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OC 1

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 mpkCCDcl4 cells, a model of collecting duct principal cells, we showed that sodium transport stimulation by aldosterone activates HIF signaling pathway revealed by HIF1 α 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 mpkCCDcl4 cells. HIF1 α or HIF2 α silencing using lentivirus encoding specific shRNAs results in a strong increase of sodium transport via increased β and γ ENaC expression in mpkCCDcl4 cells. In vivo, C57Bl6 mice exposed to hypoxia display a down-regulation of ENaC subunits whereas NKCC2 and NCC are up-regulated. To clearly discriminate the role of HIF1 α and HIF2 α , we started to investigate the consequences of HIF1 α or/and HIF2 α knock-out on renal sodium handling using PAX8-rtTA/TRE- Hif1 α or/and 2 α fl/fl 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 reabsorption along the renal tubule have been analyzed by real-time PCR, Western blotting and immunohistochemistry. Preliminary results in mice challenged with low sodium diet, that stimulates sodium reabsorption via RAAS activation, revealed a down-regulation of NKCC2 and NCC whereas β and γ ENaC were up-regulated in HIF1 α 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.

OC 2

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 fluids 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

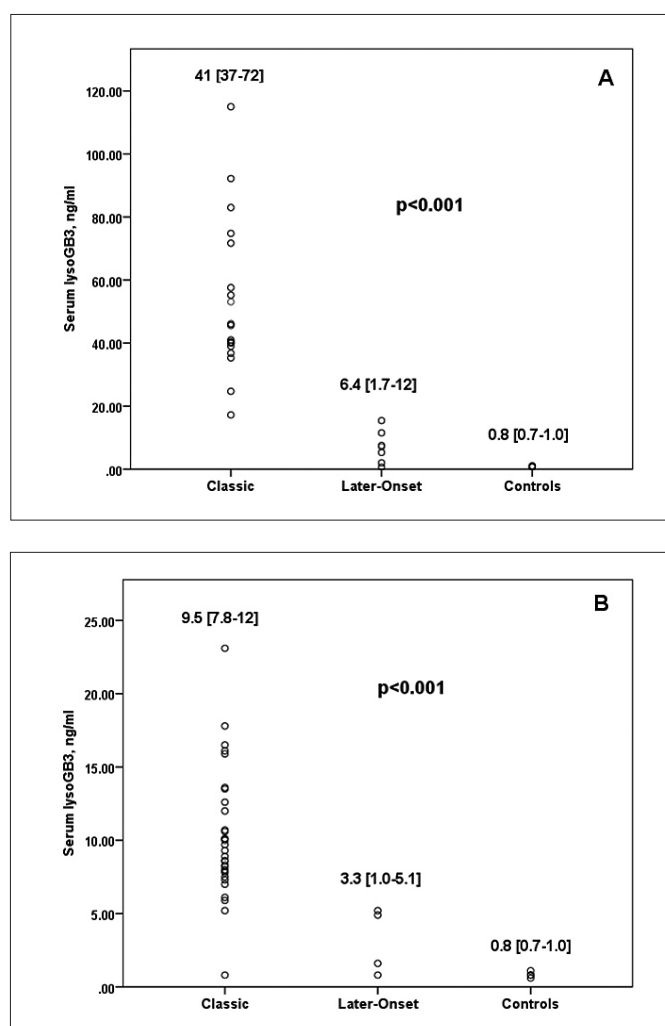


Figure 1A und B

the serum mediated inhibition of enzyme replacement therapy (table 1).

Conclusion: LysoGB3 helps to distinguish between patients without FD and with the Classic 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.

OC 3

Hypophosphatasia in mice deleted for the redox protein MEMO. NCCR Kidney.CH project

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Background: Hypophosphatasia is a bone mineralization disorder generally caused by mutations in the gene coding for tissue-nonspecific alkaline phosphatase (ALPL). Mediator of ErbB2-driven Cell Motility 1 (Memo) is a redox protein and an intracellular signaling modulator of growth factors. We previously showed that renal FGF23-induced signaling requires Memo. Now, we report that Memo deficiency in mice causes a disease resembling human hypophosphatasia.

Methods: Exon 2 of the MEMO1 gene was deleted in Memo fl/fl mice using a tamoxifen-inducible Cre recombinase to obtain conditional knockout (cKO) mice. Bones were studied by micro-computed tomography and histomorphometry. Serum, tissue and urinary

Characteristics	Univariate		Multivariate *	
	β (95% CI)	P Value	β (95% CI)	P Value
MSI, points	1.27 (0.88-1.67)	<0.001	0.58 (0.14-1.01)	0.01
eGFR, ml/min/1.73 m ²	-0.42 (-0.57 to -0.26)	<0.001	-0.18 (-0.34 to -0.02)	0.03
Cardiomyopathy	20.3 (8.60-31.9)	0.001	9.33 (0.11-18.6)	0.048
Serum-mediated ERT inhibition, %	1.02 (0.62-1.43)	<0.001	0.77 (0.47-1.06)	<0.001

Table 1

chemistry were analyzed. Primary bone cells were isolated and cultured for functional and metabolic studies.

Results: Memo cKO mice display severely reduced trabecular structure and mineral apposition in distal femoral metaphysis. The mice have higher plasma calcium levels, hypercalciuria, and increased urinary inorganic pyrophosphate excretion. Serum and bone tissue ALP activities were decreased in cKO, and intracellular redox state was altered in bone tissue of Memo cKO mice. Native PAGE analysis and thiol conjugation studies revealed no difference in bone ALP protein between genotypes, but bone tissue from Memo cKO animals revealed a diminished ALP stability. Primary cultured osteoclasts and osteoblasts from Memo control and cKO animals were of comparable cellular function, but Memo null osteoblasts revealed an altered metabolic profile.

Conclusion: Memo deletion leads to a mineral disorder that resembles a secondary and functional form of hypophosphatasia associated with distinct metabolic changes in the bone. Memo is thus a new candidate gene for hypophosphatasia.

OC 4

A single nucleotide polymorphism (SNP) in FSHR determines degree of liver involvement in female ADPKD patients (NCCR project)

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Background: Macroscopic cysts of the liver are the most common extra-renal manifestations of ADPKD. Females are more prone to liver involvement than males, cysts develop earlier, grow larger and are more numerous. Potentially, female sex hormones and gonadotropins could influence hepatic cystogenesis. It has been recently shown that FSH and FSH receptor are expressed in hepatic cyst-lining epithelial cells, activating the cAMP-MAPK pathway. Furthermore, genetic variants of FSHR have been described to modify the signaling outcome. In this project, we determined the A2039G polymorphism distribution in a small patient cohort and assessed the degree of hepatic cyst involvement. Furthermore, we overexpressed both FSHR variants in hepatic cell lines and investigated the signaling cascade upon FSH exposure.

Methods: Patient DNA was amplified and subjected to restriction fragment length polymorphism analysis. The degree of hepatic cyst formation was quantified with abdominal MRI. For the in-vitro experiments, hepatic cell lines were transfected with FSHR variants and stimulated with FSH. Cell lysates were subjected to Western blot and cAMP measurements.

Results: The observed FSHR allele frequency in the 35 assessed patients is similar to expected genotypes in the general population. Interestingly, the AG or GG genotype was significantly enriched in female ADPKD patients suffering from significant hepatic involvement, also at an earlier time point compared to the AA genotype. In line with this, our in-vitro experiments revealed different pathway activities for the A and G haplotype.

Conclusions: The G haplotype of the A2039A polymorphism promotes preterm formation of hepatic cysts in female ADPKD patients. This might be due to a potential serine phosphorylation site that is present for the G haplotype, which could influence the receptor signaling activity. Future research will be dedicated to uncover the causal link between sex hormones and the expression and activity of FSH and FSHR in the liver.

OC 5

The effect of dietary phosphate intake on blood pressure regulation and renal sodium chloride excretion in healthy male volunteers (NCCR Project)

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Background: High dietary phosphate intake is associated with a higher risk for developing kidney and cardiovascular disease with an increased overall mortality. Over the past decades dietary phosphate intake has risen dramatically mostly because of a high rate of consumption of phosphate containing beverages and food. Whereas

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 NaCl 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 high-phosphate diet included oral 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 urinary 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.

OC 6

Renal erythropoietin producing cells in vivo_NCCR Project

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Background: The adult kidney is an important sensor of molecular oxygen (O₂) and the PHD/VHL/HIF pathway is essential for the physiological response to reduced O₂ supply. In order to unravel the mechanisms involved in hypoxia-induced erythropoietin (Epo) expression, a greater understanding of the nature of renal Epo producing (REP) cells is required.

Methods: We developed a novel transgenic mouse model (Epo-CreERT2) with inducible Cre recombinase expression under the control of a 220 kb DNA fragment containing the mouse Epo gene locus which, when crossed with the Rosa26-flStopfl-tTomato reporter, allows us to permanently tag REP cells in response to Epo inducing stimuli. We investigated localization of REP cells in normoxia, following 8% FiO₂ (physiological stimulus) and 0.1% CO inspiration (profound tissue hypoxia) and followed cell fate over time. Using RNAscope technology we have localised Epo mRNA and semi-quantitatively evaluated Epo mRNA expression. We have applied tissue clearing techniques for 3-dimensional visualisation of REP cell clustering and interaction with blood vessels.

Results: Our results demonstrate that REP cells are clustered predominantly in the interstitium of the juxtamedullary cortex and that few cells are needed to maintain Epo production under physiological conditions. Under conditions of reduced O₂ availability, recruitment of additional REP cells, as well as an increase in the Epo mRNA produced per cell is required to meet the demand for increased Epo. Our data indicate REP cell proliferation following hypoxic exposure. Furthermore, we have demonstrated that previously tagged REPs are capable of Epo mRNA expression following subsequent hypoxic exposure.

Conclusions: Our data indicate that REP cells are a unique and dynamic population of cells which respond with exquisite sensitivity to changes in O₂ availability. Proliferation of these cells suggests a physiological adaptation to hypoxia and the generation of a population of REP cells primed for a subsequent or chronic hypoxic response.

P 1

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 forty 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.

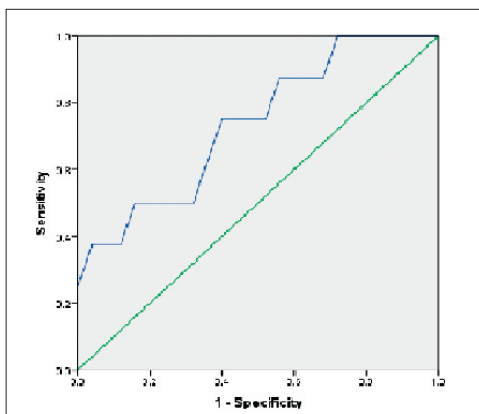
Results: The mean value of RRI was statistically significantly higher in group I than that of group II and group III. Out of 33 cases of LN cases, 6 patients had RRI of 0.7 and above giving a percentage of 18.18%. LN patients with RRI higher than 0.7 had statistically significantly higher age, mean serum 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, and therefore modifying treatment accordingly, but further follow-up studies are needed to evaluate its role in predicting response to treatment.

Demographic and clinical features of renal SLE patients grouped according to RI value

Variable	RI = < 0.7 (N = 27)	RI = 0.7+ (N = 6)	P
Male/female	5/22	3/3	1.04
Age (yr)	28.12 ± 9.465	41.80 ± 17.020	.017*
Disease duration (mo)	14.90 ± 20.129	24.1 ± 19.41	.487
Renal function			
Creatinine (mg/dL)	1.46 ± .914	5.32 ± 3.016	.000*
Blood urea (mg/dL)	57.50 ± 37.469	110.20 ± 65.155	.018*
eGFR (mL/min)	60.65 ± 34.427	33.80 ± 42.669	.141
Urine protein (g/24 h)	1.62 ± 0.868	3.50 ± 3.725	.241
Inflammatory markers			
ESR	59.54 ± 35.671	34.80 ± 22.151	.184
C-reactive protein	19.79 ± 31.092	12.70 ± 14.848	.625
Immunologic parameters			
Antinuclear Antibody	26 (96.3%)	6 (100%)	.632
Anti-dsDNA	24 (0.84 ± 30.158)	39.80 ± 78.951	.317
Serum complement C3	55.57 ± 27.924	65.00 ± 27.630	.497
Serum complement C4	12.79 ± 9.738	13.62 ± 11.324	.857
SLEDAI	21.85 ± 5.520	17.50 ± 9.983	.185
SLECRAS	10.20 ± 4.010	62.5 ± 2.061	.067
Renal SLEDAI	10.65 ± 3.472	11.00 ± 2.00	.855
Histologic class			
Class II	3 (11.1%)	-	0.202
Class III	3 (11.1%)	1 (16.7%)	
Class IV	17 (62.96%)	3 (50%)	
Class V	4 (14.82%)	1 (16.7%)	
Class VI	-	1 (16.7%)	
Activity Index (range 0-24)	7.87 ± 3.904	6.40 ± 2.965	.434
Chronicity Index (range 0-12)	2.16 ± 1.522	4.4000 ± 2.607	.014*
Mean blood pressure	108.12 ± 18.285	116.00 ± 20.756	.398

Table



Figure

ROC curve of Doppler-Based Renal Resistive index as a predictor of renal.

P 2

An in vitro model of idiopathic membranous nephropathy reveals PLA2R- 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 (PLA2R). The definitive proof for pathogenicity of PLA2R 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-PLA2R-antibody mediated injury to podocytes.

Methods: PLA2R expression levels in conditionally immortalized human podocytes were modulated by infection with a lentivirus vector carrying FLAG-tagged full length human PLA2R or by siRNA-mediated knock down. These cells were then pretreated with sera from PLA2R-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 PLA2R treated with a high-titer (1:1000) PLA2R 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 a noticeable synaptopodin rearrangement. The complement sublytic effect on podocytes is likely to involve the activation of the lectin pathway and C3aR1 and C5aR1 signaling as knock down of these receptors partially rescued synaptopodin. Synaptopodin and NEPH1 degradation appeared to occur via two independent pathways that require cysteine and aspartate proteases, respectively.

Conclusion: Podocyte injury by iMN serum and sublytic complement includes synaptopodin and NEPH1 degradation as well as Akt and ERK pathways inhibition. In addition, we have developed an in vitro assay to specifically assess the complement-dependent podocytopathic effect of iMN sera that will allow to screen for protective compounds.

P 3

Demography of the dialysis population in Switzerland

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Background: The national Swiss Dialysis Registry (srrqap) 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 srrqap is to provide quality control and quality improvement for dialysis therapy in Switzerland. In the present analysis, select demographic characteristics of the Swiss dialysis population are given.

Methods: All medical establishments in Switzerland (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 = 4453). 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 (68.1 vs. 67.9 years, respectively). However, women have been significantly longer on dialysis compared to men (51.5 vs. 45.5 months, respectively).

Conclusions: 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

Table

	All (100%)		In Centre (89.6%)		Home (10.4%)	
	Mean	Median	Mean	Median	Mean	Median
Age, yr	68.0	70.8	68.7	71.5	61.2	63.8
Dialysis vintage, months	47.7	34.0	49.8	36.0	29.3	17.0
Comorbidities, N	2.43	2.00	2.50	2.00	1.82	1.00
Charlson Comorbidity Index	4.42	4.00	4.50	4.00	3.78	4.00
Hypertensive, %	62.7		62.0		70.9	
Sex (male), %	64.0		64.3		61.6	

dialysis patients is over 70 years old, with both mean and median age having increased by approximately 6 months compared to the 2013 census. Moreover, patients are substantially ill with 50% having two or more comorbidities. Of note, approximately one third of the dialysis population is suffering from chronic heart disease (CHD = 36.5%). Home dialysis patients are clearly younger and healthier compared to patients treated by in-center hemodialysis.

P 4

Familial nephrotic syndrome caused by COQ2 mutations, an inherited mitochondriopathy

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Background: The majority of familial steroid-resistant nephrotic syndrome (SRNS) is genetically determined. Recessive coenzyme Q2 (COQ2) mutations leading to a mitochondriopathy have recently been identified. Most affected individuals presented with neurological and muscular symptoms, whereas nephrotic syndrome (NS) has been reported very rarely. We here present siblings with SRNS. 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 severe NS, microhematuria and oliguria. No known consanguinity. Treatment with prednisolone for 8 weeks followed by cyclosporine A and ACE inhibitors was not effective. Two months after admission right-side hemi-myoclonus and hydrocephalus documented by MRI were diagnosed. NS persisted, renal function deteriorated (serum creatinine at the age of 2 y 3 months was 463 µmol/l) leading to death. No renal biopsy or genetic analysis could be done. Two years later her younger brother aged 18 months was admitted with NS, microhematuria and oliguria. No extrarenal abnormalities were detected. Renal biopsy revealed FSGS (NOS, not otherwise specified) and mild irregularities of the glomerular basement membrane. No abnormal mitochondria were seen. Genetic analysis showed compound heterozygous mutations in COQ2 (maternally, COQ2 p. Leu340Val; paternally, COQ2 p.Arg173Leu). Spontaneous clinical and laboratory improvement were noticed. Currently, the patient shows non-nephrotic proteinuria and preserved renal function.

Conclusion: Isolated SRNS due to COQ2 mutations is extremely rare. Treatment with ubiquinone (coenzyme Q10) may reverse the NS. Genetic analysis in familial cases with early renal manifestations is therefore of utmost importance. This is a good example of cooperation of different laboratories and centres in Europe.

P 5

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., 2013). 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, Non-essential aas, Branched chain aas or all aas in the same

proportion as in the protein mix). Both GFR and RPF were measured in free moving animals. GFR measurements were performed transcutaneously using FITC-sinistrin. RPF was determined by using radiolabelled 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.

P 6

Fetuin-A aggravates lipotoxicity in podocytes via interleukin-1 signaling

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Background: Sterile inflammation is considered critical in the pathogenesis of diabetic nephropathy (DN).

Objective: The objective of the present study was to investigate whether palmitic acid, Fetuin-A (FetA), or their combination elicit an inflammatory response in podocytes and whether they modify podocyte survival. In addition, we explored the potential role of interleukin-1 (IL-1) signaling in these processes. In vivo, the short-term effect of an anti-IL-1 antibody was tested.

Methods: Immortalized murine podocytes were used. FetA was used alone or in combination with palmitic acid. Monocyte chemoattractant protein-1 (MCP-1) was measured by ELISA. Podocyte death was determined by annexin V and propidium iodide staining. Diabetes was induced in DBA mice by intraperitoneal (i.p.) injections of streptozotocin for five days. Control mice were injected with sodium citrate buffer. Anti-IL-1β antibody was injected i.p. weekly at 10 mg/kg of body weight for the first two weeks and at 5 mg/kg for the following two weeks. Vehicle (saline solution) was injected to the control group.

Results: FetA or lipopolysaccharide (LPS) exacerbate palmitic acid-induced podocyte death, which is associated with induction of MCP-1. Moreover, blockage of TLR4 by the specific inhibitor TAK-242 prevents MCP-1 and attenuates podocyte death induced by palmitic acid alone or combined with FetA. In addition, inhibition of IL-1 signaling by anakinra, a recombinant human IL-1Ra, or a murinized

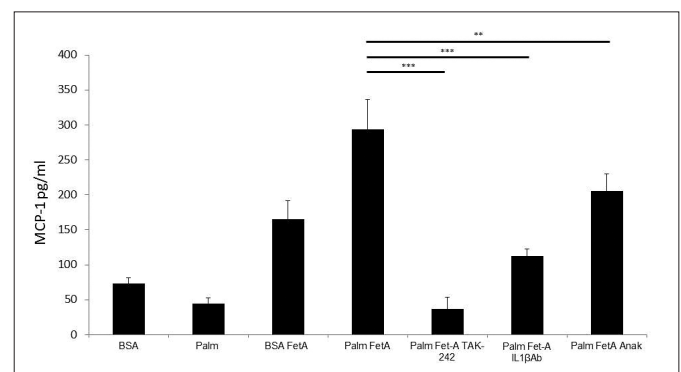


Figure 1

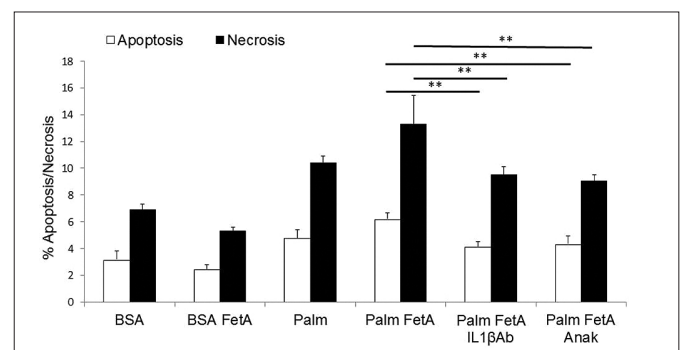


Figure 2

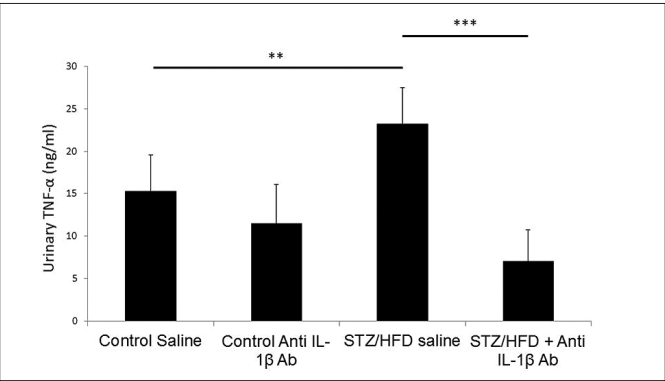


Figure 3

anti-IL-1β antibody attenuates the inflammatory and ultimate cell death response elicited by FetA alone or combined with palmitic acid. In vivo, short-term therapy of diabetic DBA/2J mice with an anti-IL-1β antibody prevented an increase in serum FetA and considerably decreased urinary tumor necrosis alpha (TNFα), a known risk factor for DN progression.

Summary: FetA similarly to LPS leads to an inflammatory response in podocytes, which exacerbates palmitic acid-induced podocyte death and our data imply a critical role for IL-1β signaling in this process.

P 7

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 monitoring.

	Female 1	Female 2	Female 3
Lyso GB3 level, ng/ml; cut-off <1.16 ng/ml	8.6	7.8	7.9
Current age, years	57	42	20
Age at diagnosis, years	55	39	12
Diagnosed as	index patient	family screening	family screening
Mutation	c.796G>T	c.1033T>C	c.744_745delTA
Predicted amino acid change	p.Asp266Tyr	p.Ser345Pro	p.Phe248LeufsX7
Category	missense	missense	deletion
Phenotype	classic	classic	classic
On ERT	+	+	+
Hypohidrosis	+	-	-
Acroparesthesia	+	-	+
Angiokeratoma	+	-	-
Cornea verticillata	+	+	+
Cardiomyopathy	-	-	-
eGFR ^{***} , ml/min/1.73m ²	94	86	128
Urine prot/creatinine, mg/mmol	normal	normal	900
Stroke history [†]	5	0	0

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.

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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.

P 9

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: 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-MetaboChip (Illumina) and 817/1041 individuals were available for this analysis after quality control on both array types. We extracted 58 known variants (53 missense and 5 loss-of-function) from the ExAC database (<http://exac.broadinstitute.org>), including the two classical PCSK9 nonsense SNPs (CYS679TER, rs28362286; 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.

CHR	SNP	Amino acid change	A1	A2	Minor allele frequency (A1) in SKIPOGH	MAF (European Non-Finnish) in ExAC (A1)
1	rs72646510	p.Met283Leu	A	C	0.15%	0
1	rs11591147	p.Leu46Arg	T	G	1.54%	3.49%
1	rs11583680	p.Val53Ala	T	C	13.73%	22.88%
1	rs540796	p.Tyr243Cys	A	G	18.67%	16.74%
1	rs562556	p.Val474Ile	G	A	18.67%	16.73%
1	rs505151	p.Gly670Glu	G	A	2.47%	3.97%

Table 1

Missense SNPs in PCSK9 segregating in the SKIPOGH study.

Lack of Fetuin-A exacerbates interstitial kidney fibrosis

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Background: Fetuin-A (FetA) is a circulating glycoprotein principally secreted by the liver into the circulation, mainly known for its inhibiting role in calcification processes. A less well known feature of FetA is its capacity to mimic TGF- β receptor and therefore its potential to compete with epithelial cells and fibroblasts for the profibrotic cytokine TGF- β . In CKD (chronic kidney diseases), renal fibrosis is one of the main features correlating with kidney function impairment, in addition CKD patients display low levels of FetA.

Aim: We hypothesize that in CKD, low levels of FetA could be a factor favoring progression of renal fibrosis. Here we investigate the effect of lack of Fetuin A on kidney fibrosis induced by Unilateral Ureter Obstruction (UUO).

Methods: Kidneys (contralateral and obstructed), liver and blood of FetA $-/-$, $+/-$ and $+/+$ (wild type) mice were harvested 1–2 weeks after UUO, and analysed by immunohistochemistry (IHC) Western Blot (WB) and qPCR.

Results and outlook: IHC showed that FetA $-/-$ obstructed kidneys displayed higher contents of Collagen, α -SMA and N-cadherin after 1 and 2 weeks of UUO when compared to wild-type or heterozygotes. Western blot analysis demonstrated a higher upregulation of mesenchymal and fibrotic markers (vimentin, α -SMA and N-cadherin) in obstructed kidneys of FetA $-/-$ than in wild-type or heterozygotes ones. In addition, Smad3 expression and phosphorylation was significantly increased.

Conclusions: Renal interstitial fibrosis following UUO was more pronounced in the absence of FetA. Thus lower FetA levels, which can be encountered in CKD patients, could facilitate the progression of kidney fibrosis. Next, we plan to reproduce these findings in another model of fibrosis, decipher the regulation of FetA expression and treat mice with recombinant FetA in order to counteract fibrosis progression.

TRANSPLANTATION

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) (34.9% 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 herpes simplex infections (5.5% vs 4.0%). Episodes of lower urinary tract infection (cystitis) occurred more often in the denosumab than in the control

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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 extent week/non-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

OC 8

using subclass specific reporter antibodies – for the degree of corresponding bound mAb. IgG3 needed the lowest concentration to achieve maximum C1q-binding, followed by IgG1, while IgG2 and IgG4 did not show a considerable C1q-binding. C1q-binding occurred only after a critical amount of IgG1/3 has bound, and abruptly increased thereafter. If both, C-binding and week/non-C-binding IgG subclasses were mixed, C1q-binding was diminished proportionally to the fraction of IgG2/4. A two- to four-fold excess of IgG2/4 inhibited C1q-binding by 50% and very high levels (10-fold excess) almost (i.e. IgG2) or completely (i.e. IgG4) abrogated C1q-binding even in the presence of significant IgG1/3 levels that would usually lead to strong C1q-binding. Clinical pre-transplant serum samples of sensitized patients showed 1618/2813 SAB (57.5%) with bound HLA antibodies representing mixtures of at least one C-binding and one week/non-C-binding IgG subclass, with an excess of IgG2/IgG4 (i.e. ≥ 2 fold the level of IgG1/3) on 197/1618 SAB (12.2%) present in 21/73 (28.8%) patients. In conclusion, if quantitatively exceeding the amount of C-binding IgG subclasses targeting the same epitope, the presence of IgG2/4 inhibited the extent of IgG1/3 triggered C1q-binding on SAB in vitro. Roughly one in four sensitized patients revealed such an HLA Ab IgG subclass pattern.

OC 9

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 donor age >70 years was significantly associated with major complications (Clavien >3) (OR 3.99; 95% CI 1.37, 11.67), genitourinary complications (urinary tract infection; OR 5.85 (95% CI 2.01, 16.59) and urinary retention; OR 6.61 (95% CI 2.29, 19.11). There were more severe 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.

OC 10

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: (Sub)clinical 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.

OC 11

Long-term outcome of kidney transplantation in Fabry disease

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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) activity. As a result, glycosphingolipid substrates accumulate in plasma, urine and tissue lysosomes. Enzyme replacement therapy (ERT) with the recombinant enzyme is available since 2001.

Fabry nephropathy can lead to end stage renal disease requiring kidney transplantation (KTx). Little is known about its long-term outcomes. Moreover, because the donor kidney produces α -GalA, it is controversially discussed, if FD can be recurrent on the graft raising the question if ERT is needed to preserve KTx.

Methods: We are reporting 12 consecutive patients (mean age 51 [35–70] years) with genetically proven FD and kidney transplantation, all males, who were treated and followed-up at the University Hospitals Zurich and Bern.

Results: The longest follow-up of the kidney transplant was 25 years. During the median follow-up time of 182 [118–229] months, 5 patients died: three due to cardiac events, one due to suicide and one unknown (fig. 1). Two kidney transplants were lost due to chronic transplant failure (after 23 and 8 years). One patient was retransplanted. In

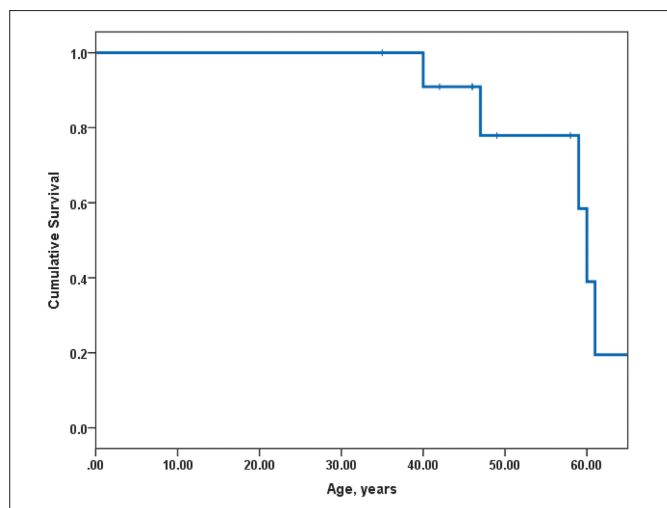


Figure 1
Survival of Fabry disease males after kidney transplantation.

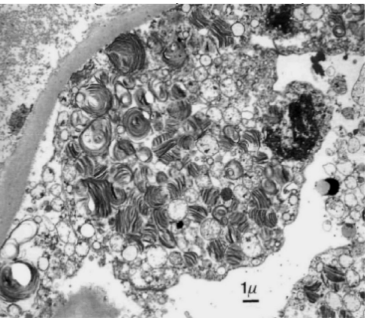


Figure 2
Kidney transplant (EM × 3700, inset × 83 700).
Formalin fixed and refixed in glutaraldehyde. Endothelial cell showing extensive glycosphingolipid substrates deposition 14 years without Enzyme replacement therapy (Gantenbein et al. 1995).

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.

Patient	Year of KTx	Year of ERT start	No ERT after KTx (months)	Age of transplant at last microscopy (months)	FD specific ultrastructural changes	Other histological changes	GLA mutation, predicted amino acid change
1	2005	2004	0	0.3	no	Rejection Banff 1B	c.125T>C p.Met42Thr
2	1995	2001	66	4	no	Intima fibrosis, acute interstitial nephritis	c.1033T>C p.Ser345Pro
3	1993	-	185	0.3	no	Intima proliferation	c.1033T>C p.Ser345Pro
4	2007	2001	0	8	no	Rejection Banff 2A	c.902G>A p.Arg301Gln
5	1999	2004	54	68	no	Interstitial fibrosis, tubular atrophy	c.899T>A p.Leu300His
	2011		0	12	no	Chronic glomerulitis, interstitial fibrosis, tubular atrophy	
6	2011	2004	0	12	no	Acute tubulus necrosis	c.613C>T p.Pro205Ser
7	1991	2001	120	262	no	Rejection Banff 2A, papillary renal carcinoma	c.370-2A>G Splicing defect
8	1993	2001	101	272	Scant myelin-figures in endothelial cells	Capillaritis with C4d positive staining	c.1167dupT p.Val390CysfsX9
9	1979	-	166	166	Extensive sphingolipid deposition in tubular epithelial and endothelial cells	Not reported	c.1167dupT p.Val390CysfsX9

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

Table 1
FD patients with kidney transplant biopsies.

Significance of isolated v-lesions on long-term graft survival in kidney transplantation
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Aim: The aim was to investigate the impact of isolated v-lesions appearing <1 year after kidney transplantation on long-term graft function and survival in the era of the current antirejection treatment.

Methods: In this retrospective analysis were included 574 recipients with different pre-transplant risks (ABO-compatible without pre-transplant HLA-DSA: n = 419, with HLA-DSA: n = 103, and ABO-incompatible: n = 52, respectively) who underwent ≥1 protocol and/or indication biopsy within the first year post-transplant. Based on the result of the index biopsy (defined as the most intense rejection episode), the recipients were divided into the following groups: (i) rejection with vascular involvement (v-lesions positive group), (ii) rejection without vascular involvement (v-lesions negative group), and (iii) no/borderline rejection. Within the v-lesions positive group, isolated v-lesions were defined as v1-3 but ≤1 and/or ≤1.

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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.

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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; ptDSAPos: 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 ptDSAPos patients (25% vs 27%). In both groups, 'suspicious for rejection' phenotypes were more frequent in surveillance than in indication biopsies (28% vs 16% in ptDSANeg patients, and 37% vs 29% in ptDSAPos 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 ptDSAPos patients. Inclusion of 'suspicious for rejection' phenotypes increased the one-year incidence of clinical (ptDSANeg patients: 18% vs 8%, p = 0.0005; ptDSAPos patients: 24% vs 18%, p = 0.31) and (sub)clinical rejection (ptDSANeg patients: 59% vs 22%, p < 0.0001; ptDSAPos 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'.

P 12

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 donor renal transplantation 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 and a strict blood pressure control, the initial 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. Due to the uncontrollable nephrotic syndrome, deteriorating renal function and a rapid progression of hyperfiltration injury in the re-biopsy, transplant nephrectomy was performed at 10 months post-transplant.

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.

P 13

Compartmentalization 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 serum CXCL10 discriminates subclinical compartment-specific inflammation. Therefore, the objective of this study was to investigate whether serum/urinary CXCL10 reflect subclinical allograft inflammation within different renal compartments (i.e. tubulointerstitial, microvascular and v-lesions only) and to identify compartment-specific confounders for their use as non-invasive biomarkers.

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 ≥ 2 (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 ≥ 2 vs. normal histology: 1.23 ng/mmol vs. 0.46 ng/mmol; p = 0.02), and microvascular compartments (median urinary CXCL10/creatinine ratios of microvascular inflammation vs. normal histology: 1.72 ng/mmol vs. 0.46 ng/mmol; p = 0.03), respectively. Conversely, elevated serum CXCL10 was not associated with inflammation within the micro-/vascular compartments (p ≥ 0.20), although it correlated with tubulitis (median serum CXCL10 concentration in the isolated tubulitis ≥ 2 group compared to the normal histology: 64.5 pg/ml vs. 41.4 pg/ml, respectively; p = 0.01). Urinary CXCL10 AUCs to discriminate tubulointerstitial/microvascular inflammation vs. normal histology were both 0.69 (p = 0.001 and p = 0.02, respectively). Furthermore, both urinary and serum CXCL10 were confounded by infection. Specifically, elevated urinary CXCL10 was triggered by BKV-viremia compared to CMV-viremia (p = 0.02), whereas serum CXCL10 levels in patients with either BKV- or CMV-viremia were equally elevated (p = 0.44), consistent with virus-specific inflammatory responses in different compartments (fig. 1).

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.

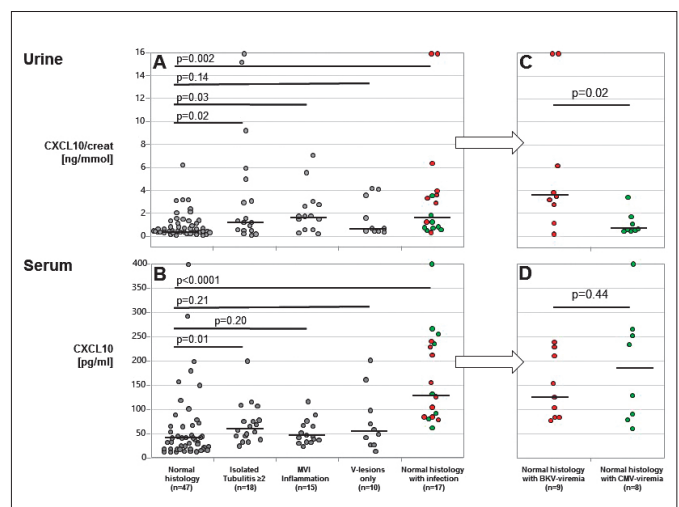


Figure 1

P 14

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

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Background: Kidney transplantation is the treatment of choice for patients with ESRD. Short- and long-term graft survival after kidney transplantation 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 years (for each patient), 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/fibrosis such as endothelin and aldosterone.

CLINICAL NEPHROLOGY / HYPERTENSION / MINERAL / ELECTROLYTES

OC 13

Comparison of furosemide/fludrocortisone with ammonium chloride test in the diagnosis of incomplete dRTA in recurrent stone formers: a prospective study (NCCR project)

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Background: Incomplete dRTA (idRTA) is a frequently encountered entity in stone formers (SF) that requires unmasking by an urinary acidification test. Since the description by Wrong and Davies in 1959, the short ammonium chloride (NH₄Cl) loading test is considered the gold standard for the diagnosis of idRTA. The furosemide/fludrocortisone (F/F) test has recently been proposed as a test with improved tolerability. However, the validity of the different provocative tests employed is currently unknown. Furthermore, it remains unclear which group of recurrent SF should undergo testing for idRTA.

Methods: We performed a prospective study in an unselected group of recurrent SF referred to our stone clinic to assess the reliability of the F/F test in the diagnosis of idRTA. All patients underwent metabolic work up for nephrolithiasis and sequential F/F and NH₄Cl testing.

Results: 142 recurrent SF were recruited for the study over a period of 3 years. Mean age was 45.7 ± 13.4 years and 73.2% were men. Prevalence of idRTA was 22.6% with the F/F test and 9.2% with the NH₄Cl test. Assuming failure to lower urinary pH <5.3 during the NH₄Cl test as gold standard for diagnosis, the F/F test had a positive predictive value (PPV) of 37% and a negative predictive value (NPV) of 97 % for the diagnosis of idRTA. Comparison of fasting urinary pH and urinary acidification capacity during F/F and NH₄Cl tests indicates that only a morning fasting urinary pH <5.3 reliably excludes idRTA.

Conclusion: The F/F test is an excellent screening test for idRTA in recurrent SF with a high NPV. Due to the low PPV, patients with a pathological F/F test need confirmation by NH₄Cl testing for idRTA diagnosis. In the absence of provocative testing, a diagnosis of idRTA can only be ruled out confidently with a morning fasting urinary pH <5.3.

OC 14

Changes of Urinary Risk Profile after short dietary intervention in Swiss Kidney Stone Formers

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Background: Calcium-containing kidney stones are frequent with high recurrence rates. Several studies have described a significant relation between nephrolithiasis and adverse renal outcomes, including ESRD. While hypercalciuria is a well-known risk factor, restricted intake of animal protein and salt, combined with normal calcium, has been shown to be more effective in stone prevention compared with a low-calcium diet. Notably, the average salt intake in Switzerland is twice as high as the WHO recommends, while surprisingly the intake of milk and dairy products is low. Thus, we wanted to test the effect of a low salt and low calcium diet on the urinary risk profile of recurrent calcium oxalate (CaOx) kidney stone formers (rKSF).

Methods: Standardized metabolic evaluation was performed, including a first 24-hour urine collection (normal diet), followed by a second collection after a 7-day low salt and low calcium diet.

Results: Out of 215 patients, 169 patients had calcium oxalate-containing stones. Of these 169 patients, 49 were hypercalciuric at baseline. Diet produced a highly significant reduction in 24-h urinary sodium and calcium excretions: from 201 ± 89 at baseline to 128 ± 88 mmol/d for sodium (p < 0.0001), and from 5.67 ± 3.01 to 4.06 ± 2.46 mmol/d (p < 0.0001) for calcium. Urine volume remained unchanged. Notably, no increase in oxalate excretion occurred on the low calcium diet (0.39 ± 0.26 vs 0.39 ± 0.19 mmol/d, p = 0.277). Calculated P_{sf} values were only predictive for calcium phosphate stones.

Conclusions: In conclusion, diet low in calcium, as in the wider Swiss population, and here tested as a short intervention did not result in an increase in oxalate excretion in rKSF. The recommendation of a low salt diet in a population with too little dietary milk and dairy products does not seem to increase the risk for CaOx stone formation. However, assessment and correction of low calcium intake in hypercalciuric KSF remains important.

OC 15

Serum calcification propensity is associated with renal tissue oxygenation and resistive index in patients with CKD or Hypertension

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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 (AHT) 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 applanation tonometry, and renal Doppler ultrasound was performed to measure renal resistive index (RRI).

Results: 145 participants were included. Mean T50 was 246 ± 129 min in 58 CKD patients, 275 ± 111 min in 48 AHT patients, and 324 ± 96 min in 39 healthy controls (ANOVA = 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 -0.13 ± 0.05, p = 0.016) R2* levels, RRI (β -0.005 ± 0.002, p = 0.009), and PWV (β -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.

OC 16

Association of kidney stone with chronic cadmium exposure in the general adult population

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The association between cadmium exposure and the prevalence of kidney stones (lithiasis) is well established in occupational exposure studies, but data in the general population are scarce and inconsistent. Tobacco is an important source of cadmium and, among non-smokers, food is the main source of cadmium exposure.

We explore the association between kidney stone and 24-hour urinary cadmium excretion in a multicentric population-based study (the Swiss Kidney Project on Gene and Hypertension or SKIPOGH). Participants were randomly selected from the adult population in three large areas: Bern, Geneva and Lausanne between 2009 and 2012. Urinary electrolytes and cadmium levels were determined in 24h urine using an inductively coupled plasma mass spectrometer (ICP-MS) with a hexapole collision cell. Kidney stone was diagnosed using ultrasound. The association between kidney stone and urinary cadmium was analysed by mixed logistic regression using different adjustment models according to the covariates significance (P < 0.05). Age, sex, center, diabetes, smoking, urinary electrolytes (Na, K, Ca, Mg, PO4)

and uric acid, kidney function and history of kidney stone were used for adjustment after performing backward regression. The 471 and 531 males and females had mean age 47.6 ± 17.5 years. Median urinary cadmium levels were 0.25 µg/24h (IQR: 0.15–0.39) and the prevalence of kidney stone was 6.7% (n = 67). The presence of kidney stone was associated positively with urinary cadmium excretion in models including age, sex and center [OR 11.3 (95%CI: 1.9–67.7), P < 0.001] and remained significant when adjusting for the other significant covariates [OR 12.7 (95%CI: 1.7–93.0), P < 0.001]. At low level chronic cadmium exposure, high urinary cadmium is associated with higher prevalence of kidney stones. More research is needed to understand the underlying mechanisms.

OC 17

Resistant hypertensive patients display lower exosomal thiazide-sensitive NaCl cotransporter expression after renal denervation. NCCR Kidney.CH project

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

Results: 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 possibly other renal transport proteins involved in blood pressure control.

OC 18

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 is meant to foster research in this field and collects epidemiological and biological data. We now report on patients included in 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

the five centers, including 2 × 24h urine collection, food and activity questionnaires, food diary and cristalluria measurements. Samples of urine, blood and DNA were stored in a biobank. All lab analysis were centralized. Follow-up visits are organized at 3 months and annually. **Results:** Between May 2014 and September 2016, 359 patients were recruited, 29% females and 71% males and data at 3-month follow-up visit were available for 138 patients. At baseline, mean BMI was 26.9 ± 4.7 kg/m². Mean 24h urine volume was 1804 ± 795 ml/d, Sodium 190.6 ± 41.3 mmol/d, Calcium 6.52 ± 1.64 mmol/d and oxalate 229 ± 75 umol/d. Noteworthy, 4.6% patients had primary

hyperparathyroidism discovered at baseline. At three month follow-up visit, urine volume increased to 2067 ± 729 ml/d. Sodium decreased to 167.1 ± 29.1 mmol/d, while calcium and oxalate remained unchanged. Metabolic parameters such as plasma cholesterol and Hb1Ac were unchanged.

Conclusion: Swiss stone formers show propensity to change nutrition habits at three months follow-up visit by decreasing sodium and increasing fluid intake. Longer follow-up is needed to confirm these encouraging data.

P 15

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

phosphate, FGF23, PTH, T50, Klotho and vitamin D level may be useful markers of IF and chronic vascular lesion in this population.

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.

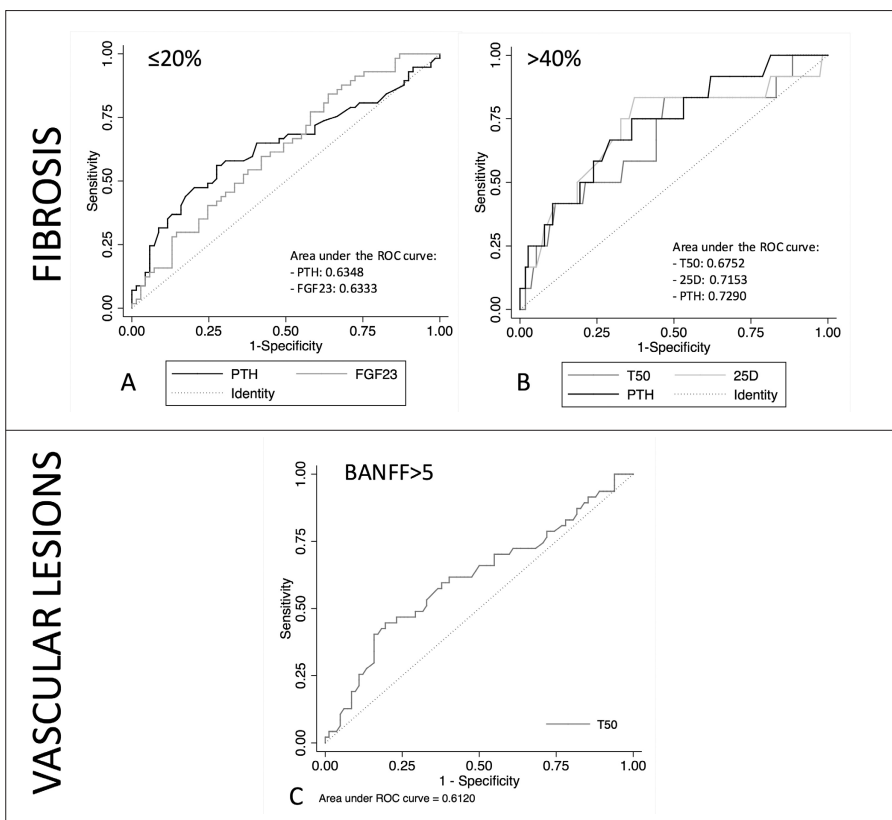


Figure 1: A: ROC curves of PTH and FGF23 in predicting fibrosis $\leq 20\%$; B: ROC curves of T50, 25D and PTH in predicting fibrosis $> 40\%$; C: Vascular lesions estimated by BANFF: ROC curve of T₅₀ in predicting significant vascular lesions (BANFF cv+ah+aah > 5).

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 on a natural logarithm due to abnormal distribution. 25D: 25-hydroxyvitamin D; FGF23: Fibroblast growth factor 23; PTH: parathyroid hormone; ROC: Receiver Operating Characteristic; T₅₀: Calcification propensity.

P 16

Airborne interstitial nephritis

Stefan Kalbermatter¹, Anne Tschacher¹, Peter Graber¹,
Marc Gutmann², Helmut Hoyer³, Denes Kiss¹

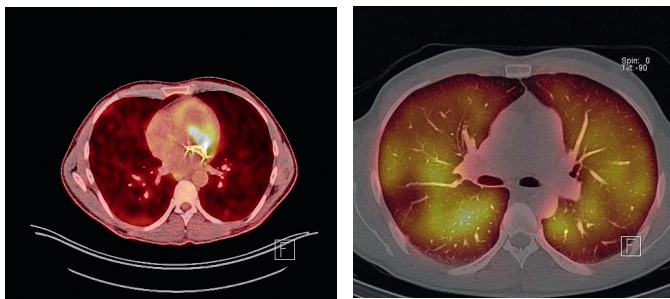
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Background: A 50-year-old man with a history of mitral valve repair one and a half years ago was complaining of dry cough, dyspnoea, fatigue, weight loss and night sweat for six months. Chest X-ray showed few small nodules and SPECT-CT peripheral perfusion 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 µmol/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



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.

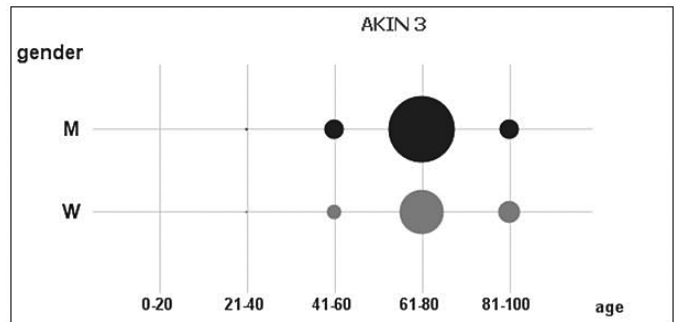


Figure 1
Repartition of gender and age in AKIN3.

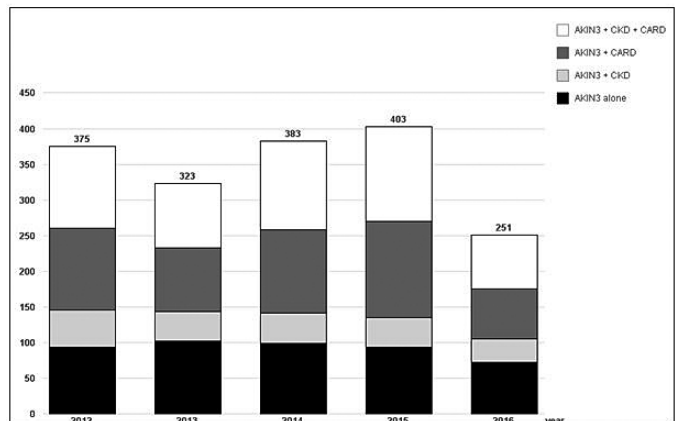


Figure 2
Evolution of AKIN3 categories per year (2016: only until 30.6.2016).

P 17

Acute kidney injury in a tertiary hospital: can we learn from medical coding?

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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 1'735 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+CKD+CARD. Figure 2 shows

Risk of brain ischemia due to carotid artery stenosis in the very elderly treated with antihypertensives: a hospital survey

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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 hypotension 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 and external carotid artery (ICC/ECC) stenosis were analysed together with sitting BPs 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

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disease). On admission, 76% were on antihypertensive drugs and 43% had their number changed. Mean BP was 149/88 mm Hg (36% sBP <140, 2/63 with sBP <100 mm Hg) vs. 129/72 mm Hg at discharge (64% sBP <140 mm Hg; $p < 0.05$, 0/63 <100 mm Hg). Mean IMD (right/left) was 8.7/9.4 mm. Frequencies of non-stenotic plaque were (right/left): CCA 13/16%, ICC 13/16%, ECC 19/29%, bulb 62/70%; of significant ($\geq 60\%$) ICC stenosis 5/5%, ECC stenosis 10/19%, bilateral ICC stenosis 2% (1/63), unilateral ICC occlusion 2/2%; none with bilateral ICC occlusion.

Conclusions: The risk of carotid stenosis-associated brain ischemia appears to be low in very old patients on antihypertensive treatment and sBP targets <140 mm Hg should be safe in this respect.

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Assessment of vascular age with a cuff-based oscillometric method in southern Switzerland: results from a drugstore survey

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Background: The Swiss Salt Survey pointed out a lower prevalence of hypertension and lower values of Body Mass Index (BMI) in the Italian-speaking part of Switzerland (ICH) compared to the other regions. An assessment of vascular age using a cuff-based oscillometric method estimating pulse wave velocity (PWV) is currently offered in a network of ICH pharmacies. We hypothesized that the peculiar cardio-vascular risk profile of this sub-population could shape a younger vascular age pattern.

Methods: We collected the demographic and clinical data of a drugstore survey performed in an unselected population in 24 ICH pharmacies between May 2015 and March 2016. PWV was measured with a cuff-based oscillometric method (Agedio B900) providing both arterial stiffness and blood pressure (BP) parameters. Data have been compared to the results of a population based European reference study.

Results: A total of 257 patients (mean age \pm SD, 55.8 ± 15.7 ; 27% women) were screened. Mean values (\pm SD) of systolic/diastolic BP were: $124.7 \pm 15.6/78.4 \pm 10.3$ mm Hg. The prevalence of hypertension was 21.5%. A large proportion of patients presented BMI in normal range (normal vs overweight/obese) according to the WHO classification (55.9%vs44.1%; p -value <0.001). The mean PWV of the population was 8.2 ± 2.1 m/sec. Patients were classified in high- vs normal-/borderline-PWV groups (26.56% vs 73.44%; p -value <0.0001). PWV by age groups was: 18–30 y: 4.8 ± 0.4 m/sec (European study reference value 6.2 ± 2.3 m/sec); 30–40 y: 5.5 ± 0.5 m/sec (6.5 ± 1.9 m/sec); 40–50y: 6.5 ± 0.5 m/sec (7.2 ± 2.3 m/sec); 50–60y: 7.7 ± 0.6 m/sec (8.3 ± 2.2 m/sec); 60–70y: 9.3 ± 0.7 m/sec (10.3 ± 2.8 m/sec); ≥ 70 y: 11.1 ± 1.1 m/sec (10.9 ± 2.8 m/sec). The mean vascular age was 2.9 ± 4.8 y above the predicted normal value. A linear regression model confirmed the positive association between vascular age and PWV (β coefficient 0.98; Standard Error 0.12; $p < 0.001$).

Conclusion: The data confirms that in the Italian-speaking region, the pattern of vascular age could be younger than expected. Further studies, on the epidemiological level, should be performed to verify that results have not been generated by a selection bias.

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Acute regulated 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 the abundance of pendrin expression using novel technique of urinary exosomes (UEs).

Methods: After acute acid (NH₄Cl 100 mg/kg) or equimolar alkali (157 mg/kg) or NaCl (110 mg/kg) loading in fasting individuals, urinary exosomes were isolated from hourly collected spot urine 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, alkali or chloride loading significantly alter UE pendrin expression in human UE within a few hours.

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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 (Fr) and to test if Fr D-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: Poliflux®RevaclearMAX; Filter B: Helixone®Fx80, Filter C: Polyflux®H210. Findings: A total of 117 HD sessions were studied. The mean (SD) filters (Fr) D-dimers were 0.19 μ g/L (0.56) for Filter A; 0.66 μ g/L (2.81) for Filter B; 0.33 μ g/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 but not in the blood can be considered a candidate marker for the evaluation of thrombogenicity during HD. Further studies are needed to elucidate the mechanism(s) and to confirm the usefulness of filter rinsing fluid D-Dimers as a clotting activation marker during HD.

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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 thiazides 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 severity and low number of patients. 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 calcium 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 metaphylaxis 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 dyspnea 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.

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, fluctuant thrombocytopenia, hypertension and chronic kidney disease with a creatinine of 140 µmol/l, proteinuria of 1.5 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 2/1'000 fragmented erythrocytes in the context of increased serum LDH 790 U/ml, and of unmeasurable haptoglobin. Because of low platelet count and small dedifferentiated kidneys a biopsy was not performed. ADAMTS13 activity was normal, search for Shiga-toxin producing *E. coli* was negative, whereas an in vitro assay able to detect complement activation on endothelial cells was positive, suggesting an atypical HUS (aHUS). The neurologic symptoms improved spontaneously, but the kidney function did not and, after the hospital stay, haemodialysis was started. Despite a 5 week IV course with an 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 646 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 118 patients, of whom 26 had severe AKI (stage II–III AKIN). AKI was present in 33 and 36% of the patients treated with ACEIs and ARBs respectively (ns). Severe AKI developed in 5 and 12.6% 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.

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Penile calciphylaxis – a rare presentation of calciphic uraemic 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 mmol/l, iPTH 1268 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 infusions, 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 extravascular 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.



Figure 1



Figure 2

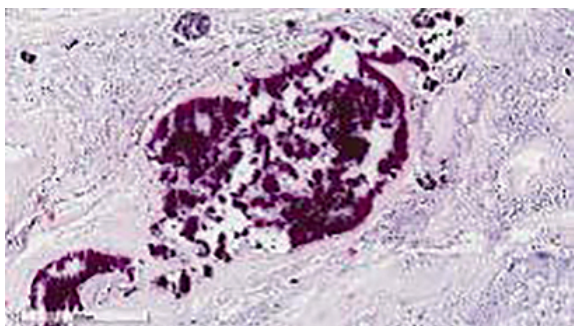


Figure 3

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Minimal change disease in SLE

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History: 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.

Clinical and Laboratory Evaluation: 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.

Course: 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.

Conclusion: In the literature several cases report a diffuse fusion of the epithelial foot processes of podocytes as a single morphologic feature in patients with SLE and nephrotic syndrome. According to some authors minimal change disease should be considered as a possible renal complication of SLE and not a coincidence.

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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 84 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 candida) in the lungs, alveolar hemorrhage was thought to be due to candida infection of the lung.

Conclusion: This case shows that even with a high clinical suspicion a completely different diagnosis is possible.

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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 hypokaliemia (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 (11062) and an elevated urinary excretion of aldosterone (28 ug/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.

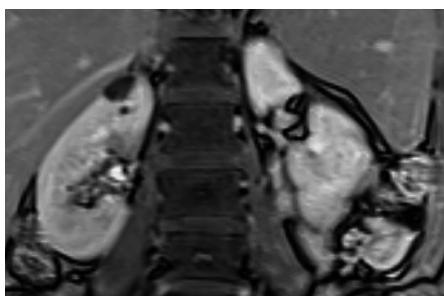


Figure 1

P 30

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-center 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 have been 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: (βcoefficient 1.867205; SE 1.280578). In a multiple adjusted regression model however, a statistically significant correlation between DB and risk of IDH (adjusted OR 1.53; 95% CI 1.03–2.28; p value 0.035) 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.

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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.

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Dialysate Chloride: an independent player in shaping the intradialytic hemodynamic pattern. Results from a cross-sectional multi-center study

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Background: Traditionally, in the multivariate analysis of blood pressure (BP) determinants during hemodialysis (HD), chloride (Cl-) was not considered as an independent player. However, increasing experimental evidence suggests that Cl- may have a role, perhaps

more important than that of sodium (Na⁺), in the regulation of BP, related to a wide spectrum of mechanisms such as vasoconstriction and renin secretion. Nevertheless a direct role of Cl⁻ on BP in HD has not been established yet, and to the best of our knowledge no study has investigated the hemodynamic intradialytic consequences of dialysate Cl⁻.

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 Δpre-post HD Cl⁻ (serum Cl⁻ pre-HD – serum Cl⁻ post-HD) with ΔBP and with the risk of hypotension. Laboratory and hemodynamic parameters were recorded. Data of 156 patients were analyzed.

Results: In a linear regression model Δ Cl⁻ showed a positive association with ΔBP (β -coefficient 0.75; $p = 0.01$), the effect was independent of serum and dialysate Na⁺ in the multivariate model (β -coefficient 0.67; p -value 0.02). A significant association was also found between dialysate Cl⁻ and ΔBP (β -coefficient 1.50; p -value 0.03). In a logistic analysis dialysate Cl⁻ was associated with hypotension risk (OR 1.87, p -value ≤ 0.001). Finally the Δ pre-post HD Cl⁻ was associated with ΔBP (β -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.

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Comparative analysis of the long-term effect of two families of high-flux polysulfone dialysers on platelet Count: a retrospective cross-sectional study in southern Switzerland

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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 (146–217) to 217 (163–253) × 10⁹/L; $p < 0.001$. A linear random-intercept model confirmed the results (β -coefficient 35.214; Standard Error 5.956; $p < 0.001$). 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 indeed, 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 (β -coefficient 2.04; p -value 0.038, $r = 0.70$) in a multivariate analysis. According to different K+Dial (2vs3vs4 mmol/L) Post-HD-SBP and MAP were, respectively: 136.3 ± 27.3vs132.8 ± 42.5vs140.1 ± 29.3 ($p = 0.013$) and 83.7 ± 11.9vs86.6 ± 18.4vs90.5 ± 19.2 ($p = 0.030$). Multivariate analysis confirmed that higher K+-Gap was associated with higher Post-HD-SBP (β -coefficient 7.7; $p = 0.031$) and with higher MAP (β -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.

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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 182 unselected hemodialysis patients treated with membranes belonging to two different polysulfone families (Fresenius FX, Helixone®, Filters A; GAMBRO, 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 PreDBP, IntraDBPmax and IntraDBPmin were 56 ± 12 , 64 ± 13 and 58 ± 10 mm Hg vs. 64 ± 13 , 68 ± 11 and 58 ± 12 mm Hg. The differences in Δ PreSBP – intraSBPmax FilterA vs FilterB were not significant, while the Δ PreSBP – IntraSBPmin was 26.2 vs 10.2 mm Hg $p \leq 0.001$. The incidence of episodes of IDH was higher for FilterA (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 chronic kidney disease provide similar, but not always congruent, strategies. The aim of the present survey was to investigate rates, determinants, and institutional variations in a Dialysis Unit network belonging to the Ente Ospedaliero Cantonale, EOC, Switzerland, in laboratory parameters of renal anemia and in costs.

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 (%HYPO). A cost-effectiveness analysis of the Erythropoietin treatment (Epo-CHF) was performed.

Results: Data of 711 patients were analysed (37.1% women). Mean Hb values (g/L) biennium 2010/2011 vs 2014/2015: $H1116.5 \pm 12.6$ vs 109.9 ± 12.45 ($p \leq 0.001$); $H2111.8 \pm 14.4$ vs 109.9 ± 13.2 ($p = 0.003$); $H3113.1 \pm 11.7$ vs 112.1 ± 11.3 (ns); $H4115.4 \pm 12.8$ vs 113.6 ± 13.5 ($p \leq 0.001$). Ferritin (μ g/L) 2010/2011 vs 2014/2015: $H1374.2 \pm 217.5$ vs 554.8 ± 278.4 ($p \leq 0.001$); $H2207.2 \pm 142.9$ vs 252.8 ± 203.1 ($p \leq 0.001$); $H3476.1 \pm 485.3$ vs 347.9 ± 198.7 ($p \leq 0.001$); $H4424.0 \pm 189.3$ vs 460.0 ± 286.3 ($p = 0.03$). %HYPO 2012/2013 vs 2014/2015: $H13.2 \pm 3.4$ vs 4.1 ± 4.4 ($p \leq 0.001$); $H25.6 \pm 5.8$ vs 6.2 ± 7.8 (ns); $H33.4 \pm 4.5$ vs 3.6 ± 4.7 (ns); $H46.8 \pm 7.1$ vs 5.9 ± 7.1 ($p = 0.02$). Significant differences in 2015 Hb and Ferritin values, %HYPO and % of patients with Hb >120 g/L were found among the Dialysis Units, with lower % Hb >120 g/L for H1, lower %HYPO for H3 and lower Ferritin for H2. In a linear multivariate model Epo-CHF was associated with Hb and %HYPO (β -coefficient -3.92; $p \leq 0.001$ and β -coefficient 14.32; $p \leq 0.001$). The mean monthly Epo-CHF among Units significantly differed $H1259.7 \pm 157.8$ $H2264.2 \pm 184.7$; $H3311.5 \pm 213.1$; $H4358.3 \pm 280.7$. The Logistic Regression confirmed a lower risk to have high cost for H1 (OR 0.57 $p = 0.03$).

Discussion: Our findings highlight a high degree of variability among institutions. The percentage of patients with Hb >120 g/L and the %HYPO partially explain differences in Epo-CHF. However the mean dialysis center Hb, %HYPO, ferritin and %Hb >120 are not predictive of the Erythropoietin costs of the dialysis unit. We can speculate that other variables, not included in this analysis, could be responsible for their variability.

Bile cast nephropathy: the unknown dangers of online shopping

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Background: Renal dysfunction in the setting of cholestatic liver disease is multifactorial. Acute kidney injury may develop secondary to hypoperfusion from vasodilatation, tubular obstruction from bile casts and direct tubular toxicity from bile acids. A growing body of evidence suggests drug-induced hepatotoxicity as cause of the underlying liver injury.

Case: A 56-year-old man presented in the emergency department due to painless icterus and severe pruritus as well as acute kidney failure with no history of kidney disease. Isolated severe hyperbilirubinemia with otherwise preserved liver function was recognized. Ultrasonography/MR-tomography revealed no cause for cholestasis and excluded a postrenal etiology of the kidney injury. Urinary sediment contained bile casts but was otherwise normal. Liver biopsy showed intracytoplasmatic/intracanalicular bilirubin stasis with no evidence of cirrhosis. During follow-up, the patient negated alcohol abuse and was repeatedly asked about over the counter medication. Hemodialysis was started due to persistent anuria. Furthermore, a kidney biopsy was performed and showed signs of acute kidney injury with dilatation/necrosis of the tubuli, as well as intraluminal pigmented casts consistent with the diagnosis of bile cast nephropathy. As there were no signs of interstitial nephritis a course of steroids was mainly applied due to the uncertain origin of the liver pathology, but without relevant impact on kidney function or hyperbilirubinemia. The pruritus remained unchanged after starting of dialysis treatment, and was therefore attributed to hyperbilirubinemia and treated with colestyramine. Finally, the patient confessed to have applied intramuscular anabolic steroids bought through internet for muscle increase. As hyperbilirubinemia improved over the course of the following weeks, kidney function recovered.

Conclusion: Bile cast nephropathy is a rare differential diagnosis of acute kidney injury in patients with severe hyperbilirubinemia. Full recovery of renal function can be expected with decreasing bilirubin levels, thus early recognition and treatment is essential.

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Successful pregnancy outcome in a patient with turner syndrome and renal malformation: a case-report

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Abstract: Background: Turner Syndrome is associated with monosomy X (45 X and mosaic) and is characterized by short stature and primary amenorrhea. In up to 50% of women with Turner Syndrome, cardiovascular and renal malformations may be present. Spontaneous pregnancies are very rare (2%) and primarily occur when the syndrome is associated with mosaicism. Pregnancy in these women carries a very high risk for life-threatening maternal complications, including aortic dissection and preeclampsia (PE).

Case-Report: We report a case of a 38yrs old woman with Turner Syndrome, who presented in her first pregnancy at 106/7 weeks of gestation (WKS). Medical history and clinical examination were otherwise unremarkable, except for short stature. Initial laboratory data showed a normal blood pressure (BP 100/60 mm Hg), normal renal function (serum creatinine 45 μ mol/L) and no proteinuria (Urine protein/creatinine ratio 0.6 mg/mmol). Tubular function showed a net uric acid (UA) reabsorption of 38 μ mol/min ($N = 21.3 \pm 4.6$). Liver function tests were normal. Further ultrasound scan evaluation revealed the presence of a horseshoe kidney. The follow-up was characterized by a physiological renal function adaptation to pregnancy, the patient remained normotensive until delivery, and she did not exhibit any maternal medical complications. At 396/7 wks of gestation a 2470 g healthy girl was delivered by Caesarian section.

Conclusion: Given the life-threatening maternal and foetal complications of pregnancy in Turner Syndrome, a work-up should be done in every patient who wishes to become pregnant, whatever her karyotype (mosaic or 45 X). A multidisciplinary obstetric-medical approach should also include specialists in cardiology, endocrinology, hepatology and nephrology.

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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 63yrs old women 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 488 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.

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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 chronic hypertension, and, rarely, glomerulonephritis. The most serious manifestation being scleroderma renal crisis (SRC), which occurs in a minority of patients.

Case 1: A 72 year-old woman was diagnosed with mixed connective tissue disease (MCTD). The initial clinical presentation was polyarthritis and raynaud disease with positive ANA titer, anti-U1-snRNP and anti-SS-A/Ro. The initial steroid sparing therapy with hydroxychloroquine/methotrexate was stopped by the patient. At admission the patient complained about dyspnoea. Polyserositis, interstitial pneumopathia and myositis was diagnosed. A therapy with prednisone and cyclophosphamide was started. However, the patient suffered from progressive myopathia and dysphagia and immunoglobulins were added. Acute kidney failure developed with hypertension, haemolytic anemia and thrombocytopenia. Renal biopsy was performed which demonstrated thrombotic microangiopathy most likely related to SRC in line with the MCTD. Prednisone dose was reduced and therapy with ACE inhibitor was established. However, kidney function deteriorated and renal replacement therapy was started. Finally, the patient decided to stop hemodialysis and died.

Case 2: A 75 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 anemia 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.

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Unsuccessful treatment with abatacept of a case of focal segmental glomerulosclerosis (FSGS) recurrence after kidney transplantation

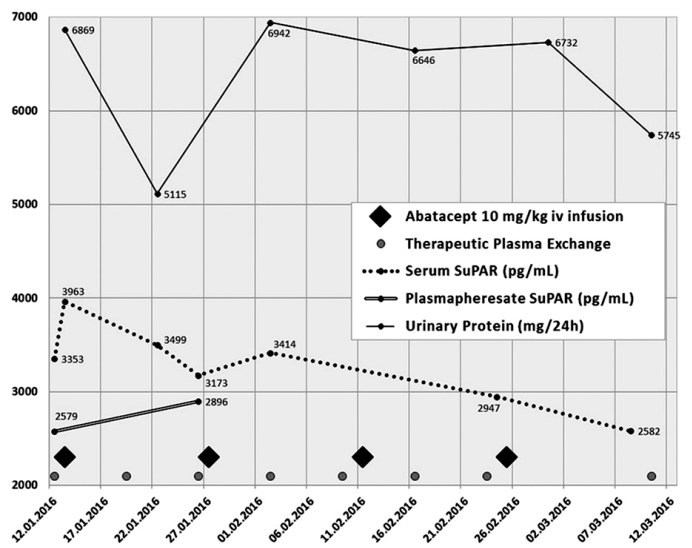
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Background: Etiopathogenesis of FSGS is an unclear topic: several circulating factors have been supposed to be involved in it. Wei et al. showed that soluble urokinase plasminogen activator receptor (suPAR) could be the circulating factor inducing FSGS: it probably promotes proteinuria by induction of B7-1 expression in podocytes, a costimulatory ligand on antigen presenting cells. This pathophysiological theory justified the treatment of FSGS with abatacept, an inhibitor of B7-1. Yu et al. reported 4 patients with B7-1 positive FSGS (NEJM, 2013), with proteinuria resolution after abatacept treatment.

Case report: A 51y.o. 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 6000 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 but at least stabilized the podocyte damage and consequently we stopped TPE. 14 days from 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 plasmapheresate 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.



Figure

Time course of 24-hour proteinuria, serum suPAR and plasmapheresate suPAR in relation to therapeutic interventions.

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24h-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) $\geq 130/80$ mm Hg whereas BP dipping $\geq 10\%$ 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/ARB use, GFR < 30 ml/min/1.72 m², diabetes, smoking status, age, gender, Hb and PTH levels. Stepwise backward regressions 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 \pm 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 ($1.4 \pm 1.6\%$ vs. $0.69 \pm 0.5\%$; $P = 0.007$) and those who developed AKI at hospital discharge ($1.3 \pm 1.5\%$ vs. $0.67 \pm 0.5\%$; $P = 0.001$) 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 ($\leq 2\%$). 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.

Variable	Total (n=69)*	LVH + (n=28)	LVH - (n=41)	P value
Echocardiography				
LVMI (g/m ²) (n=64)*	97.42 \pm 26.95	122 \pm 18.55	79.5 \pm 15.48	<0.001
Demographic				
Age (years)	69 (62-75)	71.5 (65-76)	68 (61-74)	0.352
Male, n (%)	45 (65.2%)	18 (64.2%)	27 (65.8%)	0.893
Diabetes, n (%)	33 (47.8%)	12 (42.8%)	21 (51.2%)	0.495
Smoker, n (%)	20 (28.9%)	10 (35.7%)	10 (24.3%)	0.309
Laboratory				
GFR (ml/min/1.73m ²)	36 (29-40)	34 (24.5-40)	37 (30-41)	0.265
GFR < 30 ml/min/1.73m ² , n (%)	19 (27.5%)	11 (39.2%)	8 (19.5%)	0.071
Hb (g/l)	113.54 \pm 19.44	113.43 \pm 20.67	113.61 \pm 18.81	0.970
PTH (ng/l)	7.1 (4.6-14.5)	9.25 (5.4-17.5)	7.0 (3.8 - 12.0)	0.106
Medication				
BP treatment, n (%)	59 (85.5%)	26 (92.8%)	33 (80.4%)	0.152
ACE/ARB, n (%)	48 (69.5%)	21 (75%)	27 (65.8%)	0.417
Blood pressure				
ABPM systolic BP (mmHg)	132.55 \pm 18.57	132.64 \pm 18.97	132.48 \pm 18.53	0.973
ABPM diastolic BP (mmHg)	77 (71-83)	78 (70.5-82.5)	75 (71-84)	0.941
ABPM mean BP (mmHg)	94.66 (89-102)	95.33 (89.16-102.16)	94.33 (88.33-101)	0.956
ABPM $> 130/80$ mmHg, n (%)	46 (66.6%)	23 (82.1%)	23 (56.1%)	0.024
Percent of systolic dipping	7.34 \pm 8.55	4.47 \pm 7.74	9.31 \pm 8.61	0.020
Percent of diastolic dipping	11.70 (6.25-18)	10.60 (5.20-14.97)	12.85 (6.32-18.86)	0.346
Percent of mean dipping	9.75 \pm 8.43	7.85 \pm 7.33	11.05 \pm 8.96	0.122
Systolic dipping status, n (%)	29 (42%)	6 (21.4%)	23 (56.1%)	0.004
Diastolic dipping status, n (%)	41 (59.4%)	16 (57.1%)	25 (60.9%)	0.750
Mean dipping status, n (%)	34 (49.2%)	9 (32.1%)	25 (60.9%)	0.019

Continuous parametric variables are given as: mean \pm standard deviation
 Continuous non-parametric variables are given as: median (interquartile range)
 Categorical variables are given as: % of n
 * LVMI was unavailable in 5 echocardiographic reports

Table 1
 Baseline characteristics according to the presence of LVH.

OC 19

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 stage 4/5.

Methods: 224 patients with HCV genotype (G)1 (G1a 52%, G1b 48%) and CKD 4/5 ± hemodialysis (HD) were randomized to EBR/GZR 50/100 mg (immediate treatment group, n = 111) or placebo for 12 weeks. Placebo patients (deferred treatment group, n = 113) received 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 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% (211/214). 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 and placebo patients was 0% and 4%, respectively. PK data indicate no need for dose adjustment in HD patients; geometric mean ratio (HD/non-HD) ranged from 0.67 to 0.85 for GZR and 1.43 to 1.67 for EBR. SF36 evaluation at treatment week 12 indicated trends towards more favorable changes from baseline in physical component summary and health domain scores among patients receiving EBR/GZR compared with placebo.

Conclusions: Once-daily EBR/GZR for 12 weeks was highly effective with a low rate of AEs in patients with CKD and HCV G1 infection. Patients with GT1a infection and baseline RAVs had only a modest decrease in efficacy.

OC 20

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 (srrqap) has been established first in the year 2006. However, participation is substantial only since 2013. Therefore, no analyses 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 hemo- and/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 is 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 9.5% 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 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.

	All (100%)		Male (64%)		Female (36%)	
	N	%	N	%	N	%
Deaths	560	12.6	366	12.9	194	12.1
Transplantations	250	5.6	151	5.3	99	6.2
Recovery of renal function	27	0.6	19	0.7	7	0.4
Stopping treatment (without recovery)	24	0.5	15	0.5	9	0.6
Loss to follow-up	4	0.09	4	0.1	0	0

Table 1

Survival probability in 2015 according age and gender	
0-19 yrs	100 %
20-44 yrs	97.4 %
45-64 yrs	93.9 %
65-74 yrs	88.5 %
75+ yrs	80.4 %
Men	87.1 %
Women	87.9 %

Table 2

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.

OC 21

Marsupialized peritoneal dialysis catheter: technique description and clinical practice advantages

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Background: Peritoneal Dialysis (PD) prevalence is low in Europe (<10%). Some of the barriers to its widespread are technical complication, 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 before starting PD, but the MC has several advantages: it's superficial, locked, and it has clear landmark for the externalization. Here we analyze our experience with the MC.

Results: A total of 140 MCs have been placed in patients with GFR <15 mL/min in Mendrisio and Como hospitals. Catheters were placed with surgical technique on local anesthesiology. The mean break-in time was 75 ± 291 days and all the MC were patent at PD-start; no severe post-operative complications were recorded (table 1). The MC doesn't require a surgical operation to be externalized (only a small skin cut) and the complications rate is lower compared to Moncrief's technique (no sieromas/hematomas). All patient accepted the operation without

PD Catheters [n°]	143
Marsupialized technique /Standard technique [n°]	140/3
Mean MC Break-in time, days [mean ± SD]	75 ± 291
Mean MC survival time, days [mean ± SD]	676 ± 508
MC patency at exteriorization time [%]	100%
Severe post-operative complications [n°]	
• Bowel – bladder injury	0
• Bleeding	0
Minor post-operative complications [n° (%)]	
• Subcutaneous hematoma	4 (2.8 %)
• Catheter tip migration	2 (1.4 %)
• Fluid leakage	0

Table 1

Marsupialized PD Catheter: functioning and complications.

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 Moncrief's 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.

OC 22

Real-Time benchmarks and the clinical information catalogue: an innovative user-friendly vascular access register

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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 (VA) survey made on prevalent patients on hemodialysis in 4 centers of our region on 30.11.2015. It analysed the hemodialysis-start modality (early-vs late-referral patients) and vascular access type at hemodialysis-start (central venous catheter = CVC vs arteriovenous fistula = AVF). 203 patients were enrolled: 127 (63%) started-hemodialysis with CVC, 76 (37%) with an AVF; to maintain VA primary and secondary patency for the group starting with CVC was needed 1 intervention every 8.2 months vs 1 intervention every 14.4 months/patients for the AVF-starting ones(p-val <0.05).

Results: The RAD (Dialysis-Access-Register) has been created. All fields (VA-history, primary and secondary patency, comorbidities and endpoint) were defined according to international literature definitions. Two benchmarks has been elaborated to improve quality with the creation of an AVR before hemodialysis-start in all patients early-referral: n°AVF preHD/n°early-referral-patients, n°CVC at-HD-start/n°early-referral-patients. This benchmarks are updated everyday.

Conclusions: – To maintain a register, multiple figure must collaborate to the project and use the same definitions. – Hospitals should easily analyze all the data available with the use of quantitative and qualitative benchmarks to quickly modify the inadequate outcomes. – These informations will be available to all register users, and this could motivate the persons directly involved.

OC 23

Increasing dialysate magnesium improves serum calcification propensity: The SoloMag study

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Background: A new blood test (T50-Test) measures calcification propensity in serum and is associated with adverse clinical outcome in renal transplant recipients, chronic kidney disease, and hemodialysis patients. Improving calcification propensity might improve outcome.

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 \pm 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.

OC 24

The serum calcification propensity of hemodialysis patients is strongly modified by serum phosphate, magnesium and bicarbonate

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Background: Serum calcification propensity as measured by the T50 test (Pasch, JASN 2012, 23:1744) has been validated as a strong predictor of morbidity and mortality in hemodialysis patients. We sought to identify biochemical determinants of the T50 test in a prospective cohort of hemodialysis patients.

Methods: 15 chronic hemodialysis patients (12 m, 3 f; mean age 73 ± 14 y.) treated with high volume hemodiafiltration (3×4 hr/wk) were studied. T50 was determined monthly over a period of 9 months ($n = 122$) together with midweek pre-dialysis plasma concentrations of Na⁺, K⁺, Calcium, ionized Calcium (iCa⁺⁺), Magnesium, Phosphate, Bicarbonate and Albumin. These biochemical parameters were evaluated as continuous predictors of T50 in a generalized regression model.

Results: The mean T50 value in this cohort was 260 minutes (± 72 [SD]; Range 105–460). In the linear model, only Magnesium, Bicarbonate, Phosphate and iCa⁺⁺ were significant predictors of T50. When the Patient ID was added to the model as a categorical predictor, iCa⁺⁺ became nonsignificant. While Phosphate shortened the T50 precipitation time (promoting calcification), Magnesium and Bicarbonate prolonged T50, inhibiting calcification. Predicted T50 changes when altering these parameters from the minimum to the maximum measured in the study were: Bicarbonate [$19 \rightarrow 30$ mmol/l]: + 84 min. Magnesium [$0.61 \rightarrow 1.21$ mmol/l]: + 99 min. Phosphate [$0.72 \rightarrow 2.66$]: –90 min.

Conclusions: Several easily measurable and modifiable parameters correlate significantly with T50. Serum Phosphate appears to promote, serum Magnesium and Bicarbonate to inhibit calcification propensity. Although the present data may be influenced by individual patients' comorbidities, they constitute a basis for prospectively studying the determinants of T50.

Parameter		Mean \pm SD	Beta	B	95% CI for B	p
Na ⁺	mmol/l	137.6 \pm 3.0	-0.026	-0.6	[-4.4 3.1]	0.73
K ⁺	mmol/l	4.4 \pm 0.5	0.013	1.9	[-16.5 20.3]	0.84
Ca ⁺⁺	mmol/l	2.09 \pm 0.14	0.456	216.1	[-383.8 816.0]	0.48
Ca ⁺⁺ _{corr}	mmol/l	2.30 \pm 0.17	-0.360	-148.0	[-743.6 447.6]	0.62
Ca ⁺⁺ _{ionized}	mmol/l	1.10 \pm 0.09	-0.136	-102.1	[-276.3 72.0]	0.25
Mg ⁺⁺	mmol/l	0.94 \pm 0.13	0.291	164.2	[83.5 244.9]	0.00012
Bicarbonate	mmol/l	25.3 \pm 2.1	0.220	7.6	[2.7 12.5]	0.0027
Phosphate	mmol/l	1.49 \pm 0.39	-0.246	-46.2	[-68.3 -24.1]	0.00008
Albumin	g/l	31.4 \pm 3.0	0.180	5.2	[-9.9 20.3]	0.49

Table 1

P 44

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- β 1. SJL mice showed resistance to TGF- β 1 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 administered with adenovirus expressing TGF- β 1 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- β 1 for 24 and 48hrs. Markers of EMT including E-Cadherin, procollagen type 1 and alpha-smooth muscle actin (α SMA) were analysed at protein and gene level.

Results: Peritoneal tissue from TGF- β 1 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- β 1 treatment whereas C57 cells displayed a decreased expression. Furthermore, there was reduced expression of α SMA 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- β 1 compared to the C57 mice. Future studies will explore E-cadherin signalling pathways involved in both strains of mice.

P 45

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

P 46

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. Pre- and post-dialysis BP was the mean of the second and third value as measured with BP devices incorporated in the hemodialysis machine. IDWG was calculated as the difference between the predialytic and the postdialysis body weight after the previous session.

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.

		High salt meal	Low salt meal	P
IDWG (kg)		2.2 \pm 1.2	2.0 \pm 1.2	ns
Body Weight (kg)	BD	78.3 \pm 13.8	78.8 \pm 14.0	ns
	AD	76.1 \pm 13.5	76.7 \pm 13.6	ns
SBP (mmHg)	BD	140 \pm 24	144 \pm 23	ns
	AD	132 \pm 22	134 \pm 23	ns
DBP (mmHg)	BD	69 \pm 15	70 \pm 14	ns
	AD	68 \pm 14	68 \pm 14	ns
Pulse (beats/min)	BD	76 \pm 12	76 \pm 11	ns
	AD	76 \pm 12	76 \pm 13	ns
% BPD		6.1	4.8	0.02

Before dialysis (BD), after dialysis (AD); systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP); percentage of symptomatic drop in BP (%BPD); interdialytic weight gain (IDWG)

Table 1

P 47

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.

P 48

Unconventional hemodialysis schedule: a single center experience

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Hemodialysis treatment is generally scheduled with 3 weekly sessions. However, some patients may need less and some others more than 3 sessions. Here is an overview of the medical situation, the socioprofessional implications and the administrative burden of patients with unconventional scheduled therapy in our center.

85 years old women accepting only 2 weekly sessions for social reasons. She experiences 2 episodes of pulmonary edema before to accept 3 weekly sessions until she dies.

78 years old women accepting only 2 weekly sessions for social reasons until she dies.

83 years old men who accepts only 2 weekly sessions for social reasons.

81 years old men accepting only 2 weekly sessions for social reasons. 68 years old men requiring 6 weekly sessions for medical reasons until he dies.

65 years old men requiring 5 weekly sessions for medical reasons. 55 years old men requiring 6 weekly sessions for medical reasons as for socioprofessional reasons until a successful combined kidney-pancreas transplantation. Administrative difficulty: initially accepted, then refused (producing inability to work), then accepted again.

42 years old men requiring 6 weekly sessions for medical reasons as for socioprofessional reasons until a failed kidney transplantation. Administrative difficulty: initially accepted, then refused (producing inability to work and forcing the patient to leave the country), then accepted again.

45 years old men requiring 6 weekly sessions for medical reasons as for socioprofessional reasons until a successful domino living donor kidney transplantation. Administrative difficulty: refused, forcing the patient to initiate legal proceedings against insurance and SVK. Less frequent hemodialysis sessions are motivated by social reasons in older patients. More frequent hemodialysis sessions are motivated by medical reasons and impact directly the socioprofessional situation of patients still of working age while they are waiting for a transplantation. Administrative burden is tremendous to justify these treatments cost-effectiveness.

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Analysis of the regional multicenter vascular access survey

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Introduction: Dialysis vascular access (VA) is of critical importance for the dialysis patients. Central venous catheter (CVC) use is associated to an increased risk of morbidity and mortality especially within the first year of dialysis. Guidelines strongly recommend to start hemodialysis(HD) using an arteriovenous-fistula (AVF). The aim of this study is to determine guideline adherence and differences among VA types at HD start.

Methods: A multicenter cross-sectional observational study was made on patients undergoing HD in 4 center of our region on 30.11.2015. Patients were eligible if all the clinical records were available: age, renal failure cause, HD-vintage, time of referral (early vs late-referral), VA history (type, patency, complications).

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. These 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.

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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, overhydration, phosphate binders. Colonic diverticulosis is a relative contraindications 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 recognizable 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-antiplatelet 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 temporally to HD patient 2 solving, also in this case, the bleeding. Two months later, patient 2 restarted PD with 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.

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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 dialysis time, including clinical and dialysis 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 0.010 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 KDOQI 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 KDOQI clinical outcome goals. Bed-side flow monitoring is effective and the benefit of prolonged access patency outweighs the burden of surveillance.

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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 Gemeinschaftsaufgaben 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 hospitalized for 38 (±22) days. Most of the hospitalizations were related to PD. We registered 7 episodes of peritonitis in 5 patients

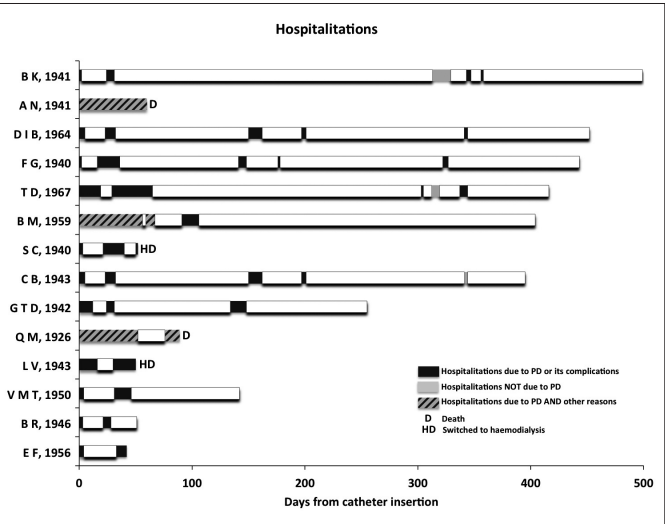


Figure 1

(1 every 1,2 dialysis year), 5 hernia repairs in 4 patients, and 1 fluid leak. There were 3 catheter replacements and 8 patients temporarily 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.

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Peritoneal dialysis is possible despite start on hemodialysis due to temporary contraindications: a case series

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Background: Peritoneal dialysis (PD) should be considered, in order to offer the most appropriate Renal Replacement Therapy (RRT) to each End Stage Renal Disease (ESRD) patient. Taking into account economical aspects, home treatments should even be preferred to in-center treatments. Patients who have chosen PD as RRT modality, but who had to be started on in-center hemodialysis (HD) for different reasons, are difficult to switch back to the initially planned treatment.

Methods: We report a case series of 3 patients, who were planned for PD, but who had to be started on HD for temporary medical contraindications.

Results: Described in table 1.

Conclusions: Starting on HD makes a switch to PD more difficult, but doesn't preclude it. The problem is well-known from patients with urgent – start on HD. A switch is even more difficult in patients who present temporary medical contraindications. We succeeded in switching 3 patients to their initially chosen RRT modality after 11±4 weeks on HD. Experienced care giver's commitment is essential to maintain patient's motivation. PD is less expensive than in-centre HD, but it may cost a lot of effort and money to overcome temporary contraindications.

Patients who chose PD as RRT	Kidney disease	Start on HD	Contraindication to PD	PD-catheter insertion	Start on PD
C.P., F, 1951	ESRD and hepatic cirrhosis	08/05/16	Listerial sepsis: 5 weeks of antibiotic treatment before PD-catheter placement	13/07/16	28/07/16
H.G., F, 1959	ESRD for chronic allograft nephropathy and cardio-renal syndrome	01/07/16	Acute Myocardial Infarction requiring dual antiplatelet therapy. We planned laparoscopic PD-catheter placement after three months, time point of clopidogrel withdrawal	planned in 09/16	planned in 10/16
E.R., F, 1971	ESRD due to oxalate nephropathy	19/07/16	Severe anemia in a renal transplant candidate, requiring iron and erythropoietin. Laparoscopic PD-catheter placement and adhesiolysis were postponed until Hb> 90 g/L	24/08/16	19/09/16

Table 1

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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 Kantonsspital 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 starting systolic pressure. All patients were on thrice weekly hemodiafiltration/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 this study. 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 ± 1.4 vs. 61.4 ± 1.3 , $p < 0.005$), 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. $87.8 \pm 0.4\%$, $p < 0.05$).

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.

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Is peritoneal dialysis a feasible option for end-stage renal disease in patients after liver transplantation and repeated abdominal surgery?

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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 thrombocytemia, 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.

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Serum calcification propensity is improved by increased dialysate bicarbonate and dialysate magnesium: The BicMag pilot study

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Background and Aims: Serum Calcification Propensity can be measured by a novel blood test, which determines the transformation time (T50) from amorphous primary to crystalline secondary Calciprotein Particles. Epidemiological and in vitro data suggest that Bicarbonate and Magnesium may be of beneficial influence on T50.

Methods: We conducted a 7-week prospective open label pilot study in $n = 12$ prevalent dialysis patients with a baseline T50 ≥ 200 min. (10 male, vintage 31 [14–92] months). T50 was determined twice at baseline, twice after increase of dialysate bicarbonate from 32 to 37 mmol/L ($n = 6$) or dialysate magnesium from 0.75 to 1.0 mmol/L ($n = 6$), and twice during the combined increase of bicarbonate and magnesium ($n = 12$). Furthermore, T50 was determined after a washout phase of 1 week.

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 1.04 ± 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.

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Therapeutic plasma exchange [tpe] with standard renal replacement equipment: a 10 year single-center experience

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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

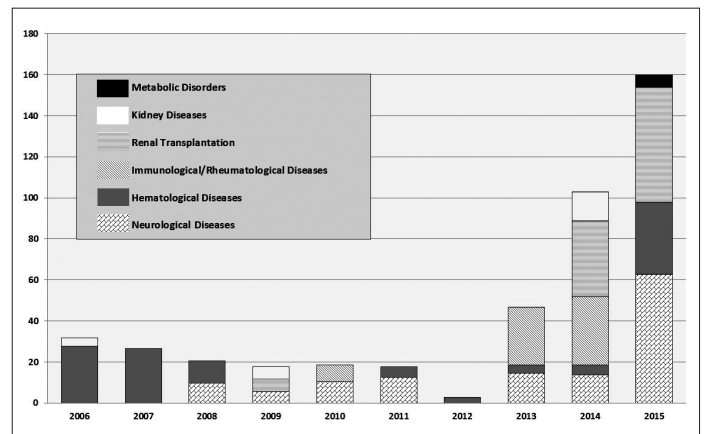


Figure 1

Number of TPE treatments performed per year and per indication.

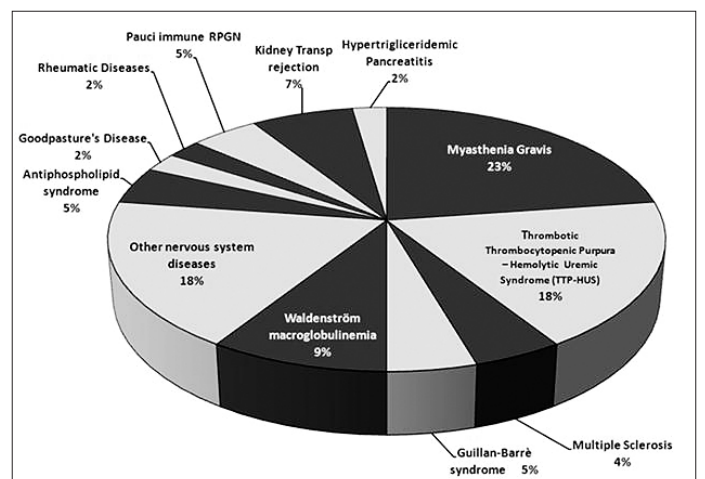


Figure 2

Percentage of diseases treated with TPE.

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%), Guillain-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).

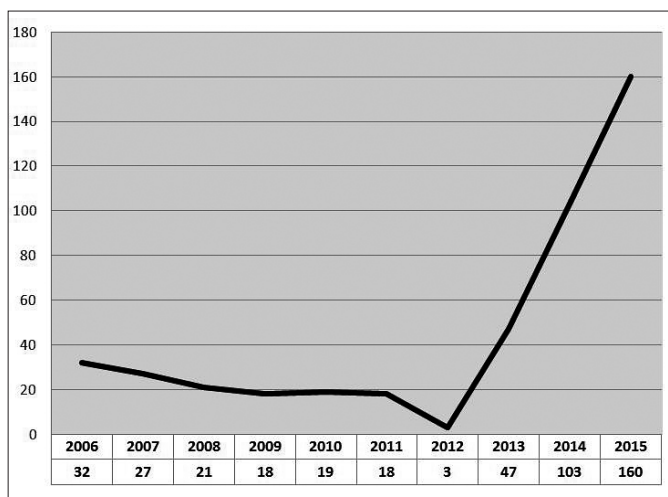


Figure 3
Number of TPE treatments per year.

Conclusions: In our 10 years of experience in TPE we have increased the number of TPE procedures mainly in collaboration with other departments. Although more used for extrarenal disorders, in our hospital TPE is a procedure managed by nephrologists. This is justified by several reasons, such as the need of a suitable vascular access, the anticoagulation of the extracorporeal circuit, the clearance of solutes and the knowledge of body volumes and the associated electrolyte disturbances.

Measuring creatinine in peritoneal dialysate: determination of the glucose correction factor

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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.

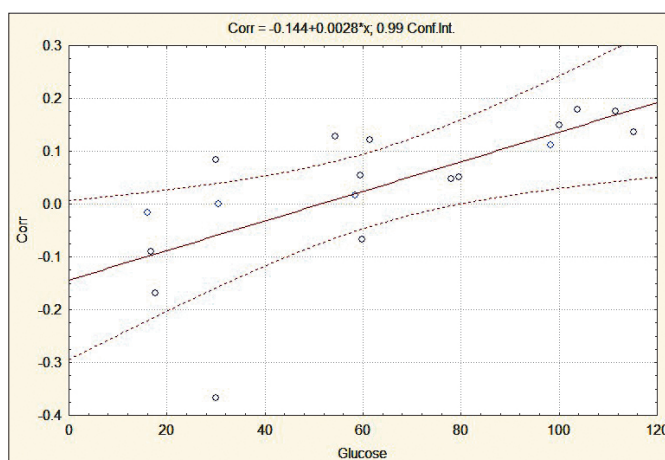


Figure 1

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.

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