (GFR) and to kidney function deterioration is not known.

Methods and Results: In our experiments we address the question of which amino acids might increase or decrease the progression of renal disease. The experimental model that we use, is the well-established 5/6th nephrectomy (5/6th Nx) in rats. The 5/6th Nx Wistar Han rats were randomly divided into groups receiving either the control diet (18% protein) or one of different diets, in each case containing 10% protein supplemented with 8% amino acid mix (Essential aas, Branched chain aas or all aas in the same proportion as in the protein mix). Both GFR and RPF were measured in in free moving animals. GFR measurements were performed transcutaneously using FITC-sinistrin, RPF was determined by using radio-labelled para-aminohippurate (PAH). Our preliminary data suggests that the EAA diets seem to slow the pace of progression the most while the BCAAs have the most detrimental effects, both in terms of the GFR and the RPF measurements. Our next studies focus on which specific amino acid or combination of amino acids could be a major contributor to the progression of the disease detrimentally or beneficially.
Plasma LysoGb3: a useful biomarker to diagnose Fabry disease heterozygotes

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Background: Fabry disease (FD) is a rare X-linked lysosomal storage disorder due to mutations in the α-galactosidase A gene (GLA) that markedly reduce α-galactosidase A (α-GalA) enzymatic activity. As a result, the enzymes glycosphingolipid substrates, globotriaosylceramide (Gb3) and globotriaosylsphingosine (LysoGb3) accumulate in plasma, urine and tissue lysosomes. In females, the diagnosis can be complicated by the fact that 40–50% of GLA-mutation confirmed heterozygotes have normal or only slightly decreased leukocyte α-GalA activities. Recently, LysoGb3 has been appreciated as a novel FD biomarker, especially for therapeutic evaluation. We identified three unrelated females in whom the accumulating LysoGb3 was increased, whereas their leukocyte α-GalA activities were in the normal range. Their clinical and biochemical characteristics are summarized in the table 1.

Methods: Among our GLA-mutation proven FD patients, we screened the 18 heterozygotes whose leukocyte α-GalA activity was determined at initial diagnosis. For these females, we measured their serum LysoGb3 levels using highly-sensitive electrospray ionization liquid chromatography tandem mass spectrometry.

Results: We identified three unrelated females in whom the accumulating LysoGb3 was increased, whereas their leukocyte α-GalA activities were in the normal range. Their clinical and biochemical characteristics are summarized in the table 1.

Conclusion: LysoGb3 serves as an useful biomarker to improve the initial diagnosis of FD heterozygotes for therapeutic evaluation.

Reduced β-catenin levels affect Uromodulin expression in mouse kidneys (NCCR project)

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Background and Aim: During kidney development, a β-catenin activity gradient exists along the nephron, with the lowest activity towards the future glomerulus. Ex-vivo chemical up-regulation of β-catenin activity leads to an expansion of distal segment identity, whereas down-regulation promotes proximal positional identity. However, it is not known, if the middle segment of the nephron, formed by the loop of Henle, is affected by these manipulations as well. Its thick ascending limb (TAL) is characterized by the production of Uromodulin also known as Tamm-Horsfall glycoprotein (THP). THP is the most abundant protein secreted in normal urine and plays a role in bacterial defense and renal transport. In this project, we used a genetic means to lower the amount of β-catenin during nephrogenesis in-vivo, and assessed whether this would affect TAL specification and THP expression.

Methods: β-catenin expression in embryonic kidneys was reduced to 25% compared to wild type mice by genetic means. Kidneys were isolated at E17.5 and P10 and analyzed histologically, by qRT-PCR or Western blot. Furthermore, urine THP content was quantified.

Results: Using marker proteins of different tubular segments (AQP1, AQP2, NCC and NKCC2), we determined the distribution of renal segment in kidneys with lowered β-catenin expression. We found ectopic expression of THP independent of other TAL-specific markers. Furthermore, the expression of THP is inversely correlated to β-catenin expression levels and is more abundant in the urine of kidneys with reduced β-catenin expression.

Conclusions: Reducing β-catenin alters the expression pattern of THP in the developing kidney. Moreover, mutant kidneys also develop cysts of collecting duct origin. The mechanisms of these processes, and whether our findings could translate to human disease will be subject of future investigation.

The allele frequency spectrum of PCSK9 mutations in the Swiss general population

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Background: Genetic studies have consistently linked PCSK9 nonsense mutations with lower low-density lipoprotein cholesterol (LDL-C) levels and decreased incidence of coronary heart diseases (CAD); conversely gain-of-function of mutations lead to increased LDL-C. The discovery of PCSK9 mutations has led to the development of PCSK9 inhibitors that are now available. This study describes the spectrum of known and suspected functional PCSK9 mutations in the Swiss general population using the population-based SKIPOGH study.

Methods: For the analysis, we included all patients of Swiss ancestry who were recruited in Switzerland, Liechtenstein, or Monaco as described previously. The study was approved by the respective institutional review boards. Whole-exome sequencing was performed on 28,825 individuals from the SKIPOGH study.

Results: In total, we identified 623 carriers of 59 heterozygous PCSK9 mutations. The frequency spectrum included 55 missense mutations, five nonsense mutations, and three splice-site variants. The most common among them was the nonsense mutation c.185C>T, which was observed in 0.38% of the study population. Other frequently identified variants included c.246A>T, c.970_971insA, and c.2390+1G>A.

Conclusions: Our findings provide insights into the prevalence and spectrum of PCSK9 mutations in the Swiss general population, which may help to inform clinical decision-making and the development of effective treatment strategies.

Table 1

<table>
<thead>
<tr>
<th>Mutations</th>
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<tr>
<td>c.185C&gt;T</td>
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<tr>
<td>c.246A&gt;T</td>
<td>0.29%</td>
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<tr>
<td>c.970_971insA</td>
<td>0.24%</td>
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<tr>
<td>c.2390+1G&gt;A</td>
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Figure 3

The figure shows the expression of β-catenin in embryonic kidneys of wild-type and β-catenin-knockdown mice. The expression levels are quantified using Western blot analysis, and the data is presented as mean ± SEM. A significant reduction in β-catenin expression is observed in the knockdown group compared to the wild-type group.
Methods: SKIPOGH is a population-based family-longitudinal study following 259 Swiss families totaling 1,126 individuals from 3 regions (Geneva, Lausanne and Bern). All participants were genotyped using the Human Omni2.5 chip and the Cardio-MetaChip (Illumina) and 817/1041 individuals were available for this analysis after quality control on both array types. We extracted 58 known variants (33 missense and 5 loss-of-function) from the ExAC database (http://exac.broadinstitute.org), including the two classical PCSK9 nonsense SNPs (CY5679TER, rs3823628; TYR142TER, rs67608943) and one missense SNP (ARG46LEU, rs11591147).

Results: In this Swiss resource of European ancestry we found one PCSK9 missense variant (ARG46LEU, rs11591147) to segregate at a frequency of 1.54% (table 1). We did not detect any rare allele of either of the other two classical nonsense PCSK9 SNPs with large effect sizes. Of the remaining known missense and loss-of-function mutations at the PCSK9 locus data was available for 7 variants and 5 were found to be non-monomorphic (table 1). The observed minor allele frequencies are comparable to other European datasets.

Conclusions: Our results show that rare and common PCSK9 mutations segregate in the general population in Switzerland with a likely impact on LDL-C levels. Larger sample sizes are necessary to detect the rare variants.

Table 1 Missense SNPs in PCSK9 segregating in the SKIPOGH study.

<table>
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<th>CHR</th>
<th>SNP</th>
<th>Amino acid change</th>
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<th>A2</th>
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Infections in de novo kidney transplant recipients treated with the RANKL inhibitor denosumab

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Background: Infections are a major cause of morbidity and mortality in kidney allograft recipients. In this post-hoc analysis of a randomized clinical trial which tested the effect of denosumab on bone mineral density we assessed the impact of this drug on the incidence and severity of infections in the first year after kidney transplantation.

Methods: In this clinical trial we randomized 90 de novo kidney transplant recipients shortly after transplantation to either denosumab on top of standard treatment (calcium and vitamin D) (n = 46), or to standard treatment alone (n = 44). Among all adverse events we analyzed all infections that occurred within the first year after transplantation, and compared their incidence and severity in both groups.

Results: Overall we identified more infections (n = 146) in the denosumab group than in the control group (n = 99). The most common infections were lower urinary tract infection (cystitis) (33.4% vs 25.2%), CMV viremia (17.8% vs 24.2%), flu-like syndrome (11.6% vs 14.1%), polyoma (BK) viremia (8.2% vs 11.1%), and herpetic simplex infections (5.5% vs 4.0%). Episodes of lower urinary tract infection (cystitis) occurred more often in the denosumab group than in the control group (51 vs 25 episodes in 24 vs 11 patients, p = 0.008), whereas episodes of transplant pyelonephritis or urosepsis were not more frequent (3 vs 5 episodes).

Conclusions: This post-hoc analysis reveals that treatment with denosumab to prevent bone loss in first-year kidney transplant recipients was associated with more frequent episodes of lower urinary tract infections, whereas other infections occurred with similar frequency in both treatment groups.

C1q blocking effects of week/non-complement-binding HLA antibodies

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A modified HLA Single Antigen Bead (SAB) assay measuring C1q-binding to HLA antibodies has recently been introduced. It is unknown under which condition and to which complement(C)-binding IgG subclasses (i.e. IgG2/4) of HLA antibodies can block C1q-binding triggered by C-binding IgG subclasses (i.e. IgG1/3). The aim of this study was to investigate in vitro C1q-binding induced by IgG subclass mixtures targeting the same HLA epitope. HLA class II specific monoclonal antibodies of different IgG subclasses but identical V-region (i.e. same affinity) were incubated with HLA DRB1*07:01 beads and parallel monitored for C1q-binding and – by
Early complications after living donor nephrectomy: a prospective analysis of the Swiss Organ-Living Donor Health Registry

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Background: We evaluated the prospective collected data about the incidence of early peri- and postoperative complications and potential risk factors for adverse outcomes after living kidney donation in Switzerland during the last eighteen years.

Methods: Peri- and postoperative events were prospectively recorded on a questionnaire by the local transplant team of all Swiss transplant centers and evaluated by the Swiss Organ Living Donor Health Registry. Complications were classified according to the Clavien grading system. A total of 1649 consecutive donors between 1998 and 2015 were included in the analysis.

Results: There was no perioperative mortality observed. The overall complication rate was 13.5%. Major complications defined as Clavien >3 occurred in 2.1% of donors. The prevalence of obese and elderly donors >70 years was 11.2% and 3.5% respectively. Obesity was not associated with any complications, whereas donors age >70 years was significantly associated with major complications (Clavien >3) observed in donors with laparoscopic surgery versus open surgery (p = 0.048), but an equal overall complication rate (p = 0.094).

Conclusion: We found a low rate of major and minor complications, independent of surgical technique after living donor nephrectomy. There was no elevated complication rate in obese donors. In contrast elderly donors >70 years had an elevated risk for perioperative complications and making careful information of this category of donors mandatory.

Frequency and predictors of successful steroid withdrawal guided by surveillance biopsies

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Background: Steroid withdrawal following renal transplantation is controversial and has to balance the risk of rejection against the risk of steroid-related side effects. The aim of this retrospective study was to investigate the frequency and determinants of successful steroid withdrawal guided by surveillance biopsies.

Methods: We investigated 156 ABO-compatible DSA-negative renal transplants receiving basiliximab induction and maintenance immunosuppression with tacrolimus-mycophenolate-steroids. The absence of rejection in surveillance biopsies at 3 or 6 months post-transplant initiated steroid withdrawal, which was monitored by subsequent indication and/or surveillance biopsies. The primary outcome was the frequency of successful (i.e. rejection-free) steroid withdrawal at one year post-transplant.

Results: Successful steroid withdrawal was achieved in 74/156 patients (47%); in 45/156 patients (29%) at the first attempt (initiated at 3 months), in 29/156 patients (18%) at the second attempt (initiated at 6 months). No clinical or immunological pre-transplant parameter was predictive for successful steroid withdrawal in uni- and multivariable analysis. Steroid maintenance therapy was not associated with a significantly increased incidence of treated diabetes (23% vs 18%; p = 0.43), treated hypercholesterolemia (48% vs 37%; p = 0.19) and hypertension, but a slightly higher weight gain within the first year (>3 kg vs >1.5 kg; p = 0.02).

Conclusion: Subclinical rejection-free steroid withdrawal can be expected in half of pre-transplant DSA-negative patients. As successful steroid withdrawal cannot be predicted by pre-transplant parameters, guidance by surveillance biopsies is advisable. Metabolic steroid-related side effects within the first year post-transplant are minor.

Figure 1
Survival of Fabry disease males after kidney transplantation.
9 patients, 18 KTx biopsies were performed. In two transplants, FD-typical ultrastructural changes were identified: in one patient who died 14 years after KTx before ERT era (figure 2, previously published by Gantenbein et al. 1995) and in one who was started on ERT 14 years and biopsied 23 years after KTx (table 1).

Conclusions: The study shows an overall good long-term outcome in FD after KTx. FD recurrence on KTx is possible without ERT. It is therefore conceivable that glycosphingolipid deposition on KTx can occur from the circulation.

Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Year of KTx</th>
<th>Year of ERT start</th>
<th>No ERT after KTx (months)</th>
<th>Age of transplant at last microscopy (months)</th>
<th>FD-specific ultrastructural changes</th>
<th>Other histological changes</th>
<th>GLA mutation, predicted amino acid change</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2005</td>
<td>2004</td>
<td>0</td>
<td>0.3</td>
<td>No</td>
<td>Rejection Banff 1B</td>
<td>c.1257T&gt;C p.Met427Thr</td>
</tr>
<tr>
<td>2</td>
<td>1995</td>
<td>2001</td>
<td>66</td>
<td>4</td>
<td>No</td>
<td>Intima fibrosis, acute interstitial nephritis</td>
<td>c.1033T&gt;C p.Ser343Pro</td>
</tr>
<tr>
<td>3</td>
<td>1993</td>
<td></td>
<td>185</td>
<td>0.3</td>
<td>No</td>
<td>Intima proliferation</td>
<td>c.1033T&gt;C p.Ser343Pro</td>
</tr>
<tr>
<td>4</td>
<td>2007</td>
<td>2001</td>
<td>0</td>
<td>8</td>
<td>No</td>
<td>Rejection Banff 2A</td>
<td>c.502C&gt;A p.Ala168Thr</td>
</tr>
<tr>
<td>5</td>
<td>1999</td>
<td>2004</td>
<td>54</td>
<td>68</td>
<td>No</td>
<td>Intimal fibrosis, tubular atrophy</td>
<td>c.1207T&gt;A p.Leu390His</td>
</tr>
<tr>
<td>2011</td>
<td></td>
<td></td>
<td>0</td>
<td>12</td>
<td>No</td>
<td>Chronic glomerulitis, intimal fibrosis, tubular atrophy</td>
<td>c.613C&gt;T p.Pro204Ser</td>
</tr>
<tr>
<td>6</td>
<td>2011</td>
<td>2004</td>
<td>0</td>
<td>12</td>
<td>No</td>
<td>Acute tubular necrosis</td>
<td>c.375C&gt;T p.Arg126Tr</td>
</tr>
<tr>
<td>8</td>
<td>1993</td>
<td>2001</td>
<td>101</td>
<td>272</td>
<td>No</td>
<td>Scant myelin figures in endothelial cells, Capillaries with C4d positive staining</td>
<td>c.1167dupT p.Val390CysX9</td>
</tr>
<tr>
<td>9</td>
<td>1997</td>
<td></td>
<td>166</td>
<td>166</td>
<td>Extensive sphingolipid deposition in tubular epithelial and endothelial cells</td>
<td>Not reported</td>
<td>c.1167dupT p.Val390CysX9</td>
</tr>
</tbody>
</table>

Abbreviations: ERT, enzyme replacement therapy; FD, Fabry disease; GLA, α-galactosidase A gene; KTx, kidney transplant

Results: Out of 345 recipients with rejection, 92 (27%) were classified as ‘v-lesions positive.’ Of these, 38 (41%) presented isolated v-lesions. At 6 years post-transplant, death-censored graft survival was significantly inferior in the v-lesions positive group: 86% vs. 89% for the v-negative group and vs. 92% for the no/borderline rejection group (p = 0.01). However, isolated v-lesions were not associated with a negative impact on long-term graft survival. Recipients with isolated v-lesions showed the same death-censored graft survival as compared with the no/borderline rejection group: 95% vs. 92%, respectively (p = 0.90). Furthermore, serum creatinine at last follow-up was comparable to the no/borderline rejection group (151 µmol/l ± 70 µmol/l vs. 145 µmol/l ± 90 µmol/l, p = 0.68). Recipients with isolated v-lesions were treated with intravenously steroids (25/38, 66%), ATG (8/38, 21%), or remained untreated (5/38, 13%). Furthermore, they were not associated with a specific pre-transplant risk (p = 0.84).

Conclusions: Isolated v-lesions are common among recipients with vascular lesions. They do not negatively affect long-term graft survival when treated with currently available antirejection agents. However, the impact on long-term outcome is unknown if these lesions remain untreated.

Figure 2
Kidney transplant (EM × 3700, inset × 83 700).
Formalin fixed and refixed in glutaraldehyde. Endothelial cell showing extensive glycosphingolipid substrates deposition 14 years without Enzyme replacement therapy (Gantenbein et al. 1995).
Rejection phenotypes in the current era of immunosuppression: a single-center analysis

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Background: Besides 'definitive rejection' the Banff classification includes categories for 'suspicious for rejection' phenotypes. The aim of this study was to determine the frequency and phenotypes of rejection episodes in 316 consecutive renal transplants from 2009–2014 grouped into patients without/with pre-transplant HLA-DSA (ptDSAneg; n = 251; ptDSApso; n = 65).

Methods: All adequate indication (n = 125) and surveillance biopsies (n = 538) performed within the first year post-transplant were classified according to the current Banff criteria.

Results: Suspicious for rejection' phenotypes were 3-times more common than 'definitive rejection' phenotypes in biopsies from ptDSAneg patients (35% vs 11%) and equally common in biopsies from ptDSApso patients (25% vs 27%). In both groups, 'suspicuous for rejection' phenotypes were more frequent in surveillance than in indication biopsies (28% vs 16% in ptDSAneg patients, and 37% vs 29% in ptDSApso patients). Borderline TCMR (91%) was the dominant 'suspicious for rejection' phenotype in ptDSAneg patients, while 'borderline TCMR' (58%) and 'suspicious for ABMR' (42%) were equally frequent in biopsies from ptDSApso patients. Inclusion of 'suspicious for rejection' phenotypes increased the one-year incidence of clinical (ptDSAneg patients: 18% vs 8%, p = 0.0002; ptDSApso patients: 24% vs 16%, p = 0.31) and (sub)clinical rejection (ptDSAneg patients: 59% vs 22%, p < 0.0001; ptDSApso patients: 68% vs 40%, p = 0.004).

Conclusion: 'Suspicious for rejection' phenotypes are very common in the current era and outnumber the frequency of 'definitive rejection'.

Severe hyperfiltration injury in a transplant kidney from a pediatric donor: a case report

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Background: The growing number of patients on the deceased donor renal allograft waiting list has prompted efforts to expand the criteria for acceptable organs on both ends of the age spectrum. While pediatric deceased donors are being transplanted to adult recipients is a valuable approach to alleviate the organ shortage, there are concerns on the increased risks for vascular and urinary complications and the hyperfiltration injury resulting from insufficient nephron mass.

Case: A 55 year-old male, 171 cm, 60 kg, suffering from ESRD due to malignant nephrosclerosis was transplanted after chronic dialysis for 4 years from an 18-month-old pediatric donor weighing 12 kg. Under triple immunosuppressive therapy with tacrolimus, mycophenolate mofetil and prednisone, the patient recovered quickly with a complete regain of weight in the first post-transplant course was favorable with a creatinine of 184 μmol/l at 6 weeks post-transplant. He however developed multiple duodenal ulcers with severe bleeding and a weight loss of 10 kg after discontinuation of prophylaxis. He recovered quickly with a complete regain of weight in the next few weeks. The creatinine decreased further, however, he developed glomerular microhematuria and a rise in proteinuria resulting in severe nephrotic syndrome. The kidney biopsy at 4 months post-transplant revealed a diffuse mesangial proliferation with a transition to FSGS compatible with an acute hyperfiltration injury.

Conclusion: Our patient developed severe hyperfiltration injury in the early post-transplant period despite well-controlled blood pressure and a low body weight. Rapid fluctuation of body weight may therefore have played an important causative role. Besides the careful selection of recipients and a strict blood pressure control, avoiding post-transplant weight fluctuation may be an additional factor for a favorable outcome in the kidney transplantation from pediatric donors.

Compartimentalization and confounders of the CXCL10 chemokine as a biomarker for subclinical renal allograft inflammation

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Background: Urinary CXCL10 is a promising non-invasive biomarker for subclinical tubulointerstitial inflammation, but limited data exists regarding its correlation with (micro)vascular inflammation. Furthermore, no study has contemporaneously evaluated whether a clinically relevant association exists between urine CXCL10 and subclinical compartment-specific inflammation.

Methods: In a prospective renal transplant cohort, 107 surveillance biopsies from 107 patients were selected/classified as normal histology (n = 47), normal histology with either BKV- or CMV-viremia (n = 17), isolated tubulitis score 34 (n = 18), microvascular inflammation (n = 15), and v-lesions only (n = 10). Serum and urine CXCL10 was measured by ELISA.

Results: Elevated urinary CXCL10 reflected inflammation within both the tubulointerstitial (median urinary CXCL10/creatinine ratios of isolated tubulitis score 34 vs normal histology: 123 ng/mmol vs. 0.46 ng/mmol; p = 0.02), normal histology vs. normal histology (n = 17), isolated tubulitis score 34 vs normal histology: 123 ng/mmol vs. 0.46 ng/mmol; p = 0.03), respectively. Conversely, elevated serum CXCL10 was not associated with inflammation within the microvascular compartment.

Conclusions: In the absence of confounders (i.e. systemic or allograft-restricted infection) urinary CXCL10 reflects subclinical alloimmune inflammation within both the tubulointerstitial and microvascular compartments of renal allograft, while serum CXCL10 does not.
Preservation of kidney function in kidney transplant recipients by alkali therapy (Preserve-Transplant Study)

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1Division of Nephrology, University Hospital Zurich, Zurich; 2Grat Biostatistics, Winterthur; 3Divisions of Nephrology and Transplantation, Geneva University Hospital, Geneva; 4Department of Nephrology, Hypertension and Clinical Pharmacology, University Hospital Bern, Bern; 5Institute of Physiology, University of Zurich, Zurich

Background: Kidney transplantation is the treatment of choice for patients with ESRD. Short- and long-term graft survival after kidney transplantation has significantly improved within the last decades but there is a substantial number of patients with declining transplant function and graft loss. Metabolic acidosis (MA) is highly prevalent in renal transplant patients. Several studies have shown that MA may contribute to deterioration of kidney function. Furthermore, recent data have demonstrated that higher serum bicarbonate levels in CKD patients are associated with a lower risk of ESRD indicating a significant role for MA in CKD progression. More evidence has been provided by a series of clinical studies that demonstrated a beneficial effect of alkali therapy on progression of kidney disease in CKD patients. Given the expanding pool of CKD patients—including former kidney transplant recipients—an alkali treatment study in kidney transplant patients is of prime importance and would have the potential to show that such treatment may slow or reduce the progression towards graft failure and significantly decrease the rate of ESRD.

Methods: This study is a 2-year intervention, multi-center, prospective, randomized, single-blind (patient), placebo-controlled interventional trial to test the superiority of alkali treatment in comparison to placebo on preservation of kidney function in 300 kidney transplant recipients. The patients will be randomized into 2 arms: intervention arm (sodium hydrogen carbonate, product: Nephrotrans®) and placebo arm (placebo comparator).

Outcomes: The primary outcome of this study is the change in renal function by assessing the change in eGFR over 2 years from baseline. The secondary outcomes of this study include exploratory outcomes such as changes in measurement of specific acid-base transport proteins by urinary exosome collection, and changes in urinary ammonium excretion, inflammatory markers such as complement factors, and hormones involved in tubulo-interstitial nephritis/librosis such as endothelin and aldosterone.
Serum calcification propensity is associated with renal tissue oxygenation and resistive index in patients with CKD or hypertension
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1University Hospital of Lausanne (CHUV), Lausanne; 2Division of Nephrology, Sion; 3Department of Nephrology, Hypertension and Clinical Pharmacology, Inselhospital, Bern; 4Department of Clinical Research, University Hospital of Bern, Bern

Background and Objectives: Arterial calcifications increase arterial stiffness and are associated with cardiovascular mortality and faster decline of kidney function, yet the underlying mechanisms are incompletely understood. A novel in vitro blood test reflects the calcification propensity of serum by measuring the maturation time of calciprotein particles (T50), and is associated with greater vascular stiffness. We hypothesized that high arterial stiffness and serum calcification propensity may impair renal perfusion and oxygenation in humans.

Methods: In the cross-sectional LauBOLD (Lausanne blood oxygenation level-dependent MRI) study, T50 was measured and BOLD-MRI performed in patients with CKD or arterial hypertension (AH1) and healthy controls. Concerning BOLD-MRI, the mean R2* values of the cortex, the medulla and layers of renal parenchyma were calculated, a high R2* value corresponding to a low oxygenation. Aortic pulse wave velocity (PWV) was assessed as a measure of arterial stiffness by planimetry, and renal Doppler ultrasound was performed to measure renal resistive index (RRI).

Results: 145 participants were included. Mean T50 was 246 ± 129 mm in 58 CKD patients, 275 ± 111 mm in 48 AHT patients, and 324 ± 96 mm in 39 healthy controls (panova = 0.008, see figure for the distribution of T50 between the groups). In multivariable adjusted linear regression analysis, square-root transformed serum T50 correlated negatively with mean cortical (regression coefficient β ± SE = –0.20 ± 0.07, p = 0.003) and medullary (β ± SE = –0.91 ± 0.04, p = 0.012) PWV was positively associated with R2* levels of outer and inner layers of renal parenchyma.

Conclusion: This study provides insight in the clinical determinates of calcification propensity, and demonstrates that a high calcification propensity and arterial stiffness are closely linked to low renal tissue oxygenation and perfusion.

Association of kidney stone with chronic cadmium exposure in the general adult population
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1Institute of Social and Preventive Medicine (IUMSP), University of Lausanne, Lausanne; 2Institute of Epidemiology and Biostatistics, University of Geneva, Switzerland; 3Department of Cardiology, University Hospital of Lausanne, Lausanne; 4Clinical for Nephrology, Hypertension and Clinical Pharmacology, Inselhospital, Bern; 5Department of Nephrology, University Hospital of Lausanne, Lausanne; 6Institute of Anatomy, University of Zurich, Zurich

Background: The renal sympathetic nervous system is implicated in most forms of hypertension. In animals, norepinephrine activates the thiazide-sensitive NaCl cotransporter (NCC), which participates to sodium reabsorption in the distal part of the nephron (DCT). No data are available in humans. Now, we used urinary exosomes from timed urine collection before and after renal denervation (RDN) in resistant hypertensive patients and investigated the acute effect of renal denervation on NCC abundance and phosphorylation.

Methods: Baseline 24-hour blood pressure and sodium excretion were measured before RDN. Timed urines were collected the morning before and the morning after renal denervation. Exosomes were freshly isolated by ultracentrifugation and stored at –80°C. NCC abundance and phosphorylation were analyzed by Western blot.

Results: Detection of TSG101 was used to confirm exosome quality and as loading control.

Conclusion: Thirteen patients were included in the study. All patients displayed low baseline plasma renin activity despite the use of hypertensive drugs. In the isolated urinary exosomes, the levels of total and phosphorylated NCC normalized to TSG101 varied several folds at baseline (pre-denervation), and showed a clear trend towards lower expression levels post-denervation, but without reaching statistical significance.

Conclusion: Thus, RDN may reduce total NCC abundance. Analysis of NCC phosphorylation in urinary exosomes may represent a mean to monitor the acute effects of RDN. Additional studies are necessary to confirm these initial observations and to assess the long term effects of RDN on renal NCC and other renal transport proteins involved in blood pressure control.

Kidney stone formers change nutritional habits at three months
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Background: Kidney stones represent a significant burden to patients and the health system, but their cause remains poorly understood. The Swiss Kidney Stone Cohort (SKSC) between May 2014 and September 2016 and their follow-up.

Methods: Adult patients were recruited in the five Swiss University Clinics of Nephrology (Basel, Bern, Geneva, Lausanne, and Zurich) if they were recurrent stone formers or had a single episode with pre-determined risk factors. Work-ups were standardized between

Resistant hypertensive patients display lower exosomal thiazide-sensitive NaCl cotransporter expression after renal denervation. NCCR Kidney.CH project
Olivier Bonny1, Fanny Durusse2, Candice Stoudmann3, Marc Maillard1, Johannes Loffing3, Grégoire Wuerzner1
1University Hospital Lausanne (CHUV), Lausanne; 2Department of Pharmacology and Toxicology, University of Lausanne, Lausanne; 3Service of Nephrology, University Hospital of Lausanne, Lausanne; 4Institute of Anatomy, University of Zurich, Zurich

Background: The renal sympathetic nervous system is implicated in most forms of hypertension. In animals, norepinephrine activates the thiazide-sensitive NaCl cotransporter (NCC), which participates to sodium reabsorption in the distal part of the nephron (DCT). No data are available in humans. Now, we used urinary exosomes from timed urine collection before and after renal denervation (RDN) in resistant hypertensive patients and investigated the acute effect of renal denervation on NCC abundance and phosphorylation.

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Results: Detection of TSG101 was used to confirm exosome quality and as loading control.

Conclusion: Thirteen patients were included in the study. All patients displayed low baseline plasma renin activity despite the use of hypertensive drugs. In the isolated urinary exosomes, the levels of total and phosphorylated NCC normalized to TSG101 varied several folds at baseline (pre-denervation), and showed a clear trend towards lower expression levels post-denervation, but without reaching statistical significance.

Conclusion: Thus, RDN may reduce total NCC abundance. Analysis of NCC phosphorylation in urinary exosomes may represent a mean to monitor the acute effects of RDN. Additional studies are necessary to confirm these initial observations and to assess the long term effects of RDN on renal NCC and other renal transport proteins involved in blood pressure control.
Phosphocalcic markers and calcification propensity for assessment of interstitial fibrosis and vascular lesions in kidney allograft recipients.

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Background: Renal interstitial fibrosis (IF) and arterial lesions predict loss of function in chronic kidney disease. Currently, IF and arterial lesions are evaluated invasively through random kidney biopsies. There are however many limitations to histopathological assessment. Noninvasive Method: In this retrospective study, we analyzed the associations and predictive values of phosphocalcic markers and T50 (calcification propensity) with chronic histological changes in 129 Kidney allograft recipients undergoing protocol biopsies. We hypothesized that

Results: PTH, T50 and vitamin D levels were independently associated to IF. PTH elevation was associated with increasing IF (r = 0.29, p = 0.001) severity while T50 (r = −0.20, p = 0.025) and vitamin D (r = −0.23, p = 0.009) were protective. On the contrary, FGF23 (r = 0.18, p = 0.045) and Klotho (r = −0.18, p = 0.045) correlated only modestly with IF whereas calcium and phosphate were not associated with IF. PTH, vitamin D and T50 were predictors of extensive fibrosis (>40% AUC: 0.73, 0.72 and 0.68 respectively) (fig. 1B), whereas PTH and FGF23 were modestly predictive of low fibrosis (<20% AUC 0.63) (fig. 1A). T50 was the only marker associated with chronic vascular lesions assessed by the Banff score. T50 decreased with increasing arterial lesions (r = −0.21, p = 0.038) (fig. 1C). The discriminative performance of T50 in predicting significant vascular lesions was modest (AUC 0.61) but was the only significant one.

Conclusion: In summary, we demonstrate that PTH, vitamin D and T50 may be useful in the noninvasive assessment of IF and vascular lesions in kidney allograft recipients. FGF23 and Klotho are in contrast of lower value in this context.

Figure 1: A: ROC curves of PTH and FGF23 in predicting fibrosis ≤20%; B: ROC curves of T50, 25D and PTH in predicting fibrosis >40%; C: Vascular lesions estimated by Banff: ROC curve of T50 in predicting significant vascular lesions (Banff ≥4 vs 0, 1, 2).

As 25D and T50 are markers that are negatively associated with fibrosis we used the opposite values of those markers. FGF23 and PTH values were logarithmically transformed as a natural log transformation was due to abnormal distribution. 25D: 25-hydroxyvitamin D; FGF23: Fibroblast growth factor 23; PTH: parathyroid hormone; ROC: Receiver Operating Characteristic; T50: Calcification propensity.
Airborne interstitial nephritis
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Background: A 50-year-old man with a history of mitral valve repair one and a half years ago was complaining of dry cough, dyspnoea, fatigue, weight loss and night sweat for six month. Chest X-ray showed few small nodules and SPECT-CT peripheral perfusion deficits, probably caused by pulmonary emboli. No signs of endocarditis were seen in echocardiography. T-spot was negative. Because of rising serum creatinine the patient was sent for diagnostic evaluation.

Methods: BP 109/62, P 98; 80.4 kg; 189 cm; Serum creatinine 166 umol/l, CRP 8 mg/l, urine analysis was normal, urine protein-creatinine ratio 28.1 mg/mmol. Ultrasound showed normal sized kidneys. Kidney biopsy revealed a diffuse acute tubulo-interstitial nephritis with epithelioid cell granulomas without necrosis.

Results: Under treatment with cortico-steroids of the interstitial nephritis and the hypersensitivity pneumopathy suspected, kidney function and the other symptoms were improving, but were worsening after reducing the steroid dose again. Systemic granulomatous disease was suspected and a PET-CT was performed, which showed a significant uptake of the reconstructed mitral valve ring. In heparin blood cultures there was a growth of mycobacterium chimaera, which was recently described to cause hospital acquired prosthetic heart valve infections. M. chimaera is a waterborne bacteria and a part of the mycobacterium avium complex (MAC). One study could show evidence of airborne transmission of M. chimaera from water tanks of contaminated heater-cooler to patients during open-heart surgery. We could not detect DNA of M. chimaera neither in the renal biopsy nor in the pulmonary biopsy so we can therefore assume that the granulomas are an immunological phenomenon in this rare chronic infection.

Conclusion: In a case of unexplained acute interstitial nephritis and a history of surgery involving the heart lung machine, special blood cultures have to be taken to detect possible mycobacterium chimaera infection.

Acute kidney injury in a tertiary hospital: can we learn from medical coding?
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1Medical controlling, Kantonsspital St Gallen, St. Gallen; 2Nephrology and Transplantation medicine, Kantonsspital St Gallen, St. Gallen

Background: Acute kidney Injury (AKI) is a diagnosis which impacts overall, cardiac and renal outcome. The aim of this study was to take advantage of medical coding in SwissDRG to analyse the diagnosis AKI Network Grade 3 (AKIN3) since 2012.

Methods: All discharge letters from our tertiary hospital between 01.01.2012 and 30.6.2016 were sorted for the diagnosis of AKIN3, CKD (all stages of chronic kidney disease) and CARD (cardiac diagnosis: hypertension, ischemic heart disease). Demographics and outcome were analysed.

Results: In total 160’277 discharge letters were analysed over the 4.5 years (on average 35’821 ± 1’073/year). AKIN3 was identified in 1735 cases representing 1.1% of discharged patients (range 0.9 to 1.3%). Figure 1 demonstrates the effect of gender and age on the occurrence of AKIN3. Among all AKIN3, 12% had AKIN3+CKD, 30% had AKIN3+CARD and 31% had AKIN3+CARD+CARD. Figure 2 shows the evolution of these categories over the years. While the overall incidence of AKIN3 was 1.1%, the overall death rate with AKIN3 reached 12.4%. Among AKIN3 patients 26% died in hospital (range 23 to 30%).

Conclusion: Identification of the AKIN3 diagnosis is essential for coding and thus data analysis. 1 in 10 patients with AKIN3 also has CKD, 1 in 3 has a cardiac diagnosis on top of acute on chronic kidney disease and 1 in 4 is at risk of death. Analysis derived from coding reveals the impact of AKIN3 in a tertiary hospital and can be used to develop strategies to prevent the occurrence of AKIN3 especially in a vulnerable population at high risk.

Risk of brain ischemia due to carotid artery stenosis in the very elderly treated with antihypertensives: a hospital survey
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1Department of Nephrology, Hypertension and Clinical Pharmacology, Inselspital, University Hospital, Bern; 2Angiology Service, Centre Hospitalier Universitaire Vaudois, Lausanne; 3General practitioner, Germany

Background: In elderly patients, systolic blood pressure (sBP) goals by European and international guidelines are more liberal because of higher risks of side-effects and hypertension with drug treatment. Carotid artery stenosis increases with age and may cause brain ischemia if hypotension occurs but its relevance for the treatment of elderly hypertensives remains unclear. To evaluate this risk, we analysed precerebral artery morphology and clinical BP data from a survey of aged hospitalised patients.

Methods: All patients ≥90 years admitted to the medical ward of a primary care hospital period were included over a period of 15 months. Ultrasound exams of the precerebral arteries were performed as a clinical routine to evaluate cardiovascular risk in the elderly. Intima-media thickness (IMT) of the common carotid (CCA), and internal carotid and external carotid artery (ICC/ECC) stenosis were analysed together with sitting BP’s and therapy (admission vs. discharge). Patients who died, with circulatory shock and readmissions were excluded (n = 9).

Results: Sixty-three patients aged 92 ± 3 years (mean ± SD; range 90–101) with a median hospital stay of 11 days were analysed (78% female, 35% diabetics, 24% atrial fibrillation, 41% coronary heart
Acute renal expression of pendrin in human urinary exosomes (UEs)

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Background: The kidneys play a paramount role in maintaining acid-base homeostasis by reabsorbing bicarbonates and excreting acid equivalent generated by metabolism. Apical protein pendrin is pivotal in this process. However there is a paucity of data on the regulation of pendrin in the human kidney. Here we studied effect of acute acidosis, alkalosis and sodium chloride loading in humans on urinary pendrin expression using novel technique of urinary exosomes (UEs).

Methods: After acute acid (NH4Cl 100 mg/kg) or equimolar alkalai (157 mg/kg) or NaCl (110 mg/kg) loading in fasting individuals, urinary exosomes were isolated from hourly collected samples. Pendrin and the housekeeping UE protein alix were detected by immunoblotting. UE pendrin expression was normalized to alix expression.

Results: Acute NH4Cl loading (n = 8) elicited a systemic acidosis with a drop in urinary pH and an increase of urinary NH4 excretion. Nadir urinary pH was achieved 5 hrs after NH4Cl loading. UE pendrin expression was first significantly reduced after 3 hrs, lowest UE pendrin levels were observed after 4 hrs. In contrast, after acute equimolar NaHCO3 loading (n = 8), urinary and blood pH rose rapidly and urinary NH4 excretion decreased. Densitometric analysis of immunoblots revealed rapid upregulation of UE pendrin expression already after 1 hr of NaHCO3 loading. However, UE pendrin levels returned to baseline after 2 hrs. To analyze the effect of acute NaCl loading, we administered an oral equimolar amount of NaCl to healthy individuals (n = 7). Urinary Na and Cl excretion increased significantly and rapidly after NaCl loading. Urinary pH, blood pH and urinary ammonia were unaltered throughout the experiment. Compared to baseline levels, UE pendrin abundance fell and was significantly lower at 3 hrs after NaCl loading.

Conclusion: Acute acid, alkalai or chloride loading significantly alter UE pendrin expression in human UE within a few hours.

Assessing the contact-activation of coagulation during hemodialysis with three different polysulfone filters: a prospective randomized cross-over trial

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Introduction: During hemodialysis (HD) the interaction of the blood with the dialyzer triggers both an inflammatory reaction and an activation of the coagulation cascade. An accepted parameter to quantify the extent of coagulation activation during HD is not available. This study aims to evaluate its amplitude, comparing dialyzers made of different polysulfone polymers, by measuring D-dimers in the filter rinsing fluids (FrF) and to test if FrF-dimers are suitable candidate marker to assess contact coagulation activation during HD.

Methods: In a prospective, cross-over study 41 hemodialysis patients were randomly allocated to 9 HD sessions with three types of polysulfone membranes: Filter A: Polistik®RevaclerMAX; Filter B: Helixone®Fx80, Filter C: Polyflux®H210. Findings: A total of 117 HD sessions were studied. The mean (SD) filters (FrF) D-dimers were 0.19 μg/l (0.56) for Filter A, 0.06 μg/l (2.81) for Filter B and 0.33 μg/l (1.13) for Filter C. Significant differences were found: A vs. B (p < 0.01), A vs. C (p = 0.01); B vs. C not significant. A large between-patients variability of D-dimer filters level was found. D-dimers in blood showed a similar trend but differences were not significant.

Discussion: The contact activation of coagulation during HD may vary also among filters made up with similar polysulfones. D-dimer in the filter rinsing fluid can be a standard approach to identify candidate marker for the evaluation of thrombogenicity during HD. Further studies are needed to elucidate the mechanism(s) and to confirm the usefulness of the rinse fluid D-Dimers as a clotting activation marker during HD.

Acute expression of pendrin in human urinary exosomes (UEs)

Randomized double-blind placebo-controlled trial assessing the efficacy of standard and low dose hydrochlorothiazide treatment in the prevention of recurrent nephrolithiasis – the "NOSTONE trial"

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Background: Nephrolithiasis is a global healthcare problem with a current lifetime risk of 18.8% in men and 9.4% in women. Thiazides have been the cornerstone of stone metaphylaxis for decades. Efficacy of the diuretics was tested in several RCTs. However, all of these RCTs have major methodological deficiencies including: lack of double-blinding and intention-to-treat analysis, unclear allocation concealment, lack of adverse event and drop out reporting, unknown baseline risk of disease recurrence and urine sample collection. Furthermore, only high doses were used, in the case of...
hydrochlorothiazide (HCTZ), 50 and 100 mg daily. Nowadays, thiazides are commonly used in the treatment of recurrent nephrolithiasis and arterial hypertension, but at significantly lower doses. In the case of nephrolithiasis, however, this practice is not supported by randomized evidence.

**Rationale:** There is a lack of evidence for the benefit of thiazides in the prevention of stone reformation. Several randomized trials containing kidney stones in general. In addition, the efficacy of the currently employed low dose thiazide regimens to prevent stone recurrence is not known.

**Methods:** The NOSTONE trial will be a 3 year prospective, multicenter, randomized, placebo-controlled, double-blind, parallel-group trial. We will include 416 adult patients with recurrent calcium containing kidney stones. Patients with active pharmacologic metabolically or with secondary causes of calcareous nephrolithiasis will be excluded from the study. Patients will be randomly allocated to once daily 50 mg or 25 mg or 12.5 mg HCTZ or placebo. All patients will receive concomitant counseling for non-pharmacologic interventions according to current guidelines to prevent stone recurrence.

**Outcomes:** Primary: Incidence of stone recurrences (a composite of symptomatic or radiologic recurrence, the latter assessed by low dose CT). Secondary: Individual components of the primary outcome, changes in urinary biochemistry elicited by HCTZ treatment and impact of baseline disease severity, biochemical abnormalities and stone composition on treatment response.

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**Failure of rituximab induction therapy in MPO-ANCA vasculitis**

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**Background:** A 54-year-old Asian female was admitted to our outpatient clinic due to newly detected renal failure and microhaematuria. She had suffered from arthralgia and muscle pain for two years and was diagnosed previously for "fibromyalgia." Kidney biopsy revealed pauci-immune glomerulonephritis with crescent formation and the titer of ANCA was highly increased (>1:640, MPO-ANCA; >134 U/ml). There was no history of coughing or haemoptysis and Chest-X-ray was normal.

**Method:** Steroid pulse therapy in combination with 1 g rituximab and prednisolone (1 mg/kg/day) followed by a second course of rituximab (1 g) 14 days later was started. Peripheral blood monitoring indicated B-cell depletion but ANCA titers remained elevated.

**Result:** 5 weeks after induction therapy and under Prednisolone (40 mg/d) the patient developed dyspepsia and haemoptysis due to pulmonary hemorrhage. CT scan and bronchoscopy confirmed the diagnosis and lower respiratory tract infection including Pneumocystis jirovecii was excluded. Due to progressive respiratory failure she was transmitted to the intensive care unit. Plasmapheresis was initiated, followed by administration of intravenous cyclophosphamide (500–750 mg) every four weeks. ANCA titers never returned normal while peripheral blood samples showed persistent B-cell depletion. The condition of the patient slowly improved and renal function remained stable. Over the time lung volumes normalized but with persisting restriction in diffusion capacity, and the radiologically signs of pulmonary haemorrhage disappeared.

**Conclusion:** Granulomatosis with polyangiitis and microscopic polyangiitis are small vessel vasculitides characterized by circulating antineutrophil antibodies. The RAVE and RITUXVAS trials demonstrated that rituximab is an alternative and noninferior to standard cyclophosphamide-based treatment, particular in patients with refractory disease and cyclophosphamide intolerance. Usually rituximab can be considered superior over cyclophosphamide in patients who have relapsing or refractory disease. However, its role in patients with severe renal disease warrants further investigations. We report a case with microscopic polyangiitis who had progressive pulmonary disease in spite of persistent B-cell depletion.

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**The crucial role of a Complement deposition endothelial cells Test in the diagnosis of an atypical HUS**

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**Case Report:** A 70 year old woman, known for long pre-existent epilepsy, fluctuating thrombocytopenia, hypertension and chronic kidney disease with a creatinine of 140 µmol/l, proteinuria of 1.9 g/day and microhaematuria was hospitalized after an accidental fall. During her stay she developed a bloodstream infection with E. coli, mental changes with absences, a worsening of her renal function (maximum creatinine 450 µmol/l), proteinuria (maximum 8 g/day), and thrombocytopenia (minimum 68 G/l). A peripheral blood smear showed 21/000 fragmented erythrocytes in the context of increased serum LDH 790 U/l, and of unmeasurable haptoglobin. Because of low platelet count and small deredifferentiated kidneys a biopsy was not performed. ADAMTS13 activity was normal, search for Shiga-toxin producing E. coli was negative, the presence of anti-C5 humanized monoclonal antibody (Eculizumab) and normalized ex vivo complement deposition on ADP-activated endothelial cells, there was no improvement in the renal function. Complement deposition on ADP-activated endothelial cells Test The Remuzzi group in Bergamo developed an in vitro assay able to detect complement activation on endothelial cells. This test might be interesting to diagnose aHUS in complex situations. It detects surface endothelial complement activation, as seen in active or resolved aHUS, while it is negative in other clinical situations where the complement is reduced, as membranoproliferative or c3 glomerulonephritis. Besides being diagnostic, it could help to monitor and personalize the Eculizumab therapy.

**Conclusions:** The complement deposition endothelial cells test, recently added to the nephrologist toolkit, potentially offers a way out in complex unresolved differential diagnosis.

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**Occurrence of community-acquired acute kidney injury in patients hospitalized for acute heart failure: impact of Renin-Angiotensin-Aldosterone blocking drugs**

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**Introduction:** A recent meta-analysis suggested that angiotensin-converting enzyme inhibitors (ACEIs) induce less acute kidney injury than angiotensin II receptor blocker (ARBs) in patients with chronic kidney disease (CKD). We investigated what is the risk of community-acquired acute kidney injury (CA-AKI) in patients hospitalized for acute heart failure (AHF) and previously treated by ACEIs and ARBs.

**Methods:** In a post-hoc analysis of a previous retrospective study including 648 patients admitted for AHF, AKI prevalence and its severity were analyzed in the 339 patients treated by either ACEIs (n = 200) or ARBs (n = 119). ACEIs and ARBs were classified in low, medium and high dosages. Multivariate analysis was performed with type of RAA blockers, age, gender, diabetes, coronary artery disease, chronic kidney disease and concomitant diuretic use as covariates.

**Results:** AKI was present in 116 patients, of whom 26 had severe AKI (stage II–III AKIN). AKI was present in 33 and 36% of these two groups (p = 0.014) Multiple logistic analysis showed that occurrence of severe AKI was associated with diabetes (OR 2.77; 95% CI: 1.17–6.55, p = 0.02) and use of ARBs (OR 2.39; 95% CI: 1.04–5.49, p = 0.04). There was no difference in dosage between the two types of RAA blockers. One year mortality rates were 12 and 18 % in patients treated with ACEIs and ARBs respectively (ns).

**Conclusion:** Compared to ACEIs, use of ARBs in patients admitted with acute heart failure was associated with double the risk of concomitant severe AKI within this retrospective study. Further clinical trials should be implemented in patients admitted for acute heart failure to examine whether ARBs are more detrimental than ACEIs in terms of risk of superimposed CA-AKI.
Penile calciphylaxis – a rare presentation of calcific uremic arteriolopathy
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Background: Calcific uremic arteriolopathy (calciphylaxis) is a rare disease presenting predominantly in ESRD and dialysis patients. Calciphylaxis is characterized by calcification of cutaneous arterioles with consecutive painful skin ulcerations and associated with high mortality mostly due to septic complications and gangrene. While the lower extremities are most frequently affected, necrotic lesions can occur at any site of the skin. Penile ulcerations have been described but are not well known as the primary manifestation of calciphylaxis.

Methods: We describe the case of a 54-year-old male patient with advanced diabetic nephropathy, who had so far refused renal replacement therapy, presenting with skin ulcerations exclusively on the glans penis (fig. 1). The patient was primarily seen by his family doctor, referred to dermatologists and urologists, and the differential diagnosis was focused on infectious or inflammatory diseases. However, biopsy results and a microbiological workup were non-diagnostic.

Results: After hospital admission and interdisciplinary nephrology and dermatology consulting, a tentative diagnosis of penile calciphylaxis was finally made from the history of longstanding untreated ESRD, the clinical presentation, laboratory findings (serum phosphate 4.28 mg/dL, iPTH 128 pg/mL) and exclusion of differential diagnoses. Despite local debridement of necroses, start of intensive hemodialysis therapy, treatment with phosphate binders and cinacalcet as well as sodium thiosulfate, penectomy could not be prevented (fig. 2). Histological analysis of the penectomy specimen revealed characteristic calcific infiltration of small and medium sized arterial vessels, vascular thrombosis and extracutaneous calcifications (fig. 3), that had not been detectable on biopsies of penile lesions. Only in the course of disease, additional characteristic skin lesions of the lower extremities developed.

Conclusion: After six months of treatment with dialysis, sodium thiosulfate, cinacalcet, phosphate binders, antibiotic treatments, local necrosectomies and skin grafts finally a stabilization of all wounds could be achieved.

Minimal change disease in SLE
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Background: A 54-year-old woman with a history of a systemic lupus erythematosus (SLE) treated with hydroxychloroquine and corticosteroids for seven years presented with a new onset of progressive edema since one week. There were no additional lupus specific symptoms.

Methods: On presentation she was hypertensive (bp: 160/100 mm Hg), showed generalized edema and reported a weight gain of 4 kg. Urine analysis revealed a selective glomerular proteinuria of almost 10 g per day. Nephrotic syndrome was diagnosed. Serum creatinine was elevated from recently 60 µmol/l to 104 µmol/l, CRP was not elevated.

The ANA titer was 1:640, anti ds DNA, anti ribosomal P protein antibodies and PLA-2 receptor antibodies were negative. There was a consumption of complement factors C3 was 0.71 g/l (normal 0.8–1.8) and C4 0.07 g/l (normal 0.1–0.4). On initial lupus diagnosis in 2009 the ANA titer was 1:1280, anti histon and anti ribosomal P protein antibodies were positive, anti ds DNA antibodies were negative. Kidney biopsy revealed normal mesangial cells and intact capillary loops with no endocapillary proliferation on light microscopy. Despite a slight granular deposition of C5-9 and IgG but no C3 on immunofluorescence no subepithelial electron-dense deposits were seen in electron microscopy. Instead diffuse fusion of the epithelial foot processes of podocytes was evident and minimal change disease was diagnosed.

Conclusion: The patients low dose corticosteroids were raised to 1 mg/kg body weight for a 12 week course and were then tapered. The serum creatinine returned to normal and proteinuria dropped to 0.2 g/day.

Not always what you expect
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Background: A 76-year-old man was admitted to our tertiary care clinic because of anemia and acute kidney failure. One month before admission, the patient suffered from diarrhea and vomiting with spontaneous resolution after two weeks. On physical examination, the temperature was 36 °C, the blood pressure 122/59 mm Hg, pulse rate 110 beats/min, respiratory rate 28 breaths/min with mild basal crackles on pulmonary auscultation, and oxygen saturation 98% on room air. On laboratory studies, serum creatinine was 741 µmol/l, CRP 10 mg/l, hemoglobin 64 g/l, leucocytes 10 x 109/l, and blood gas analysis showed mild metabolic acidosis.

Method: The initial diagnosis was dehydration with acute prerenal kidney failure, volume resuscitation was started. 24-hours after admission, the patient complained about dyspnea. Progressive respiratory insufficiency developed and the patient was transferred to the ICU where orotracheal intubation was performed. A pulmonary CT-scan showed a “crazy paving” pattern suspicious for diffuse alveolar hemorrhage which was confirmed by bronchoscopy. With pulmonary hemorrhage and acute kidney failure small vessel vasculitis was suspected, immunosuppressive therapy with high dose prednisone was started. Surprisingly, a kidney biopsy revealed acute tubular injury without any signs of small vessel vasculitis and serum ANCA were negative. Bronchoalveolar lavage showed no signs of infection without any growth of pathogens or viral replication. A lung biopsy was suspicious for pulmonary fibrosis.

Results: The patient’s condition further deteriorated and he died of respiratory failure. An autopsy was performed. Liver cirrhosis compatible with alcohol abuse and acute tubular injury in the kidneys was diagnosed. No signs of vasculitis were present and pulmonary fibrosis could not be confirmed. With signs of fungi (type candidas) in the lungs, alveolar hemorrhage was thought to be due to candidias infection of the lung.

Conclusion: This case shows that even with a high clinical suspicion a completely different diagnosis is possible.
Primary Aldosteronism caused by an unusual “Adrenal Adenoma”
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Introduction: Primary aldosteronism is a common cause of secondary hypertension, and can be associated with an adrenal adenoma or with bilateral adrenal hyperplasia. We report a case of an uncommon localization of adrenal adenoma.

Case presentation: We describe a 46 years old woman who was diagnosed with a new grade 3 hypertension associated with severe hypokalemia (2.2 mmol/l). Primary aldosteronism was suspected, and confirmed by peripheral blood testing: increased plasma aldosterone (885 pg/ml), suppressed plasma renin activity PRA (<0.08 ng/ml/h), a very high Aldo/PRA ratio (11082) and an elevated urinary excretion of aldosterone (28 µg/24h). Abdominal imaging (MRI and ultrasound) was performed to exclude a renovascular hypertension. A 2 cm lesion was found on the upper pole of the right kidney, inside the cortex, but no adrenal nodule or hyperplasia was detected on either side. A first selective adrenal venous sampling showed no difference between the right and left measurements of plasma aldosterone. Because the blood pressure remained high and the potassium values low, despite three medications on optimal doses, the same procedure was performed again. This time a right lateralization of aldosterone secretion was detected, justifying a right laparoscopic adrenalectomy. The surgical exploration showed that the suspicious 2 cm lesion seen on the MRI inside the right renal cortex corresponded in fact to an adrenal adenoma adherent to the kidney tissue. A complete resection was performed. Plasma aldosterone was low and the blood pressure was normalized after the surgery. It is possible that the failure of the first adrenal venous sampling could be explained by the unusual localization of the adrenal adenoma.

Conclusion: This very rare case of reno-adrenal adenoma highlights the fact that adrenal vein sampling was essential as a decision aid to perform surgery in this patient with a curable form of secondary hypertension.

Figure 1

The influence of dialysate bicarbonate concentration on the risk of intradialytic hypotension: a retrospective cross-sectional study in southern Switzerland
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Background: Higher concentrations of dialysate bicarbonate (DB) have been associated with many adverse outcomes ranging from clinical manifestations to a higher risk of mortality. In a multi-centered cohort study (DOPPS) a positive, although not significant, association between DB and the incidence of intradialytic hypotension (IDH) (HR, 1.12 [95% CI, 0.96–1.32) was found. Furthermore, in two previous randomized cross-over trials, we showed a direct correlation between DB and BP decrease during haemodialysis. Nevertheless, the clinical impact of the postulated DB hypotensive effect was not investigated exhaustively and the results of the DOPPS could be influenced by confounding factors related to the quality of the data. We therefore aim to investigate, in an unselected population, the association among DB, intradialytic BP behaviour and risk of IDH.

Methods: We performed a cross-sectional multi-center study, in 4 Dialysis Units in Southern Switzerland. Laboratory, blood pressure parameters and episodes of IDH, defined as systolic BP <100 mm Hg in one or more of three consecutive HD-sessions were recorded. Data of 156 patients were analyzed.

Results: The minimum (min) intradialytic blood pressure (BP) was 110.6 ± 19.0 systolic (SBP) and 56.6 ± 11 .5 mm Hg diastolic (DBP), with a mean ΔBP (pre HD SBP – intra HD min SBP) of 25.3 ± 15.1 mmHg. The multivariate linear regression showed a positive, although not significant correlation between ΔBP and DB: (coefficient 1.867205; SE 1.280578). In a multiple adjusted regression model however, a statistically significant correlation between DB and risk of IDH (adjusted OR 1.52; 95% CI 1.03–2.28; p value 0.033) was found. The Δ bicarbonate (DB – pre HD bicarbonate) reduced the risk of IDH in the crude and adjusted regression models (OR 0.87,p value:0.010).

Conclusion: Our data confirms that both, the DB content and the Δ bicarbonate significantly affect the intradialytic BP and the risk of IDH.

Fibronectin glomerulopathy in a patient with systemic lupus erythematosus: case report and literature review
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Introduction: Fibronectin glomerulopathy (FG) is a rare autosomal dominant disorder associated with massive deposition of fibronectin in glomeruli. It presents with proteinuria, often in a nephrotic range, in the third to fourth decade and slowly progresses to end-stage renal disease. We present a case of a young woman with early diagnosis of systemic lupus erythematosus (SLE) and later development of nephrotic syndrome in a context of FG. To our knowledge, only one case is reported in literature describing atypical fibrillary deposits in the glomerular mesangium and subendothelium in association with SLE.

Case report: We present the case of a 34-year-old woman with diagnosis of SLE in 1996. At this point she presented erythema, arthralgias and arthritis, Raynaud phenomenon, hemolytic anemia. ANA/anti-dsDNA were positive. Glucocorticoid therapy was introduced in association with Chloroquine. In 1997 she developed nephrotic proteinuria in a context of lupus glomerulonephritis Grade WHO III (documented in a first renal biopsy). In 1999 she underwent a second renal biopsy because of persistent proteinuria in course of immunosuppression; the biopsy showed a lupus nephritis grade IV. Steroidal treatment was associated with Cyclophosphamide and Azathioprine. In June 2015 she had a premature twin childbirth, Since the third trimester she developed a progressive proteinuria with hypertension in a pre-eclampsy context. Over the 6 months after delivery, we observed a persisting proteinuria (more than 2 g/die), without hypertension. A third renal biopsy was performed: fibronectin glomerulopathy was found.

Conclusion: We present a case of fibronectin glomerulopathy in a patient with SLE. This to encourage us to be careful researching autoimmune disorders in patient presenting glomerular deposition of paraprotein.
A cross-sectional retrospective study was performed.

Methods: We designed a cross-sectional multi-center study aimed to investigate the association of Cl− in dialysate and of ΔCl− (serum Cl− pre-HD – dialysate Cl−) with intradialytic BP changes (ΔBP: pre-HD SBP – lower intra-HD SBP) and with the risk of hypotension, testing at the same time the association between ΔCl− and serum Cl− post-HD with ΔBP and with the risk of hypotension. Laboratory and hemodynamic parameters were recorded.

Data of 182 unselected hemodialysis patients treated with membranes belonging to two polysulfone families (Fresenius FX, Helixone®, Filters A; Gambro, Polyflux®, Filters B) were collected. Pre- and post-dialysis systolic and diastolic BP and heart rate were measured at the same time the association between ΔCl− and serum Cl− post-HD with ΔBP and with the risk of hypotension. Laboratory and hemodynamic parameters were recorded.

Results: In a linear regression model the long-term association between ΔCl− and serum Cl− post-HD was not significant (coefficient 0.150; p-value 0.03). In a logistic analysis association between Cl− was associated with hypotension risk (OR 0.87, p-value 0.001). Finally Δ pre-post HD Cl− was associated with ΔBP (coefficient 1.02; p = 0.02) and with the risk of hypotension (OR 1.14; p = 0.05).

Discussion: Our findings confirm a possible independent role of chloride in the complex genesis of the hemodynamic intradialytic pattern. Further studies are needed to elucidate the role of this still neglected electrolyte.

Background: Thrombocytopenia is a potential complication of hemodialysis (HD) and its occurrence has been described even with high-biocompatible polysulfone membranes. Dialysis units routinely monitor platelet count at the beginning of HD-sessions. However considering that the long-term effects on platelet count could be easily missed, the prevalence of HD-related thrombocytopenia could be underestimated. In the present study we aimed to investigate: i) the long-term impact of HD treatment on platelet count, comparing two families of dialysis membranes made up of similar polysulfones ii) whether the switch between the dialysis membranes studied significantly affects platelet count iii) the prevalence and the risk of HD-induced thrombocytopenia according to the dialysis membranes used.

Methods: A cross-sectional retrospective study was performed comprising 157 adult chronic HD-patients. The HD-membranes under investigation were of the series FX, Helixone® Fresenius (Filters A), and Polyflux® Gambro (Filters B). Patients were treated in 4 Dialysis Units in Southern Switzerland. Data were collected from a centralized computing platform.

Results: Platelet count significantly differs between filter A and B with respectively 188 (153–243)×109/L vs 214(179–255)×109/L; p = 0.036. The prevalence of thrombocytopenia was higher for Filter A compared to Filter B (28.4% vs 12.8%; p < 0.001). The switch from filter A to B significantly affected platelet count: 189 (148–217) to 217 (163–253)×109/L; p < 0.001. A linear random-intercept model confirmed the results (coefficient 0.254; Standard Error 0.956; p < 0.001). In a mixed-effects logistic regression model the risk of thrombocytopenia for filter B was 0.157, CI 0.056–0.442.

Conclusion: Our data suggest that among the polysulfone membranes studied, the FX membrane induced a lasting decrease in PLT count and caused significantly more thrombocytopenia. Prospective studies are warranted to verify our findings.

The yo-yo hemodynamic effect of dialysate potassium. A retrospective cross-sectional study

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Background: The dialysate potassium concentration (K+ Dial) could impact in a relevant way on the blood pressure profile during haemodialysis (HD). Previous findings of our group, from a randomised single blind crossover study, suggested instead, that a rapid decrease in the concentration of serum K+ during HD was associated with a decrease of systolic (SBP) and mean blood pressure (BP) mediated by a decrease in peripheral resistance. Furthermore, results of a previous study showed that a rapid decrease of serum K+ concentration translates into a BP rebound at the end of the HD session. Considering the relative small sample of the studies above mentioned, we aimed to investigate respectively: i) the impact of K+-Gap (pre-dialysis serum K+ minus K+ Dial) on ΔBP (Pre-HD-SBP minus minimum intra-HD-SBP) ii) the contribution of K+-Gap and K+ Dial on Post-HD-SBP and on mean BP (MAP).

Methods: A multi-center cross-sectional-retrospective study was performed, Pre/intra/post haemodialysis BP and heart rate parameters of 159 patients of 4 Dialysis Units in Southern Switzerland were collected. Dialysate electrolyte content, ultrafiltration rate and covariate known to impact BP were recorded.

Results: Mean K+-Gap (mEq/L) was 2.00 ± 1.03 (range 1.03–4.5); ΔBP (mm Hg) 25.4 ± 15.4; Pre-MAP: 87.4 ± 13.4; Post-MAP 86.4 ± 17.4. Higher K+-Gap (and, therefore, lower K+-dialysate-concentration) was associated with higher ΔBP (coefficient 2.04; p-value 0.038, r = 0.70) in a multivariate analysis. According to different K+Dial (2vs3vs4 mEq/L) Post-HD-SBP and MAP were, respectively: 136.3 ± 27.3±132.8 ± 42.5±140.1 ± 29.3 (p = 0.013) and 83.7 ± 11.9vs86.6 ± 17.4vs90.5 ± 19.2 (p = 0.030). Multivariate analysis confirmed that higher K+-Gap was associated with higher Post-HD-SBP (coefficient 0.77; p = 0.031) and with higher MAP (coefficient 3.8; p = 0.015).

Conclusion: We confirmed that dialysate potassium concentration significantly impact on hemodynamic during and after HD. Our findings, as expected, pointed out a bidirectional effect of K+Dial on one hand it contributes in lowering intradialytic BP and on the other in generating a post-HD BP rebound.

Polysulfone hemodialysis membranes and intra-dialysis blood pressure variability: a multicenter observational survey

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Background: Blood pressure (BP) variability increases in hemodialysis (HD) patients and is associated with a higher risk of cardiovascular events and mortality. The impact of the physico-chemical characteristics of HD-membranes on the intra-dialytic BP-profile and on its variability has not been exhaustively established till now. In a previous cross-over study comparing high- and low-flux HD-membranes we observed that not only the permeability but also the structure of the membrane could translate into a peculiar hemodynamic behavior. The purpose of this survey was to investigate among polysulfone dialyzers, whether the choice of the membrane influences the tendency to BP decrease during hemodialysis.

Methods: We performed a cross-sectional study in 4 Dialysis Units belonging to the Ente Ospedaliero Cantonale. Data of 128 unselected hemodialysis patients treated with membranes belonging to two different polysulfone families (Fresenius FX, Helixone®, Filters A; GAMIBRO, Polyflux®, Filters B) were collected. Pre- and post-dialysis systolic and diastolic BP (PreSBP, PostSBP, PreDBP and PostDBP) and Intra-dialysis maximum(max) and minimum(min) SBP and DBP were recorded. Episodes of Intradialytic hypotension (IDH) defined as
SBP <100 mm Hg in one or more of three consecutive HD-sessions were recorded.

**Results:** The PreSBP, IntraSBPmax and IntraSBPmin for Filter A and B were as follows: 134 ± 21, 143 ± 23 and 111 ± 20 mm Hg vs. 140 ± 22, 151 ± 21 and 113 ± 20 mm Hg. The PreSBP, IntraSBPmax and IntraSBPmin were 56 ± 12, 64 ± 13 and 58 ± 10 mm Hg vs. 64 ± 13, 68 ± 11 and 58 ± 12 mm Hg. The differences in PreSBP – intraSBPmax Filter A vs FilterB were not significant, while the ∆ PreSBP – IntraSBPmin was 26.2 ± 10.2 mm Hg p ≤0.001. The incidence of episodes of IDH was higher for Filter A (A vs. B: 76.8% vs. 23.1%; p = 0.005).

**Conclusion:** Our data suggest that even among high-flux HD-membranes BP-variability could be influenced by their physico-chemical characteristics. Further research is needed to confirm that the results have not been generated by the basic characteristics of the population.

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**Clinical Management and Inter-Institutional Variability of Renal Anemia Determinants among Dialysis Units in Southern Switzerland**

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**Background:** Variations in healthcare management between institutions and health care professionals have been addressed in several studies and correlated with clinical outcomes and performance measurements. International treatment guidelines for anemia in dialysis patients treated with hemodialysis in the 4 EOC Dialysis Units (H1,H2,H3,H4). Data from all patients treated during the period under review (2008–2016) were collected. Parameters investigated were: hemoglobin (Hb), serum ferritin and hypochromic red blood cells (%HYP0). A cost-effectiveness analysis of the Erythropoetin treatment (Epo-CHF) was performed.

**Methods:** Retrospective cross-sectional multicenter analysis in adult patients treated with hemodialysis in the 4 EOC Dialysis Units (H1,H2,H3,H4). Data from all patients treated during the period under review (2008–2016) were collected. Parameters investigated were: hemoglobin (Hb), serum ferritin and hypochromic red blood cells (%HYP0). A cost-effectiveness analysis of the Erythropoetin treatment (Epo-CHF) was performed.

**Results:** Data of 711 patients were analysed (37.1% women). Mean Hb values (g/L) biennial 2010/2011 vs 2014/2015: H1116.5 ± 12.6 vs 109.9 ± 12.5 (p = 0.001); H21111.8 ± 14.4 vs 109.9 ± 13.2 (p = 0.003); H3113.1 ± 11.7 vs 112.1 ± 11.3 (ns); H4115.4 ± 12.8 vs 113.6 ± 13.5 (p = 0.001). Ferritin (µg/L) 2010/2011 vs 2014/2015: H1374.2 ± 217.5 vs 554.8 ± 278.4 (p = 0.001); H22072 ± 142.9 vs 252.8 ± 203.1 (p = 0.001); H33476.1 ± 485.3 vs 3479 ± 198.7 (p ≤0.001); H44240.0 ± 189.3 vs 468.0 (p = 0.03).%HYP2010/2011 vs 2014/2015: H132.3 ± 3.4 vs 4.1 ± 4.4 (p ≤0.001); H225.6 ± 5.8 vs 6.2 ± 7.8 (ns); H334.5 ± 4.5 vs 3.6 ± 4.7 (ns); H446.8 ± 7.1 vs 5.9 ± 7.1 (p = 0.02).

**Discussion:** Significant differences in 2015 Hb and Ferritin values, %HYP0 and % of patients with Hb >150g/L were found among the Dialysis Units, with lower %Hb >120 g/L for H1, lower %HYP0 for H3 and lower Ferritin for H2. In a linear multivariate model Epo-CHF was associated with hemoglobin (Hb), serum ferritin and %Hypochromic red blood cells (%HYP0). A cost-effectiveness analysis of the Erythropoetin treatment (Epo-CHF) was performed.

**Conclusion:** Our data suggest that even among high-flux HD-membranes BP-variability could be influenced by their physico-chemical characteristics. Further research is needed to confirm that the results have not been generated by the basic characteristics of the population.
Kidney failure after long-term low-dose methotrexate therapy: a case report
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Background: Acute kidney failure is a well-known adverse effect of high-dose methotrexate (MTX) chemotherapy. The mechanisms of MTX-induced nephropathy is probably a combination of crystal deposition and tubular necrosis. Whether long-term low-dose MTX therapy may favour or accelerate the development of chronic kidney injury is not clear. Pre-existing risk factors for kidney disease such as hypertension, use of NSAID's, concomitant acute illness and aging may worsen kidney function and consequently increase MTX toxicity by reducing its clearance.

Case Report: We report a case of a 63-year-old woman with psoriatic arthritis under long-term treatment with low-dose MTX (20 mg/week). The medical history was characterized by untreated arterial hypertension. Laboratory data showed a decline in eGFR between 2010 and February 2016 from 72 to 51 ml/min/1.73 m². In May 2016 she developed acute diarrhea. In June 2016 she was hospitalized with symptoms of severe MTX toxicity, stomatitis, acute kidney failure (creatinine 486 µmol/l) and pancytopenia. Interestingly initial MTX blood level was relatively low (0.31 µmol/l). Though rapid decrease of serum MTX level (<0.04 µmol/l) with urine alkalinisation and diuretic therapy, the patient developed hypervolemia and underwent a short course haemodialysis treatment. A partial recovery of the kidney disease was observed after 2 months (eGFR 40 ml/min/1.73 m²).

Conclusion: In the presence of pre-existing risk factors, MTX may contribute to development of chronic nephropathy. The progressive cumulative dose of MTX over the years and diarrhea-induced prerenal injury may have precipitate the acute renal failure and MTX toxicity. A careful renal follow-up is mandatory in every patient under treatment with MTX even with low dose.

Scleroderma renal crisis: a serious complication
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Background: Renal involvement is common in patients with systemic sclerosis and may reflect prerenal failure, direct drug toxicity, effects of hypertension, use of NSAID's, concomitant acute illness and aging. Hypertension, use of NSAID's, concomitant acute illness and aging may worsen kidney function and consequently increase MTX toxicity by reducing its clearance.

Case-Report: A 72-year-old woman with known systemic sclerosis with skin, lung, gastrointestinal involvement and repeated cardiac effusions under therapy with low dose prednisone and rituximab was admitted to the hospital because of acute on chronic kidney failure with hypertension, haemolytic anaemia and thrombocytopenia. Therapy with ACE inhibitor was stopped because of progressive kidney failure. Renal biopsy was performed and revealed an older but still active thrombotic microangiopathy. Once again, this patient decided not to continue dialysis and deceased.

Conclusion: SRC is a major complication of systemic sclerosis. Despite treatment with ACE inhibitors, approximately 20 to 50 percent of patients with SRC require dialysis. Furthermore, survival on dialysis in patients with SRC is worse compared to other etiologies of ESRD.

Unsuccessful treatment with abatacept of a case of focial segmental glomerulosclerosis (FSGS) recurrence after kidney transplantation
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Background: Pathophysiological theory justified the treatment of FSGS with abatacept. Yu et al. reported 4 patients with B7-1 (CD80) deficiency. Whether long-term low-dose MTX therapy may favour or accelerate the development of chronic kidney deposition and tubular necrosis. Whether long-term low-dose MTX therapy may favour or accelerate the development of chronic kidney injury is not clear. Pre-existing risk factors for kidney disease such as hypertension, use of NSAID's, concomitant acute illness and aging may worsen kidney function and consequently increase MTX toxicity by reducing its clearance.

Case report: A 51-year-old woman affected by primary FSGS started weekly therapeutic plasma exchange (TPE) for acute recurrence of FSGS after kidney transplantation (02/2014). Under treatment with weekly TPE, renal function remained stable (serum creatinine level: 110–130 µmol/L) with an unchanged proteinuria of around 8000 mg/24 hours. From 01/2016, we administered abatacept (10 mg/kg iv), one dose every 2 weeks. Since we didn’t observe a decrease of proteinuria after 2 doses, as described by Yu et al., we decided to administer a total of 4 doses. We hypothesized that abatacept didn’t reduce proteinuria at least stabilized the podocyte damage and consequently we stopped TPE. 14 days after the last TPE treatment there was no significant proteinuria reduction and serum creatinine remained stable. Serum suPAR levels slightly decreased during the treatment period, while suPAR concentration in the plasmaphereses didn’t change after the first abatacept administration. No adverse reactions were observed, except for a mild headache for half an hour after the first 2 abatacept administrations. We didn’t find Polyoma BK or JC virus activation in our patient following abatacept therapy.

Conclusion: According to recent reports, abatacept didn’t significantly decrease proteinuria, but we have to consider that we didn’t perform kidney biopsy for B7-1 research, considering the risk/benefit ratio. So we decided to continue chronic TPE & other investigations.
24-h ambulatory blood pressure monitoring and left ventricular hypertrophy in chronic kidney disease (CKD)

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Background: Few studies have assessed the role of 24-h ambulatory blood pressure monitoring (ABPM) in a general population of adults suffering from non-dialysis CKD. We examined potential determinants of left ventricular hypertrophy (LVH) and mass index (LVMI) in this population.

Methods: From a cohort of 242 stage IIIb-IV CKD adults, 69 patients had ABPM and transthoracic echocardiography performed simultaneously. Hypertension (HT) was defined as 24h blood pressure (BP) ≥130/80 mm Hg whereas BP dipping ≥10% was considered normal. We used multivariate linear and logistic regressions to assess determinants of LVH and LVMI. In the models, we entered dipping statuses, HT, ACEI/ARAII use, GFR <30 ml/min/1.72 m2, diabetes, smoking status, age, gender, Hb and PTH levels. Stepwise backward regression were performed.

Results: LVH was present in 28 (40.5%) patients. Characteristics according to LVH status are displayed in the Table. Although, ABPM readings were not statistically different between groups, patients with LVH were more likely to meet HT criteria, and had lower prevalence of systolic and mean dipping status. In linear regression analysis, only GFR <30 ml/min/1.72 m2 (coef = 21.05, 95% CI: 7.37 to 34.74, p = 0.003), systolic (coef = –13.19, 95% CI: –25.52 to –0.87, p = 0.036) and mean (coef = –14.41, 95% CI: –26.45 to –2.37, p = 0.020) dipping statuses were associated with LVMI. Diastolic dipping status and other confounders were not associated with LVMI. Logistic regression confirmed the association of systolic (OR = 0.19, 95% CI: 0.06 to 0.60, p = 0.005) and mean (OR = 0.23, 95% CI: 0.07 to 0.70, p = 0.010) dipping status with LVH. HT was also associated with LVH (OR = 4.12, 95% CI: 1.21 to 14.01, p = 0.023) whereas GFR <30 ml/min/1.72 m2 was not.

Conclusions: These data confirm the high incidence of LVH amongst CKD patients. Moreover, it suggests that systolic and mean BP non-dipping statuses measured by ABPM are a strong predictor of LVH in this population.

Baseline fractional excretion of sodium (FE-Na) may serve as an early diagnostic marker for the development of acute kidney injury in myocardial infarction patients

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Background: Acute kidney injury (AKI) after acute myocardial infarction (MI) is associated with higher rates of morbidity and mortality. Data regarding the diagnostic ability of fractional excretion of sodium (FE-Na) for AKIN in acute MI patients is scarce. We investigated the diagnostic value of FE-Na regarding the development of AKI in acute MI patients.

Methods: This is a post-hoc analysis of 436 patients (341 male, 63 ± 13 years) with acute MI (308 with ST-elevation and 128 with non-ST elevation MI). Patients were assessed for presence of AKI at 48 hours post admission and at hospital discharge using either the AKIN, the RIFLE or the KDIGO criteria.

Results: The incidence of AKI in the study population was 9.4% (n = 41) at 48 hours and 14.2% (n = 62) at hospital discharge. Patients who developed AKI at 48 hours (1.4 ± 1.6% vs. 0.69 ± 0.5%; P = 0.007) and those who developed AKI at hospital discharge (1.3 ± 1.5% vs. 0.67 ± 0.5%; P = 0.001) had increased baseline FE-Na in urine compared to patients without kidney injury. Patients with high FE-Na in urine (>2%) at baseline had an increased relative risk (RR) for developing in-hospital AKI both at 48 hours (RR 9.1 95%CI 5.5–14.8; P <0.001) and at hospital discharge (RR 7.4 95%CI 5.4–10.4; P <0.001) compared to patients with low FE-Na levels (<2%). Presence of high FE-Na in urine (>2%) at baseline was inversely associated with observed changes in glomerular filtration rate at 48 hours (Kendall’s tau-b –0.144; P <0.001) and at hospital discharge (Kendall’s tau-b –0.200; P <0.001).

Conclusion: Elevated baseline FE-Na (>2%) is associated with increased risk for developing AKI during hospitalization in patients presenting with acute MI and may serve as an early diagnostic marker.
**Elbasvir/Grazoprevir (EBR/GZR) treatment of Hepatitis C Virus (HCV) infection in patients with chronic kidney disease (CKD) stage 4/5: clinical, virological, and health-related quality of life outcomes in the C-SURFER study**

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**Background:** Introduction and Aims: Limited options are available for treating HCV patients with advanced kidney disease. C-SURFER is the first randomized, placebo-controlled, phase 3 study to evaluate an all-oral, ribavirin-free regimen in patients with CKD and HCV G1 infection.

**Methods:** 224 patients with HCV genotype (G)1 (G1a 52%, G1b 48%) and CKD 4/5 ± hemodialysis (HD) were randomized to EBR/GZR 224 mg/112 mcg once daily or placebo. Primary endpoint: SVR12. The impact of baseline resistance-associated variants (RAVs) on SVR12 in EBR/GZR after placebo therapy. Primary endpoint: SVR12. The impact of baseline resistance-associated variants (RAVs) on SVR12 in GT1a-infected patients was assessed, and health-related quality of life (HRQoL) was evaluated using the SF-36v2® Health Survey.

**Results:** SVR12 in patients who received EBR/GZR was 94.6% (211/223). Twelve patients failed to attain SVR12 (relapse, n = 3; discontinuation for AE, n = 1; administrative reason, n = 8). Excluding patients who discontinued for reasons unrelated to study drug, SVR12 was 98.6% (211/212). Among G1a-infected patients, baseline RAVs were present in 11.7% (13/111) of patients. SVR12 was achieved by all patients without RAVs (98/98 [100%]) and by 84.6% (11/13) of those with RAVs. Serious adverse events (AEs) occurred in 16 (14%) EBR/ GZR and 17 (15%) placebo patients; discontinuation due to an AE in EBR/GZR was 1% (n = 1), while in placebo patients was 0% and 4%, respectively. PK data indicate no need for dose adjustment in HD patients; geometric mean AUC0-24 ratio (HD/non-HD) ranged from 0.67 to 0.85 for GZR and 1.43 to 1.67 for EBR.

**Conclusions:** Once-daily EBR/GZR for 12 weeks was highly effective for treating HCV patients with advanced kidney disease. C-SURFER is the first randomized, placebo-controlled, phase 3 study to evaluate an all-oral, ribavirin-free regimen in patients with CKD and HCV G1 infection. Patients with GT1a infection and baseline RAVs had only a modest decrease in efficacy.

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**Mortality and other relevant clinical endpoints in the Swiss dialysis population for the 2015 census**

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**Background:** The national Swiss Dialysis Registry (srmqp) has been established first in the year 2006. However, participation is substantial only since 2013. Therefore, no analysis regarding endpoints have been available so far as for this large cohort of maintenance dialysis patients in the Swiss Dialysis Registry. In the present study, we evaluated the following endpoints: Death, transplantation, recovery of renal function, treatment stop (without recovery of renal function) and loss to follow-up

**Methods:** All medical establishments in Switzerland (both public and private; N = 88) providing chronic treatment by either hemodialysis (HD) or peritoneal dialysis had to provide relevant data for the year 2015. All individuals being on chronic dialytic therapy in 2015 were enrolled (N = 4453).

**Results:** The main cause of death was cardiac arrest / sudden death with an incidence of 11.9%. Patient refusing further treatment for ESRD is the second common cause of death in Switzerland with a percentage of 10.6%. In 8.5% of the patients, the cause of death is unknown. Survival probability is not different between men and women as shown in table 2. Three-quarters of all transplantations were performed from cadaveric kidneys. Fifty patients were transplanted preemptively (not included in table 1; data kindly provided by the Swiss Transplant Cohort Study). One third of all transplantations were performed in adolescents aged from 0 to 19 years.

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**Peritoneal Dialysis (PD) prevalence is low in Europe (<10%). Some of the barriers to its widespread are technical complications, late referral patients to surgery and patient reluctance to place a PD-catheter when uremic symptoms are still mild.**

**Methods:** To overcome these obstacles our group introduced in the clinical practice the use of the marsupialized PD-catheter (MC), a technical variation of Moncrief’s technique. The external part of the MC, as Moncrief’s one, is embedded in the subcutaneous tissue and the complications rate is lower compared to Moncrief’s technique (no sieromas/hematomas). All patient accepted the operation without complications.

**Conclusions:** There is no obvious gender difference regarding deaths and transplantations between men and women. Despite the fact that dialysis patients in Switzerland are older compared to other countries, the survival probability is still higher in Switzerland. However, in order to validate these data, prospective analyses over the upcoming years are required.
any discomfort before PD-start. The mean training time was short (5 days), in 88% outpatient and, whenever possible, it started on Monday to be completed on Friday.

Conclusions: – The MC is feasible and easy to externalize. – The low complication rate is the consequence of the complete abdominal scar healing before starting PD, without the risk of pulling the catheter, and the technical improvement of the Moncrieff Technique. – Patients accepted the operation some months before PD-start because they had no changes in physical appearance or discomfort, reducing the risk of late-referring to surgery. – The MC allowed us to reduce possible organizational problems. This made easier starting PD outpatient.

Methods: We conducted a prospective, single-center, open-label 8-week study to test whether the T50-value is amenable to therapeutic interventions. As a therapeutic intervention, dialysate magnesium was increased from 0.5 mmol/L to 0.75 mmol/L, and later reduced back to baseline concentrations (0.5 mmol/L).

Results: We included 33 chronic stable hemodialysis patients. A mixed linear model was used for data analysis. Increasing dialysate magnesium from 0.5 to 0.75 mmol/L during 6 dialysis sessions resulted in a mean increase of serum magnesium from 0.93 ± 0.13 (mean ± SD) to 1.02 ± 0.14 (P < 0.0001) as compared with three dialysis each before and after the increase of dialysate magnesium. A concomitant increase of T50 (219 ± 60 vs 240 ± 62, P < 0.0006) and of serum albumin (36.1 ± 3.7 vs 37.0 ± 3.6 g/L, P < 0.0103) was observed, while serum levels of sodium, potassium calcium, phosphate and bicarbonate remained unaltered. Modelling the combined effects of serum magnesium and albumin on T50 revealed an independent effect of serum magnesium on T50.

Conclusion: T50 can be therapeutically improved by increasing dialysate magnesium. The clinical significance of this improvement remains to be established.

Increasing dialysate magnesium improves serum calcification propensity: The SoloMag study

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Background: Clinical registers are fundamental tools for quality-control and monitoring, but filling them with complete data requires time, commitment and motivation of the involved persons. Usually all data are inserted manually, at the end of the year, and they are often incomplete, useless in the short time period, and unavailable for many people.

Methods: Our institution created the Clinical Information Catalogue (CIC) that automatically extracts all the data present in all the clinical register of the different departments. The CIC avoids data redoubling, guarantees complete information and it allows immediate data analysis with Business Intelligence Instruments. This strategy has been made available also for the Dialysis Units after a multicenter vascular access register catalogue: an innovative user-friendly vascular access register

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Exploring predispositions to peritoneal fibrosis in two mouse strains

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Introduction: Peritoneal fibrosis (PF) occurs in patients on long-term peritoneal dialysis and the degree of PF varies between patients suggesting involvement of a genetic component. Previous work showed genetically different strains of mice display different degrees of PF in response to the profibrotic mediator, TGF-β1. SJL mice showed resistance to TGF-B1 effects whereas C57 mice were most susceptible. The aim of this project was to identify the cellular mechanisms leading to PF susceptibility in particular the role of epithelial–mesenchymal transition (EMT).

Methods: Adult C57 and SJL mice were intraperitoneally administrated with adenovirus expressing TGF-β1 or control construct. Tissue was harvested at day 14 and processed for histology, protein and gene expression analysis. Peritoneal cells were also isolated from C57 and SJL mice and treated with TGF-β1 for 24 and 48hrs. Markers of EMT including E-Cadherin, procollagen type 1 and alpha-smooth muscle actin (αSMA) were analysed at protein and gene level.

Results: Peritoneal tissue from TGF-β1 treated C57 mice showed a marked increase in thickness compared with SJL mice. SJL peritoneal cells showed increased expression of E-cadherin following 24hrs TGF-β1 treatment whereas C57 cells displayed a decreased expression. Furthermore, there was reduced expression of αSMA in the SJL cells compared to C57 cells.

Conclusion: Mouse mesothelial cells are difficult to culture and the method requires further optimisation. SJL mice may be resistant to EMT due to the reduced response of E-cadherin after TGF-β1 compared to the C57 mice. Future studies will explore E-cadherin signalling pathways involved in both strains of mice.

New access, new problems

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Background: The transradial approach to cardiac catheterization has many advantages over the transfemoral approach and is increasingly being used for diagnostic coronary angiography and percutaneous coronary intervention. It is associated with fewer vascular access complications and reduced major bleeding. However there is still a risk of 1–10% for radial artery complications including radial artery occlusion.

Case: A 56 year old patient with ADPKD started chronic hemodialysis after allograft failure. A 6 years old cimino fistula on her left forearm was used as dialysis access. Three months after initiation of hemodialysis she presented with painful splinter hemorrhages of the fingers on her right hand. Evaluation for infectious endocarditis with blood cultures and transthoracic echocardiography were negative. Two weeks before, a percutaneous coronary intervention was performed due to cardiac ischemia. As access a transradial approach on the right side was used. Further investigation with a duplex sonography of the radial artery revealed a pseudoaneurysm of the radial artery at the site of the puncture, which was probably the cause of peripheral embolism. Surgical repair of the pseudoaneurysm was performed to eliminate the source of embolism and to save the radial artery for future AV-fistula creation.

Conclusion: In patient with severe chronic renal insufficiency or on dialysis transradial approach for cardiac catheterization should be avoided, as there is a risk of radial artery complication limiting the use for future AV-fistula creation.

Figure 1

Impact of reducing salt content of meals consumed during hemodialysis sessions on hemodynamic stability and interdialytic weight gain

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Background: Hemodialysis patients are advised to reduce daily salt intake in order to reduce interdialytic weight gain (IDWG). In order to counterbalance protein-losses, protein-rich meals are provided during hemodialysis sessions in many centers, but their sodium content is not always taken into account. The aim of this study was to assess the influence of the sodium content of sandwiches provided during hemodialysis sessions on IDWG, dry weight, and hemodynamic stability during dialysis.

Methods: Monocentric, interventional, prospective study. In August 2015, sodium content of the sandwiches given to all patients during dialysis was reduced by 1 g, from 2.4 to 1.4 g. All patients treated with three weekly hemodialysis sessions and free of hospitalisation, transplantation, and transfer to another center or death throughout the four-month study period were included in the study. Mean BP, body weight, IDWG and dry weight was assessed two month before and two months after the reduction of sodium content of the sandwich. Results: A total of 78 patients were screened, and 40 included in the final analysis. Median age was 63 years (range 28–90), 35% female, 22.5% had a residual diuresis >0.5 l/day and median BMI was 26 kg/m² (19–36). Overall, there was no significant change in the values before and after the change of the salt content of the sandwich, except in the percentage of symptomatic drops in BP (6.1% in high salt versus 4.8% of HD sessions low salt sandwich, p = 0.02).

Conclusion: Blood pressure and interdialytic weight gain were not altered when reducing salt content of the meals consumed during hemodialysis, whereas hemodynamic stability was slightly improved.

Table 1

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<td>% BF D</td>
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Before dialysis (BD), after dialysis (AD); systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP), percentage of symptomatic drop in BP (APD); interdialytic weight gain (IDWG)

An iPad application to support training by self-instruction for PD

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Background: Many efforts have been undertaken to increase the prevalence of home dialysis, i.e. peritoneal dialysis (PD), in Switzerland. Towards this goal, recruitment of candidates that formerly have been considered ineligible for this treatment modality, needs to be improved. Specifically, patients with difficulties to learn the PD handling should be targeted by using audiovisual training enhancement tools.

Methods: A specific, multistep audiovisual learning program was developed and implemented as an Apple iPad application.

Results: After regular real life PD handling instructions and training given by the nephrology nursing staff patients can achieve further
practice by self-instruction through the iPad application. Each individual aspect of the PD process is illustrated step-by-step in short video clips. Informations are supplemented through parallel vocal instructions and written text provided as captions. The patient can select, stop, and repeat each section of the instruction process by easy on-screen touch interaction.

Conclusions: An interactive iPad app to enhance the PD learning process by the patient has been developed and implemented at our institution. Future evaluations will show whether audiovisual techniques are helpful for better promotion and implementation of home dialysis modalities in patients with endstage renal disease.

Results: 203 out of 210 prevalent patients were enrolled: age 73 ± 12 years, 62% male, HD-vintage 3.9 ± 3.3 years, 41% diabetic. 149(73%) patients undergo HD with AVF; 54 (27%) patients with CVC. 28 (14%) patients didn't undergo any AVF placement because of unsuitable anatomy/clinical conditions and 26 (13%) patients were late-referral. 127 (63%) started with CVC (CVC-first) and only 76 (37%) patients started with AVF (AVF-first). Patients were divided in two groups according to VA type used at HD start. 638 new VA were created (456 CVC-first vs 128 AVF-first, p <0.05). 295 rescue intervention, surgical or endovascular, were made (162 CVC-first vs 128 AVF-first, p <0.05) in a follow up time of 9706 months (5030 CVC-first vs 4676 AVF-first). Incidence rate of VA interventions expressed as n intervention/patient/year was 1.47 in CVC-first, 0.8 in AVF-first (p <0.05).

Conclusions: According to guidelines, AVF prevalence rate is acceptable. Late referral and unsuitable anatomy do not justify the low rate of AVF-first patients. CVC-first patients are exposed to higher risks of new intervention to keep primary and secondary patency. This data suggest that a timely referral to surgeons and early creation of permanent VA by dedicated teamwork improves the success rate of AVF decreasing HD-bridge CVC so enhancing survival and life-quality.

Colonic angiodysplasia and peritoneal dialysis: two case reports

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Background: Colonic Angiodysplasia (AD) is the most common gastrointestinal vascular lesion and a frequent cause of hidden bleeding. AD is an acquired dilatation of arterioles and veins and it’s supposed to be caused by intermittent venous congestion. AD is frequent in patients with chronic kidney disease, with increased complication risks in patients with end stage renal disease, that usually have multiple bleeding causes: uremic milieu, antiplatelet and anticoagulant drugs, also during hemodialysis (HD) session, overhydratation, phosphate binders. Colonic diverticulosis is a relative contraindication for PD, no recommendations about colonic-AD are given by guidelines.

Clinical cases: We present the case of two 60-years-old male patients with severe colonic AD-related anemia on PD. Both patients after more than 2 years from PD-start (APD by night plus icodextrin 2L by day) developed severe anemia: the only recognisable cause was a colonic-AD bleeding. For them PD was considered better than HD because no anticoagulation is needed, nevertheless all the attempts to stop the bleeding (multiple Argon-plasma sessions, anticoagulant-antiplatet therapy discontinuation, colic angiography with embolization) have been vain. Patient 1 was shifted from PD to HD for two reasons: to plan a colic resection and also because of an ultrafiltration decline. One month after the shift we noticed that the bleeding stopped so he never underwent to surgery. For this reason we decided to shift temporarily to HD patient 2 solving, also in this case, the bleeding. Two months later, patient 2 restarted PD while lower PD-solution volume and no further bleeding episodes in the next 6 months recurred.

Discussion: We believe that filling the abdomen with PD-solution could sustain the bleeding as consequence of an increase of the peritoneal pressure that worsen the colic venous congestion.

Conclusions: In patient with colonic-AD, DP indication should be evaluated with attention for its uncertain effect on bleeding.

Prospective arteriovenous access management in clinical practice

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Background: KDOQI guidelines recommend an organized monitoring and surveillance approach to improve access survival and to decrease hospital admissions for access dysfunction in haemodialysis population. We present our experience with prospective dialysis access surveillance since 2007.

Methods: Since 2007, all consecutive patients treated for at least 90 days after access creation at our centre underwent standardized access surveillance during their dialysis time, including clinical, biochemical, imaging, and function parameters as well as flow monitoring. Data of dialysis access,
surveillance and complications were entered prospectively in a database.

Results: Data from 133 arteriovenous accesses (40 grafts, 93 native fistulas) were analysed. Cumulative time at risk was 93.6 patient years for grafts and 344.5 patient years for native fistulas. Median access survival was 59.3 months for grafts and >108 months for native fistulas. A functional loss occurred in 5/40 grafts after a median duration of 33.6 (range 16–61) months (0.053 events per patient-year) and in 17/93 native fistulas after a median duration of 31 (range 3–91) months (0.049 events per patient-year). Loss through thrombosis occurred in 0.070 grafts per patient-year and in 0.017 native fistulas per patient-year. No single dialysis access was lost due to infection, which means an incidence of less than 0.01 per patient-year in grafts and less than 0.003 per patient-year in native fistulas. These results compare favourably with the KDQI clinical outcome goals of thrombosis incidence (<0.25 episodes/patient-year in native fistulas, <0.5 episodes/patient-year in grafts), infection (<10% in grafts, <1% in fistulas) and overall patency (>2 years for grafts, >3 years for native fistulas).

Conclusions: Our data confirm that prospective access management performed during dialysis sessions is capable of surpassing KDQI clinical outcome goals. Bed-side flow monitoring is effective and the benefit of prolonged access patency outweighs the burden of surveillance.

Complications and hospital stays in our peritoneal dialysis population (incident patients, 01.01.2015–30.06.2016)

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Background: Observational studies suggest that survival of patients treated with Peritoneal Dialysis (PD) is not inferior to those treated with hemodialysis (HD). Different studies showed that PD might provide a short-term survival benefit, but doubts remain about possible selection biases. Since 2012 the “Schweizer Verband für Gemeinschafts-aufgaben der Krankenversicherer” (SVK) has a contract with the Hospitals (H+), to foster home treatments. Since 2015, the goal is to include 20% of the incident patients, who require a Renal Replacement Therapy (RRT), in a home treatment program. In practice PD is the main home treatment in Switzerland. As a consequence of the SVK/H+ contract, home treatment prescriptions rose from 9% (2011) to 27% (2015), in our center we observed how starting PD in older adults with multiple comorbidities, increases hospital stays and complications.

Methods: We registered hospitalizations, temporary switch to HD and incidence of main complications (peritonitis, hernias, fluid leaks and need of catheter replacement) among patients who started PD between 01.01.2015 and 30.06.2016.

Results: 14 patients (7 females, 7 males) were started on PD during the observation period, with a mean age of 68 (±11). The mean follow-up from catheter insertion to 30.06.2016, or to death or to HD, was 218 (±186) days. During the observed period, the patients were switched to HD for a mean period of 21 days.

Conclusions: Starting PD in our population caused frequent complications and prolonged hospital stays, especially in the first weeks. The SVK/H+ contract might force caregivers to suggest PD to older patients, more prone to complications.

Intradialytic hypotension correlates with age, diastolic blood pressure and relative blood volume decrease

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Background: To help preventing dialysis hypotension, newer dialysis machines estimate changes of relative blood volume (RBV) from online hematocrit measurements. However, there are no available algorithms to predict each patient’s critical RBV threshold. The present study evaluated determinants of dialysis hypotension including the role of intradialytic RBV.

Methods: A database of 24862 individual hemodialysis sessions in 199 patients of the Kantonssspital Aarau hemodialysis unit between Jan 1, 2015 and July 4, 2016 was created from the therapy data management system (TDMS). Only sessions with an initial systolic blood pressure >100 mm Hg were considered, and patients with <12
dialyses in the resulting set were excluded, resulting in 22803 dialysis sessions with evaluable blood pressure and RBV data from 151 patients. Dialysis hypotension was defined as any measured systolic blood pressure <100 mm Hg and <80% of baseline systolic pressure. All patients were on thrice weekly hemodialfiltration/hemodialysis sessions of at least 4 hours length. Dialysate Na and Ca were 140 and 1.25 mmol/L.

**Results:** Dialysis hypotension occurred in 3857 of the 22803 dialysis sessions (16.9%), 19 of 151 patients (12.5%) never had hypotension, and 71/151 (47%) experienced it in <10% of dialysis sessions, which was defined as "stable" for the purpose of calculation. Stable patients were younger (age 64.1 ± 1.9 vs. 70.1 ± 1.4, p < 0.005) and had higher predialytic diastolic blood pressures (67.5 ± 14 vs. 61.4 ± 13, p < 0.005), but similar mean systolic pressures and ultrafiltration volumes (2.7% of body weight). Mean minimal RBV per dialysis was higher in stable patients (89.1 ± 0.5 vs. 87.8 ± 0.4%, p < 0.05).

**Summary and Conclusions:** Age, low diastolic pressure and lower RBV all correlate with dialysis hypotension. Although the determination of patient-specific RBV thresholds remains empirical, target RBV thresholds should be higher in older patients with low diastolic blood pressures.

**Is peritoneal dialysis a feasible option for end-stage renal disease in patients after liver transplantation and repeated abdominal surgery?**
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Nephrology Department, Bürgerspital, Solothurn

**Background:** End-stage renal failure (ESRD) represents a frequent complication after non-renal solid organ transplantation and was reported to be especially high after liver transplantation. Limited data exists about the feasibility and safety of peritoneal dialysis (PD) after liver transplantation. Here we report a case of a 64 years old female who underwent liver transplantation, reached cyclosporine-induced ESRD and is now successfully treated with PD for more than 1 year.

**Case:** 1987 liver transplantation was performed following Budd-Chiari syndrome. At this time multiple abdominal surgical revisions were necessary before discharge from the hospital was possible. After decades of treatment with cyclosporine A the patient developed progressive kidney disease. Furthermore diagnosis of a myeloproliferative disorder (essential thrombocytocemia, JAK2 V617F mutation) was made in 1994 followed by a long-term, ongoing treatment with hydroxyurea. PD was initiated in September 2015 immediately after implantation of a Tenckhoff catheter when the patient developed uremic symptoms. In 12 months of follow-up with a regime of 4 dwells per day of a standard PD Solution neither technical nor infections complications associated to the PD procedure were observed. Actually, the patient is doing well and meets all criteria of an adequate dialysis prescription according to the actual guidelines.

**Conclusion:** Peritoneal dialysis is feasible in patients after liver transplantation, even in the presence of repeated abdominal interventions following the transplantation period. In our single case, a similar outcome in terms of complications and method-survival is observed when compared to patients without previous intraperitoneal organ transplantation.

**Serum calcification propensity is improved by increased dialysate bicarbonate and dialysate magnesium:** The BiMag pilot study
Andreas Pasch1, Matthias Bachter1, Edward Smith2, Katarina Benackova2, Dominik Uehlinger2, Anne Dschietzig, Vesna Reinmann, Stefan Farese
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**Background and aims:** Serum Calcification Propensity can be measured by a novel blood test, which determines the transformation of patient-specific RBV thresholds remains empirical, target RBV thresholds should be higher in older patients with low diastolic blood pressures.

**Results:** One patient, hospitalized during this study due to an unrelated problem, was excluded from the analysis. Increasing dialysate magnesium led to an increase of serum magnesium from 1.0 ± 0.17 to 1.15 ± 0.17 mmol/L (p <0.01) and increasing dialysate bicarbonate led to an increase of serum bicarbonate from 20.2 ± 1.7 to 23.4 ± 1.8 (p <0.01). T50 was 242 ± 40 min. at baseline, 265 ± 61 min. while on increased bicarbonate, and 267 ± 57 min. while on increased magnesium. Combining increased bicarbonate and magnesium resulted in a T50 of 282 ± 67 min. (p <0.014 when compared to baseline). After 1 week washout, serum magnesium was 1.04 ± 0.19 mmol/L, serum bicarbonate 19.6 ± 1.7 mmol/L, and T50 255 ± 52 min.

**Conclusions:** Serum calcification propensity is improved by increasing dialysate bicarbonate and magnesium. Further studies with longer observation periods are needed.

**Therapeutic plasma exchange (TPE) with standard renal replacement equipment: a 10 year single-center experience**
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Division of Nephrology, Ospedale Regionale di Lugano, Lugano

**Background:** TPE is an extracorporeal procedure, performed using a highly permeable filter with a multifunctional hemodialysis device. It removes high molecular weight substances from plasma, including pathogenic autoantibodies, immune complexes, cryoglobulins, myeloma light chains, endotoxin, cholesterol-containing lipoproteins. TPE plays a key role in the management of various diseases. We analyzed data of patients who received TPE during the last 10 years and we report our single-center experience.

**Method:** We analyzed retrospectively all TPE treatments with membrane separation technique between 2006 and 2015. During
10 years 448 TPE treatments were performed in 43 patients. The replacement fluids used were 5% albumin and fresh frozen plasma in all treatments.

Results: TPE procedures were performed for neurological diseases (n = 132), hematological diseases (n = 118), renal transplantation (n = 99), immunological/rheumatological diseases (n = 69), kidney diseases (n = 24) and metabolic disorders (n = 6) (fig. 1). Main treated diseases were myasthenia gravis (23%), other nervous system diseases (18%), including 3 cases of neuromyelitis optica, 3 cases of CIDP and 1 case of acute disseminated encephalomyelitis. Further, we treated TTP (18%), Waldenström macroglobulinemia (9%), kidney graft rejection including a case of relapsed FSGS after transplantation (7%), multiple sclerosis (4%), Guillan-Barré syndrome (5%), antiphospholipid syndrome (5%), rheumatic diseases (2%), pauci immune RPGN (5%) and finally Goodpasture’s disease (2%) and hypertriglyceridemic pancreatitis (2%) (fig. 2). The annual number of treatments has significantly increased in the last 10 years (fig. 3).

Discussion: We could not demonstrate a constant correction factor in the studied glucose concentration range. In the glucose concentration range of around 100 mmol/l a correction factor of 0.15 might be applied. As these glucose concentrations are usually only encountered in the setting of a peritoneal equilibration test, the clinical relevance of the measurement error is probably rather limited.

Conclusions: In our practice there is no need for routinely correcting the creatinine measurement in peritoneal dialysate for glucose.

Measuring creatinine in peritoneal dialysate: determination of the glucose correction factor
Florian Buchkremer, Luca Bernasconi, Andreas Bock
Kantonsspital Aarau, Aarau

Background: The Jaffe method for creatinine determination is based on the chromogenic reaction of creatinine with picrate. It continues to be in widespread use. Glucose can form a non-creatinine chromogen with picrate and may lead to erroneous results of creatinine measured in peritoneal dialysate. The use of a correction factor has been recommended. The true creatinine concentration is determined by subtracting the glucose concentration times the correction factor from the measured creatinine concentration (true Crea = measured Crea – Gluc*CF). We tried to establish a correction factor for the Jaffe method used in our lab.

Methods and Results: Following the recommendations of Tam et al. (Peritoneal Dialysis International, 2009, pp 352–357) we first applied our Jaffe method on unused dialysate. Any measurement of “creatinine” would have represented non-creatinine chromogens. Contrary to Tam et al. our measurements were – correctly – negative. Next we spiked the dialysate solutions with known amounts of creatinine. The resulting correction factors are shown in figure 1.

The correction factor correlated with the glucose concentration with an r = 0.69 (p = 0.0015). However, the 99% confidence intervals for the regression line embraced the 0 line up to 80 mmol/l of glucose, indicating no difference from zero. The mean correction factor for glucose concentrations >80 mmol/l was 0.150 ± 0.012 (SEM; n = 5) at a mean glucose concentration of 108 mmol/l.

Discussion: We could not demonstrate a constant correction factor in the studied glucose concentration range. In the glucose concentration range of around 100 mmol/l a correction factor of 0.15 might be applied. As these glucose concentrations are usually only encountered in the setting of a peritoneal equilibration test, the clinical relevance of the measurement error is probably rather limited.

Conclusions: In our practice there is no need for routinely correcting the creatinine measurement in peritoneal dialysate for glucose.
The numbers refer to the pages of this supplement.

<table>
<thead>
<tr>
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