Table of contents

Suppl. 167
ad Swiss Med Wkly
2008;138(47–48)
November 29, 2008

Oral Presentations – Basic Science 2 S

Oral Presentations – General Nephrology 3 S

Oral Presentations – Transplantation 5 S

Oral Presentations – Dialysis 7 S

Posters 9 S

Index of authors 24 S
Hypoxia-regulated gene expression in glomeruli from biopsies of patients with arterioparenchymal kidney disease (APKD) and Alport’s syndrome (AS).  

Methods and materials: We applied a non-invasive glomerular glomerulosclerosis index (GSI) to determine the extent of glomerulosclerosis in the donor kidneys by image analysis. In addition, we performed a comprehensive proteomic analysis of the urinary proteome before and after CPB.

Results: The GSI was significantly higher in patients with AKI than in controls (n = 36). The proteomic analysis revealed 139 differentially expressed proteins between CPB patients with and without AKI. These proteins are involved in various biological processes, including cell adhesion, immune response, and renal function.

Conclusion: The non-invasive GSI is a promising tool for the early detection of AKI. The proteomic analysis identifies potential biomarkers for the diagnosis and monitoring of AKI.

1.3

Proteomics for identifying mechanisms and biomarkers in acute kidney injury after extracorporeal circulation

F. Aregger1, C. Pilop1, D. E. Uehlinger1, T. Carrel1, R. Brunisholz2, H.-J. Anders3, H. Regele2, S. Segerer1, J. Jedlicka4, A. Soleiman2, O. Gross3, H. Regele2

1.4

Alport’s syndrome: another inflammatory kidney disease?

M. Kretzler3, D. Schlöndorff4, C. D. Cohen1

1Zürich/CH, 2Heidelberg/DE, 3Ann Arbor/US, 4New York/US

Proteomics for identifying mechanisms and biomarkers in acute kidney injury after extracorporeal circulation

F. Aregger1, C. Pilop1, D. E. Uehlinger1, T. Carrel1, R. Brunisholz2, F. J. Frey5, B. Frey6

1Bern/CH, 2Zürich/CH

Purpose: Alport’s syndrome is a hereditary glomerular disease linked to structural abnormalities of collagen type IV. In a mouse model interstitial T cells were involved in disease progression and fibrosis. Chemokines promote leukocyte recruitment to the kidney and the chemokine receptor CXCR3 is important for T cell infiltration in mouse models.

Methods and materials: We characterized a series of biopsies for the expression of the alpha 5 chain of collagen IV (to confirm the diagnosis), for the expression of CXCR3 and CD3 positive T cells. We compared 19 human renal biopsies, in which the diagnosis of Alport’s syndrome was based on morphological criteria, to the renal tissue from pretransplant biopsies from donor kidneys (n = 9).

Results: In 18 of 19 biopsies a complete loss of alpha-5-chain of type IV collagen from the glomerular tuft confirmed the diagnosis. A prominent number of CXCR3 positive cells was found in the tubulointerstitium, but only rarely within the glomerular tuft. Besides diffuse infiltrates the CXCR3 positive cells were found to form nodular infiltrates within the tubulointerstitium. The distribution of CXCR3 positive cells correlated with the chemokine receptor CXCL12.

Conclusion: We demonstrate that a non-inflammatory glomerular lesion with a structural defect of collagen IV leads to tubulointerstitial T cell accumulation. This is associated with the chemokine receptor CXCR3 and correlates with renal function. Targeting T lymphocytes, e.g. by CXCR3 blocking agents, might be a suitable approach to hold disease progression in patients with Alport’s syndrome.

Alport’s syndrome: another inflammatory kidney disease?

M. Kretzler3, D. Schlöndorff4, C. D. Cohen1

1Zürich/CH, 2Heidelberg/DE, 3Ann Arbor/US, 4New York/US

Proteomics for identifying mechanisms and biomarkers in acute kidney injury after extracorporeal circulation

F. Aregger1, C. Pilop1, D. E. Uehlinger1, T. Carrel1, R. Brunisholz2, F. J. Frey5, B. Frey6

1Bern/CH, 2Zürich/CH

Purpose: Alport’s syndrome is a hereditary glomerular disease linked to structural abnormalities of collagen type IV. In a mouse model interstitial T cells were involved in disease progression and fibrosis. Chemokines promote leukocyte recruitment to the kidney and the chemokine receptor CXCR3 is important for T cell infiltration in mouse models.

Methods and materials: We characterized a series of biopsies for the expression of the alpha 5 chain of collagen IV (to confirm the diagnosis), for the expression of CXCR3 and CD3 positive T cells. We compared 19 human renal biopsies, in which the diagnosis of Alport’s syndrome was based on morphological criteria, to the renal tissue from pretransplant biopsies from donor kidneys (n = 9).

Results: In 18 of 19 biopsies a complete loss of alpha-5-chain of type IV collagen from the glomerular tuft confirmed the diagnosis. A prominent number of CXCR3 positive cells was found in the tubulointerstitium, but only rarely within the glomerular tuft. Besides diffuse infiltrates the CXCR3 positive cells were found to form nodular infiltrates within the tubulointerstitium. The distribution of CXCR3 positive cells correlated with the chemokine receptor CXCL12.

Conclusion: We demonstrate that a non-inflammatory glomerular lesion with a structural defect of collagen IV leads to tubulointerstitial T cell accumulation. This is associated with the chemokine receptor CXCR3 and correlates with renal function. Targeting T lymphocytes, e.g. by CXCR3 blocking agents, might be a suitable approach to hold disease progression in patients with Alport’s syndrome.
Methods and materials:

remains to be elucidated. Thus, the aim of this study was to clarify, if correlates with the cause or mechanism of nephrocalcinosis still. Whether the histomorphological pattern of renal calcifications Various conditions leading to nephrocalcinosis are known. (n = 4), sarcoidosis (n = 3). The total number, density, location, size, and histological slides of all 48 cases were reevaluated by light microscopy. The cases were grouped into ten categories according to

tubular dysfunction of various etiology, including tubulopathy after cardiac surgery. A relevant mechanism of proximal tubular uptake of filtered proteins including RBP, AMBP, Ig light chains and albumin is receptor-mediated endocytosis by megalin and cubulin. The uregulation of RBP, AMBP and IGKV 1-5 in urine after CPB observed is in line with an impaired megalin mediated endocytosis. Second, ZAG expression is stimulated by gluocorticoids in adipocytes. After cardiac surgery total and unbound concentrations of cortisol are significantly increased. Thus, a glucocorticoid-mediated increased production is a reasonable candidate mechanism of the increased urinary ZAG excretion after CPB. Third, cardiac surgery with the aid of CPB induces a systemic inflammatory response syndrome (SIRS). The changes of the following proteins observed in the present study might be explained at least in part by CPB associated SIRS: LRG, MASP-2, HSPG. The identification of urinary markers predicting renal injury early after an insult to the kidney occurred is a tremendous undertaken. ZAG and the albumin/ZAG ratio are potential markers for early prediction of AKI after CPB.

Induction of ER stress in human diabetic nephropathy

M. Lindenmeyer1, M. P. Rastaldi2, M. Ikehata2, A. Starke1, M. A. Neusser1, M. Kretz1, D. Schönörf1, D. C. Cohen1

Zürich/CH, 2Milan/IT, 3Ann Arbor/US, 4New York/US

Purpose: Chronic proteinuria and tubulointerstitial fibrosis, characteristics of established diabetic nephropathy (DN), correlate best with a high degree of renal dysfunction. Recent studies have shown ER stress in cultured renal cells after protein overload. In this study, we therefore investigated ER stress and ER stress-induced apoptosis in kidneys of patients with proteinuria secondary to DN or minimal change disease (MCD) and in cultured human proximal tubular cells (PTC).

Methods and materials: Microarray analysis of DN patients (n = 6) and controls (n = 3, CON) were studied and confirmed by real-time RT-PCR (DN n = 15, MCD n = 4, CON n = 10). Protein levels were assessed. We then identified proteins using SDS-PAGE and LC-MS/MS techniques.

Results: 76 unique proteins were identified using these techniques. Several of these proteins were previously described as potential markers of glomerular diseases. Interestingly, one protein, the serum protein paraoxonase/arylesterase 1 (PON-1), was newly identified in human urine. We confirmed this result and demonstrated by Western blot analysis the presence of PON-1 protein in normal urines. We further demonstrated by RT-PCR that PON-1 mRNA is expressed in the normal human kidney and by immunohistochemistry that PON-1 protein is localized in podocytes.

Conclusion: These results demonstrated the potential for the urine samples enriched in podocyte vesicles as a starting material in studies aimed at disease biomarkers discovery.

1.6

Proteomic analysis of a podocyte vesicles-enriched fraction from human normal and pathological urine samples

S. Moli, P. Lescuyer1, A. Perini1, J. A. Schifferli1, D. Hochstrasser1

1Geneva/CH, 2Basel/CH

Purpose: Podocytes or glomerular visceral epithelial cells are known to release vesicles into urine in physiological conditions. This vesiculation process seems to be increased in pathological conditions such as glomerulopathies. Podocyte vesicles-enriched fractions of urine were therefore the starting material for proteomic analysis and identification of potential biomarkers of glomerular diseases.

Methods and materials: We first prepared a podocyte vesicles-enriched fraction from normal (19 healthy donors) and pathological (10 patients with biopsy-proven renal diseases) urine samples using an immunoadsorption method. Enrichment of podocyte vesicles was assessed. We then identified proteins using SDS-PAGE and LC-MS/MS techniques.

Results: 76 unique proteins were identified using these techniques. Several of these proteins were described as potential markers of glomerular diseases. Interestingly, one protein, the serum protein paraoxonase/arylesterase 1 (PON-1), was newly identified in human urine. We confirmed this result and demonstrated by Western blot analysis the presence of PON-1 protein in normal urines. We further demonstrated by RT-PCR that PON-1 mRNA is expressed in the normal human kidney and by immunohistochemistry that PON-1 protein is localized in podocytes.

Conclusion: These results demonstrated the potential for the urine samples enriched in podocyte vesicles as a starting material in studies aimed at disease biomarkers discovery.

Oral Presentations – General Nephrology

Histopathological patterns of nephrocalcinosis: the hyperphosphatemic type in acute phosphate nephropathy following colonicose can be distinguished from other types

T. Wiech1, H. Hopfer1, M. Werner1, M. J. Mihatch1

Freiburg/DE, 2Basel/CH

Purpose: Various conditions leading to nephrocalcinosis are known. Whether the histomorphological pattern of renal calcifications correlates with the cause or mechanism of nephrocalcinosis still remains to be elucidated. Thus, the aim of this study was to clarify, if the histopathological appearance of calcifications provides information about the possible etiology.

Methods and materials: Native kidney biopsies of the last 50 years (1959 to 2008) with a diagnosis of nephrocalcinosis were included and histological slides of all 48 cases were reevaluated by light microscopy. The cases were grouped into ten categories according to the likely etiology of nephrocalcinosis, such as hypercalcinemia (n = 6), hyperparathyroidism after colonicose (n = 5), hyperparathyroidism (n = 5), sarcoidosis (n = 5), oxalate deposits, respectively. Finally, the different morphological features were correlated with clinical and laboratory data.

Results: Nephrocalcinosis was one of the major diagnosis in 48 of 12000 native kidney biopsies (0.4%). The clinicopathological correlation analysis revealed a specific pattern of nephrocalcinosis in the group of hyperparathyroidism after colonicose: all five cases showed predominance of cortical, intratubular, spheroidal deposits with outer shell-like calcifications (hyperparathyroidic type). In contrast, other groups, especially the group of hypercalcinemia, had a different pattern with predominantly lumpy, homogeneous or finely granular calcifications (hypercalcinemic type). The specificity of the hyperparathyroidic type could be reconfirmed in a blinded test by two nephropathologists using these given criteria. However, nephrocalcinosis in patients with diabetes mellitus, or with both diabetes mellitus and hyperparathyroidism is also common, had a similar pattern. Compared to the post-colonoscopy group these biopsies contained calcium oxalate deposits, but often in the interstitium than in tubular lumina.

Conclusion: Hyperparathyroidism-associated nephrocalcinosis can be distinguished histopathologically from nephrocalcinosis of other
Renal amyloidosis revisited: relevance of histomorphological patterns, amyloid dynamics and chemical type

H. Hopfer, T. Wiechi, M. J. Mihatsch
Basel/CH, Freiburg/DE

Purpose: Renal amyloidosis is a well recognized disease resulting from protein misfolding of diverse precursor proteins and leads to progressive renal insufficiency. Recently management of amyloidosis has shifted from purely supportive care to an aggressive treatment depending on the amyloid precursor type present. Only few data are available concerning the relevance of the histomorphological patterns and the dynamic role of the disease process within the kidneys.

Methods and materials: We retrospectively reviewed all cases of renal amyloidosis diagnosed in native kidney biopsies between 1968 and 2007 (n = 205). All cases were systematically evaluated for the presence of amyloid in the various renal compartments and its pattern of distribution. Each the extent (focal and segmental vs. global and diffuse) and severity of glomerular amyloid deposition was scored semiquantitatively (1 = minimal, 4 = severe). A glomerular amyloid score was calculated by simple multiplication. Total glomerular involvement was defined as minimal score 1–4, mild (score 5–8), moderate (9–12), or severe (13–16). The degree of interstitial fibrosis and tubular atrophy of the cortex was estimated as area %.

Results: Morphological findings were correlated with clinical data available at the time of biopsy.

Conclusion: The mean patient age was 57.6 ± 16.1 years, the male: female ratio was 1.2:1.1. According to the predominant site of amyloid deposition 46.4% showed a glomerular, 9.4% a vascular, and 6% a tubulointerstitial pattern. Regardless of the pattern most cases had additional less suspicious amyloid deposits in one or both of the other compartments. By immunohistochemistry 84/158 cases were identified as AL lambda, 68/158 cases as AA, 9/158 as AL kappa and 1/158 as lambda. There was no correlation between the amyloid type and the histological pattern. For the glomerular pattern the dynamics of amyloid deposition was investigated. In the early stage mesangial amyloid fibrils are put down in a focal and segmental fashion. With increased deposition there is a diffuse segmental and later global affection of the glomeruli often accompanied by a vascular and/or tubulointerstitial involvement. Interstitial fibrosis with tubular atrophy is rarely in minimal or mild glomerular amyloidosis but becomes much more frequent in moderate to severe disease. Serum creatinine correlates well with interstitial fibrosis and tubular atrophy (p <0.001).

Renal volume enlargement predicts the progression to end stage renal disease in autosomal dominant polycystic kidney disease

M. M. Ragazzi, E. F. Fossali, M. G. Bianchetti
Bellinzona and Mendrisio/CH, Milano/IT

Purpose: The mechanisms underlying postural proteinuria are not well understood. In most Asian subjects with postural proteinuria ultrasonic imaging and Doppler flow scanning disclose entrapment of the left renal vein in the fork between the aorta and the mesenteric artery. Little information is available on the possible occurrence of left renal vein entrapment in European subjects with postural proteinuria.

Methods and materials: Renal ultrasound with Doppler flow imaging was performed in 24 Italian or Swiss patients with postural proteinuria (14 girls and 10 boys, aged between 5.2 and 16 years, median 14 years). The diagnosis of left renal vein nutcracker phenomenon was made when the antero-posterior diameter at the hilum divided by that at the atero-mesenteric portion (= diameter ratio) or when the peak flow velocity at the atero-mesenteric divided by that at the hilar portion (= flow velocity ratio) were >4.0.

Results: Ultrasonic imaging and Doppler flow scanning disclosed signs of aorto-mesenteric left renal vein entrapment in 18 of the 24 patients (75 percent). The diameter ratio and the flow velocity ratio were both >4.0 in 13, the flow velocity ratio was >4.0 but the diameter normal in 3 and the diameter ratio was >4.0 (but the flow velocity normal) in 2 patients. The diameter ratio and the velocity ratio were both normal, i.e. <4.0, in the remaining six patients.

Conclusion: Left renal vein nutcracker phenomenon is frequent both in Asian as well as in European subjects with postural proteinuria. We suggest ultrasonic imaging and Doppler flow scanning be useful in subjects with postural proteinuria to evaluate whether left renal vein nutcracker phenomenon is implicated or not.

Role of the antenatal and postnatal ultrasound in the diagnosis of vesicoureteral reflux

S. Graziosi, P. Parvex, L. Merlini, E. Antonelli, C. Dellhumeau, E. Girardin
Geneve/CH

Purpose: Antenatal hydronephrosis (ANH) is a frequent anomaly found on foetal ultrasound (US). There is no consensus recommendations for the postnatal follow-up and the necessity to practice a voiding cystourethrography (VCUG) for the diagnosis of the vesicoureteral reflux (VUR), thus leading to unnecessary and irradiating examinations. The goal of this study was to evaluate the role of the antenatal and postnatal US in the diagnosis of VUR in neonates with ANH.

Methods and materials: We prospectively followed 121 patients (pts) with ANH (anterior posterior diameter (APD) ≥ 5 mm or ureteral dilatation (UD) ≥ 5 mm) from birth to 1 year of age. All cases were characterized by a positive VCUG at 5 days and 1 month after birth. Only children with persistence of dilatation at an APD ≥ 5 mm or a ureteral dilatation on one or two of the postnatal US had a VCUG at 5 weeks after birth.

Results: VCUG was done in 89 pts and a VUR was detected in 10, among those, 5 had high grade reflux (> grade II). A positive correlation was found between the severity of VUR and the degree of APD on the antenatal and postnatal US (p <0.05). The ROC curve with a cut off level of 7–9 mm showed a sensibility of 90% and specificity of 12.6% for the antenatal ultrasound and a sensibility of 90% and specificity of 44.3 % for the postnatal US. Children with severe VUR had an APD ≥ 10 mm on the antenatal and prenatal US.

Conclusion: These data indicate that the US had a poor specificity for the diagnosis of the VUR. However it is useful in selecting patients at risk for a severe VUR. We recommend that all the newborns with ANH ≥ 7 mm have an US at 5 days and 1 month after birth; the VCUG should be done at 6 weeks if one of the US showed the persistence of an APD ≥10 mm or the presence of a ureteral dilatation.

Safety, tolerability and adherence of sirolimus in autosomal dominant polycystic kidney disease

Zürich/CH

Purpose: Renal volume enlargement predicts the progression to end stage renal disease in autosomal dominant polycystic kidney disease (ADPKD).

Methods and materials: We performed a randomized controlled trial to assess the effect of sirolimus on renal volume change in 100 ADPKD patients. Patients with documented renal volume progression received either sirolimus 2 mg/day (A) or no treatment (B).

Results: Baseline characteristics of the patients in the two groups were similar, including age (29.2 ± 6.2 yr), kidney volume, eGFR (109 ± 24 ml/min), albuminuria (3.8 ± 4.5 mg/mmol) and blood pressure. The most frequent adverse events were transient and mild mucositis (A: 72%, B: 12%), upper airway infection (A 52%, B: 72%), acne (A: 41%, B: 44%). No serious drug-related adverse events occurred and none of the patients discontinued the drug prematurely. Electronic monitoring of medication adherence showed a median adherence of >90%. After 6 months of treatment the eGFR and albuminuria were unchanged in both groups. Triglyceride (A: 1.4 ± 0.9, B: 1.2 ± 0.6 mmol/l), cholesterol (A: 4.5 ± 1.2, B: 4.5 ± 0.8 mmol/l) and LDL levels (A: 1.4 ± 0.4, B: 1.3 ± 0.4 mmol/l) remained in the normal range.

Conclusion: We conclude that 2 mg/day sirolimus is safe and well tolerated and that treatment adherence is excellent in ADPKD patients (ClinicalTrials.gov, NCT00346918).

Left renal vein entrapment: a frequent feature in children with postural proteinuria

M. M. Ragazzi, E. F. Fossali, M. G. Bianchetti
Bellinzona and Mendrisio/CH, Milano/IT

Purpose: The mechanisms underlying postural proteinuria are not well understood. In most Asian subjects with postural proteinuria ultrasonic imaging and Doppler flow scanning disclose entrapment of the left renal vein in the fork between the aorta and the mesenteric artery. Little information is available on the possible occurrence of left renal vein entrapment in European subjects with postural proteinuria.

Methods and materials: Renal ultrasound with Doppler flow imaging was performed in 24 Italian or Swiss patients with postural proteinuria (14 girls and 10 boys, aged between 5.2 and 16 years, median 14 years). The diagnosis of left renal vein nutcracker phenomenon was made when the antero-posterior diameter at the hilum divided by that at the atero-mesenteric portion (= diameter ratio) or when the peak flow velocity at the atero-mesenteric divided by that at the hilar portion (= flow velocity ratio) were >4.0.
Why do so many patients start haemodialysis without definitive vascular access?

A. Schenker, I. Binet, I. Koneth, D. Tsinalis
St. Gallen/CH

Purpose: Although it is widely accepted that an av fistula is the best vascular access for haemodialysis (HD), a substantial number of patients start HD without definitive access. The aim of this retrospective study was to evaluate the proportion of patients starting HD without definitive access, to understand the reasons and discuss the potential for improvement.

Methods and materials: A database review was performed on all patients who started HD at our centre between January 2005 and June 2008, collecting patients’ characteristics (age, nephropathy, evolution of kidney failure, time of referral to renal service) and the presence of definitive access when starting HD.

Results: Within the observation period 154 new HD patients were identified. We excluded 49 patients who required HD transiently and recovered renal function. Of the 105 patients analyzed only 32% (n = 34) had definitive access. 13% (14/105) were switched to HD from transplantation (n = 6) or peritoneal dialysis (n = 8), 92% (13/14) of the transplanted patients had a timely vascular access. Of PD-patients 62% (5/8) switched to HD without access due to acute complications. Of the patients naive to renal replacement therapy (RRT) 40% (36/91) were unknown to renal services until less than 4 months and started without definitive access. Of these 36 patients (n = 11) had an acute renal failure, 56% (n = 20) had CKD but recovered renal function. Of the patients naive to renal replacement therapy (RRT) 40% (36/91) were unknown to renal services until less than 4 months and started without definitive access. Of these 36 patients (n = 11) had an acute renal failure, 56% (n = 20) had CKD but recovered renal function. Of the patients naive to renal replacement therapy (RRT) 40% (36/91) were unknown to renal services until less than 4 months and started without definitive access. Of these 36 patients (n = 11) had an acute renal failure, 56% (n = 20) had CKD but recovered renal function.

Conclusion: A majority of patients with chronic renal failure in our centre starts HD without definitive vascular access. Approximately half of these patients could have started HD in a planned manner but were either not identified or were not referred to renal services. The other half was known to renal services but failed to have a definitive access. A substantial proportion explicitly refused timely surgery. Beside organisational issues, a mental barrier against accepting the need for RRT might result in the denial of practical steps towards initiation of dialysis. In conclusion there is still a need to improve detection of CKD and timely referral to a nephrologist. There is a further need to increase understanding and acceptance of timely preparation for haemodialysis for patients and maybe also for nephrologists.
Regulation of allo-reactive human CD8 T cell response by CD40 and PD-L1 expression on renal tubular epithelial cells

Y. Wüthrich-Men, A. Starke, T. Fehr, R. P. Wüthrich
Zürich/CH

Purpose: Allo-reactive cytolytic T lymphocytes (CTLs) induce tubulointerstitial injury during kidney transplant rejection. Previously we demonstrated that murine renal tubular epithelial cells (TECs) with high PD-L1 expression are partially protected from the attack of antigen-specific autologous CTLs. In the present study we investigated human allo-reactive CTL responses to renal TEC that express positive (CD40) or negative (PD-L1) costimulatory molecules.

Methods and materials: Human renal TEC line HK-2 cells or primary renal TEC cultures were pre-stimulated with IFN-γ and IFN-α to induce high surface expression of PD-L1 and MHC Class I. These cells were then used as targets of allo-reactive CD8+ CTLs isolated from PBMCs of healthy donors. Cytotoxicity of allo-reactive CTLs were measured by non-radioactive CTL assays, in the presence or absence of specific blocking mAbs for PD-L1 or activating mAbs for CD40, respectively. T cell cytokines in the co-culture supernatants were also determined by ELISA kits.

Results: Allo-reactive CTLs demonstrated a strong cytolytic activity to the positive control targets Jurkat cells but not to renal TECs, though allogen-specific IFN-γ production was detected in both cases. Blocking surface PD-L1 on HK-2 cells with a specific mAb significantly increased IFN-γ production of allo-CTLs, but was still not able to induce the lysis of renal TECs. Importantly, when the CD40 co-stimulatory signal was triggered by an activating anti-CD40 mAb, the cytolysis of TECs was induced. These results indicate that positive and negative co-stimulatory molecules CD40 and PD-L1 were directly involved in the interaction of allo-reactive CTLs and TECs.

Conclusion: Since the co-stimulatory molecules B7.1 and B7.2 are not expressed by renal TECs, CD40 becomes the unique co-stimulatory surface molecule which is capable of stimulating alloreactive TEC responses to renal TECs. Strategies to downregulate CD40 and enhance PD-L1 expression on TECs might be therapeutically useful to prevent kidney transplant rejection.

3.4

Urinary CXCR3-binding chemokine levels correlate with the extent of subclinical tubulitis

S. Schaub1, P. Nickerson2, D. Rush3, C. Hess1, M. Mayr1, W. Stefura1, K. Hayglass2
1Basel/CH, 2Winnington/CA

Purpose: Subclinical tubulitis, while occurring in less than 10% of all kidney transplants under current immunosuppression, can induce tubular atrophy and interstitial fibrosis. Defining populations at risk for subclinical tubulitis –preferably via non-invasive screening – would therefore be important. CXCR3-receptor 3 (CXCR3) binding chemokines (i.e. MIP-1β, IP10, TAF) are secreted by various leukocytes as well as tubular epithelial cells, and are involved in the recruitment of activated T cells into the site of inflammation. The aim of this study was to investigate how levels of urinary CXCR3-binding chemokines relate to the extent of subclinical tubulitis in kidney allograft recipients.

Methods and materials: Using ELISA, urinary CXCR3-binding chemokines and urinary tubular injury biomarkers (NGAL and 1-microglobulin) were measured in 65 renal allograft recipient and related to their histological grading of tubulointerstitial inflammation (normal tubular histology [n = 24], subclinical borderline tubulitis [n = 18], and subclinical tubulitis Ia/Ib [n = 23]). Glomerular filtration rates were estimated using the MDRD equation.

Results: Total proteinuria, urinary levels of NGAL and 1-microglobulin and estimated glomerular filtration rates were similar across these histologically defined patient groups. By contrast, each of the three measured urinary CXCR3-binding chemokines were significantly higher in patients with subclinical tubulitis Va/Vb as compared to patients with subclinical borderline tubulitis (p <0.01) and patients with normal histology (p <0.05). The association of urinary CXCR3-binding chemokines with NGAL was also significant.

Conclusion: These results demonstrate a correlation of urinary CXCR3-binding chemokine levels with the extent of subclinical tubulitis. If confirmed in a larger independent validation set, urinary CXCR3-binding chemokines might become a useful non-invasive biomarker to screen for subclinical tubulitis.

3.5

In vivo mechanisms leading to transplantation tolerance induced by regulatory T cells

D. Golishayev1, J.-C. Wyss2, S. Schaefer1, H.-A. Lehr3, M. Pascual1
1Lausanne/CH, 2London/UK

Purpose: The mechanisms by which CD4+CD25+Foxp3+ T cells (Tregs) regulate effector T cells in a transplantation setting and their in vivo homeostasis still remain to be clarified. Using a mouse adoptive transfer and skin transplantation model, we analyzed the in vivo expansion, effector function and trafficking of effector T cells and donor-specific Tregs, in response to an allograft.

Methods and materials: Antigen-specific Tregs were generated and expanded in vitro by culturing freshly isolated Tregs from BALB/c mice (H2d) with syngeneic dendritic cells pulsed with an allogeneic peptide (here the Kb peptide derived from the MHC class I molecule of allogeneic H2b mice). Fluorescent-labelled CD4+CD25- naive T cells and donor-antigen-specific Tregs were transferred alone or co-injected into syngeneic BALB/c Nude recipients transplanted with allogeneic C57BL/6xBALB/c donor skin.

Results: As opposed to their in vitro hyporesponsiveness, Tregs divided in vivo, migrated and accumulated in the allograft draining lymph nodes (drLN) and within the graft. The co-transfer of Tregs did not modify the early proliferation and homing of CD4+CD25+ T cells to secondary lymphoid organs. But, in the presence of Tregs, effector T cells produced significantly less IFN-γ- and IL-2 effector cytokines, while higher amounts of IL-10 were detected in the spleen and drLN of these mice. Furthermore, time-course studies showed that Tregs were recruited into the allograft at a very early stage post transplantation and prevented infiltration by effector T cells.

Conclusion: Overall, our results suggest that suppression of graft rejection involves the early recruitment of donor-specific Tregs at the sites of antigenic challenge and that Tregs mainly regulate the effector arm of T cell allosponses.
4.1 Glycynthetic acid food supplementation lowers plasma potassium concentrations in chronic hemodialysis patients

Bern/CH

Purpose: Hyperkalemia (HK) is a life threatening problem in dialysis patients. Glycynthetic acid (GA), the active ingredient of licorice, inhibits the enzyme 11-β-hydroxysteroiddehydrogenase type 2 (11-β-HSD2) and thereby increases access of cortisol to the colonic mineralocorticoid receptor. This has the potential to lower plasma potassium concentrations (K+). We hypothesized that the prolonged ingestion of GA lowers plasma K+ without inducing the renal side effects of sodium retention and hypertension.

Methods and materials: Ten patients where studied in a 6 month prospective, double blind, placebo controlled cross over study. Either cookies or bred rolls were supplemented with GA (500 mg or placebo) and given twice per day. Blood was drawn and 24-hour BP measured at baseline, week 6, 12, 18 and 24. Plasma K+ concentration was determined before each treatment session.

Results: The ratio of plasma cortisol/cortisone increased in all patients on GA (14.3 ± 3.3) when compared to the baseline (6.1 ± 2.1, p <0.001) or placebo period (5.7 ± 3.3, p <0.01), indicating inhibition of 11-β-HSD2. Nine of ten patients exhibited a rapid and persistent decrease of predialysis plasma K+. On GA, mean plasma K+ concentrations were lower (5.5 ± 0.61 mmol/l) than at baseline (5.5 ± 0.61 mmol/l, p <0.01) or during the placebo period (5.3 ± 0.53 mmol/l, p <0.05). On placebo plasma K+ levels were elevated above the upper limit of normal range in 76% (64/83), compared to 30% (107/357) on GA (p <0.01). The frequency of relevant K+ (>6 mmol/l) decreased from 9 to 0.6% (p <0.01). No differences were found concerning parameters reflecting sodium retention, i.e. weight and BP measurements. The aldosterone/rein ratio was diminished during the GA administration (19 ± 13) when compared to baseline (89 ± 67, p <0.01) or to placebo (39 ± 36, p ns), an effect best explained by the diminished plasma K+.

Conclusion: Prolonged GA supplemented food consistently lowers plasma potassium without inducing weight gain or hypertension in dialysis patients. Thus, GA might be useful to prevent serious HK and to diminish aldosterone, a culprit of myocardial fibrosis.

4.2 Predicting the risk of severe falls in maintenance haemodialysis patients with Tinetti test

P. E. Rassier, D. Hannane, M. P↵rujm, M. Burnier, D. Teta
Lausanne/CH

Purpose: Patients on maintenance haemodialysis (MHD) are at high risk of falls. In the general population, the risk of fall can be assessed by the Tinetti test. This is an easily reproducible clinical tool for balance and walking assessment with a maximal score of 26. The cut off value ≥20 predicts a high risk of falls. As this test has never been performed in patients on MHD, the purpose of this study was to assess the prevalence of severe falls and the ability of the Tinetti test to predict falls in this population.

Methods and materials: All patients on MHD in our centre between June 1, 2005 and July 31, 2008 were asked to participate. Tinetti test was performed by the same person (DH) before a dialysis session in all patients and in a subgroup of 12 patients also after dialysis. Thereafter, all severe falls defined by the need of hospitalisation and/or presentation in an emergency department, were documented prospectively.

Results: Eighty four patients (mean age 69.1 ± 14.3 years) were included, of which 33% females and 46.4% diabetics. Predialytic Tinetti score was 19.0 ± 6.6 (Mean ± SDV). In the subgroup of 12 patients tested before and after dialysis, mean scores were 20.6 ± 4.4 and 16.3 ± 7.2, respectively. After a mean follow up time of 16.6 months, severe falls were recorded in 24 patients (28.4% of all patients), resulting in 13 fractures (54.2% of patients with falls). Tinetti score in patients without falls was 20.2 ± 5.6 and 16.0 ± 7.9 in patients with falls 16.0 ± 7.9 (p = 0.001). Of the 35 patients with a “classical” Tinetti cut off value of ≥20, 34.0% fell, versus 24.5% in patients with a score ≥20 sensitivity: 50%, specificity: 61.6%; p = 0.23). Of all tested cut off values (between 20 and 24), the highest sensitivity (70.8%) and specificity (53%) was found when using a cut off value of 21. Of the 45 patients with a score ≥21, 38.5% fell, versus 17.9% of patients with a score <21 (p = 0.038). At this cut off value of 21, the negative predictive value was 82% and the positive predictive ratio was 57%.

Conclusion: Severe falls are a frequent complication in MHD patients, occurring in 21% of patients per year. Tinetti scores are remarkably low in our study, and drop further after a dialysis session, which raises questions of when to perform the test. Moreover, it suggests that the predialytic Tinetti score may underestimate the global risk, which might explain why the higher cut off value of 21 correlated better with the risk of falls. The high negative predictive value of the test predicts fairly the patients who will remain free of falls. On the contrary, in case of a lower score, attention is warranted and efforts should be made to reduce individual risk factors such as low muscle mass, orthostasis and certain medications. However, further studies are needed to assess the impact of co morbidities on the predictive value of the Tinetti test in this population.

4.3 Is PAPP-A a useful parameter to predict morbidity and mortality of patients on maintenance haemodialysis?

C. Etter1, Y. Straub1, H.-R. Räz5, T. Kistler3, D. Kiss4, R. P. Wüthrich1, H. J. Glooor9, D. Ameel2, P. Wahl1, P. Ambüh1
1Zürich/CH, 2Baden-Dättwil/CH, 3Winterthur/CH, 4Liestal/CH, 5Schaaffhausen/CH, 6Lachen/CH

Purpose: Hemodialysis (HD) treatment is associated with a high morbidity and mortality, mainly due to cardiovascular (CV) complications. Thus, it would be desirable to have simple screening tools available to assess an individual patient’s risk with regard to the occurrence of medical complications including death, PAPP-A (insulin-like growth factor binding protein-4-protease; IGFBP-4-protease), is responsible for the degradation of IGFBP-4, a potent inhibitor of IGF. Both IGF and PAPP-A are elevated in patients with acute coronary syndrome, and PAPP-A has recently been identified as a marker for plaque instability and as an independent predictor for CV mortality in patients with coronary artery disease. The aim of this study was to assess a) the prognostic value of PAPP-A as a marker of morbidity and mortality, including the frequency and duration of hospitalisations, and b) to compare PAPP-A with other cardiovascular risk markers.

Methods and materials: The study population consists of a total of 164 patients participating in the monitor1 trial, a prospective dynamic hemodialysis cohort study assessing a wide range of clinical laboratory and anthropometrical parameters. A baseline assessment including the measurement of PAPP-A in serum was performed at time of inclusion into the monitor1 cohort, which continuously occurred between summer of 2006 and winter of 2008. Medical charts of all study participants were reviewed in April 2008 for the occurrence and date of both hospitalisations and death and length of hospital stay. All events were analyzed regarding their relation to cardiovascular causes and to time of follow-up within the study cohort.

Results: Results are given as mean ± SDV for all patients and for subgroups according to tertiles of PAPP-A (low: 7–17, medium: 18–23, and high: 24–46):

<table>
<thead>
<tr>
<th>N</th>
<th>164</th>
<th>60</th>
<th>50</th>
<th>54</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAPP-A, mIEs</td>
<td>22±11</td>
<td>13±3</td>
<td>21±2</td>
<td>35±6</td>
</tr>
<tr>
<td>Age, yr</td>
<td>66±14</td>
<td>66±15</td>
<td>66±15</td>
<td>71±12</td>
</tr>
<tr>
<td>Hospital days</td>
<td>20±23</td>
<td>17±3</td>
<td>15±3</td>
<td>27±7</td>
</tr>
<tr>
<td># CV endpoints</td>
<td>6</td>
<td>0</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Comorbidities, N</td>
<td>1.8±0.9</td>
<td>1.8±0.9</td>
<td>2.3±1</td>
<td>1.7±0.7</td>
</tr>
<tr>
<td>Follow-Up, days</td>
<td>475±129</td>
<td>436±174</td>
<td>479±112</td>
<td>513±64</td>
</tr>
<tr>
<td>Days on HD</td>
<td>2104±2504</td>
<td>1409±1783</td>
<td>1442±1124</td>
<td>3328±3378</td>
</tr>
<tr>
<td>Kt/V</td>
<td>1.60±0.3</td>
<td>1.60±0.4</td>
<td>1.60±0.3</td>
<td>1.60±0.3</td>
</tr>
<tr>
<td># Death, N</td>
<td>22</td>
<td>5</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>IL-6, ng/L</td>
<td>9±10</td>
<td>7.8±9</td>
<td>9.0±9</td>
<td>10.6±13</td>
</tr>
<tr>
<td>NT-pro-BNP, ng/L</td>
<td>1278±72148</td>
<td>9600±14906</td>
<td>11251±15533</td>
<td>17273±20282</td>
</tr>
<tr>
<td>MDA, pmol/L</td>
<td>0.27±0.1</td>
<td>0.23±0.1</td>
<td>0.26±0.1</td>
<td>0.33±0.1</td>
</tr>
<tr>
<td>LDL, mmol/L</td>
<td>2.2±0.8</td>
<td>2.4±0.8</td>
<td>2.3±0.9</td>
<td>2.2±0.8</td>
</tr>
<tr>
<td>PHN, ng/L</td>
<td>281±368</td>
<td>199±125</td>
<td>297±261</td>
<td>346±335</td>
</tr>
<tr>
<td>Osteoprotegerin, PM</td>
<td>16±7</td>
<td>13.7±8</td>
<td>13.8±8</td>
<td>18±7</td>
</tr>
</tbody>
</table>

Conclusion: In this Swiss cohort of maintenance HD patients PAPP-A is associated with higher morbidity and mortality. This is reflected by more hospital days, CV occurrence, and greater number of deaths in patients with higher PAPP-A serum concentrations. It remains to be determined whether PAPP-A is merely a marker for morbidity and mortality, or whether a causal link exists to cardiovascular disease pathogenicity. An indirect causality may exist through alterations in mineral metabolism, as suggested by the correlations found for PAPP-A with PHN and osteoprotegerin.
Simple and effective treatment of 25-OH-Vitamin D3 deficiency in hemodialysis patients

A. Bock1, L. Lüthi2

*Dept. of Nephrology, CH, Aarau/CH. 1Frauenfeld/CH

Purpose: To assess the accuracy of interferon-gamma release assay (IGRA), when compared to the tuberculin skin test (TST), in the diagnosis of latent tuberculosis infection (LTBI) in immunocompetent patients. However interferon-gamma release assays (IGRA) are more specific and predict LTBI accurately in immunocompetent patients. However interferon-γ (INF-γ) secretion is impaired in HD-patients due to immunosuppression caused by uremia and this may lead to more inconclusive results.

Methods and materials: We took advantage of the mitogen positive-control reaction integrated in the Quantiferon Gold InTube (QTF-GIT), ELISA-based IGRA to assess the IGRA-accuracy in HD-patients. First the lymphocyte count, HD-treatment measured by single pool (spKt/V) and nutritional status measured by serum albumin and normalized protein catabolic rate (nPCR) was assessed on the QTF-GIT performance. Second, we performed a head to head comparison between the QTF-GIT and the TST in HD-patients. HD-patients were enrolled at the HD-centre and healthy controls at the health services of the Kantonspital St. Gallen. QTF-GIT was performed in patients and controls, TST additionally in HD-patients. HD-patients with active malignancy or under immunosuppression were excluded. Medical histories were reviewed for LTBI risk factors. The study was approved by the local ethical committee.

Results: 39 HD-patients and 52 healthy controls were enrolled. HD-patients showed a significantly reduced immune reaction measured by INF-γ secretion in the positive reaction compared to the healthy controls (p <0.05). Nevertheless, only 1/39 QTF-GIT test result was inconclusive with a positive negative control reaction; this result was obtained in a patient with diabetic nephropathy. Time on HD-treatment (median 31 months), spKt/V (median 1.6), serum albumin (median 36.1 g/dl), nPCR (median 0.86 g/kg/d), PTH (median 252 ng/l), CRP (median 135 mg/l), PTH (median 252 ng/l), CRP (median 135 mg/l), pre-albumin, hemoglobin, Kt/V, CRP, bicarbonate, PTH, TSH, were recorded.

Conclusion: The accurate diagnosis of latent tuberculosis infection (LTBI) in haemodialysis patients monitors the health status of the patients. However, the use of interferon-gamma release assays (IGRA) is more specific and predicts LTBI accurately in immunocompetent patients.

Accuracy of a interferon-gamma release assay for the diagnosis of latent tuberculosis infection in haemodialysis patients

M. Hoffmann1, D. Tainalis1, P. Vernazza1, W. Fierz1, I. Binetti1, S. Gallen/CH. 1Speicherschwend/CH, 2Kreuzlingen/CH, 3St. Gallen/CH

Purpose: To assess the accuracy of interferon-gamma release assay (IGRA), when compared to the tuberculin skin test (TST), in the diagnosis of latent tuberculosis infection (LTBI) in immunocompetent patients. However interferon-γ (INF-γ) secretion is impaired in HD-patients due to immunosuppression caused by uremia and this may lead to more inconclusive results.

Methods and materials: We took advantage of the mitogen positive-control reaction integrated in the Quantiferon Gold InTube (QTF-GIT), ELISA-based IGRA to assess the IGRA-accuracy in HD-patients. First the lymphocyte count, HD-treatment measured by single pool (spKt/V) and nutritional status measured by serum albumin and normalized protein catabolic rate (nPCR) was assessed on the QTF-GIT performance. Second, we performed a head to head comparison between the QTF-GIT and the TST in HD-patients. HD-patients were enrolled at the HD-centre and healthy controls at the health services of the Kantonspital St. Gallen. QTF-GIT was performed in patients and controls, TST additionally in HD-patients. HD-patients with active malignancy or under immunosuppression were excluded. Medical histories were reviewed for LTBI risk factors. The study was approved by the local ethical committee.

Results: 39 HD-patients and 52 healthy controls were enrolled. HD-patients showed a significantly reduced immune reaction measured by INF-γ secretion in the positive reaction compared to the healthy controls (p <0.05). Nevertheless, only 1/39 QTF-GIT test result was inconclusive with a positive negative control reaction; this result was obtained in a patient with diabetic nephropathy. Time on HD-treatment (median 31 months), spKt/V (median 1.6), serum albumin (median 36.1 g/dl), nPCR (median 0.86 g/kg/d), PTH (median 252 ng/l), CRP (median 135 mg/l), pre-albumin, hemoglobin, Kt/V, CRP, bicarbonate, PTH, TSH, were recorded.

Conclusion: The accurate diagnosis of latent tuberculosis infection (LTBI) in haemodialysis patients monitors the health status of the patients. However, the use of interferon-gamma release assays (IGRA) is more specific and predicts LTBI accurately in immunocompetent patients. However interferon-γ (INF-γ) secretion is impaired in HD-patients due to immunosuppression caused by uremia and this may lead to more inconclusive results.
lack of difference in activity (number of steps, time of physical activity) and REE. This finding was observed in MHD patients both older and younger than 60 years. However, age stratification appeared to give an influence on the REE. BUN and creatinine clearance correlated with clinical characteristics using uni- and multivariate analysis.

Results: The mean total kidney volume (TKV) was 1003 ± 568 cc/m2 at baseline and increased by 31.8 ± 72.0 ccm (2.71 ± 4.82%) in 6 months (P <0.001). The baseline cyst volume of the right and left kidney of the same patient were highly correlated (r = 0.905, P <0.001). The baseline volumes of the right and left kidneys were determined using a region-based thresholding technique applied to axial T2-weighted TSE sequences. 48 kidneys were measured twice by the same and again by an additional observer to assess the intra- and interobserver agreement. Volumetry data were correlated with clinical characteristics using uni- and multivariate analysis.

Results: The mean total kidney volume (TKV) was 1003 ± 568 cc/m2 at baseline and increased by 31.8 ± 72.0 ccm (2.71 ± 4.82%) in 6 months (P <0.001), which corresponds to an extrapolated annual growth rate of 5.36 ± 9.47%. The total cyst volume was 476 ± 440 cc/m2 at baseline and increased by 32.8 ± 52.9 ccm (5.45 ± 14.28%) (P <0.001). The change in TKV was directly correlated with the changes in TKV (r = 0.780, P <0.001). The baseline volumes of the right and left kidney of the same patient were highly correlated (r = 0.905, P <0.001) and their growth rates also (r = 0.702, P <0.001). The concordance correlation coefficient (95% CI) was 1.000 (0.999—1.000) for intraobserver and 0.996 (0.995—0.999) for interobserver agreement. The change in renal volume correlated with baseline factors. The changes in TKV correlated positively with male sex, hypertension, albuminuria and history of macrohematuria and negatively with creatinine clearance. Albuminuria was associated with accelerated volume progression. A significant volume decrease was found in 13 kidneys of 10 patients. In 7 cases, the volume decrease could be attributed to the rupture of large cysts.
Conclusion: We conclude that kidney volume progression can be determined over a period as short as 6 months on unenhanced MRI sequences in ADPKD patients with preserved GFR. The volume determinations were reliable as demonstrated by an excellent reproducibility of measurements. The measured growth rate was identical to a previously published cohort with 3 years follow up. Furthermore, the first time that cyst ruptures contribute to relevant volume changes over the short term.

Comparison of urinary oxalate assessment between six international reference laboratories
O. Borini1, A. Pasch1, B. Huet-Adams2, F. J. Frey3, N. M. Maalouf4
1Lausanne/CH, 2Bern/CH, 3Dallas/US
Purpose: Hyperoxaluria is a major risk factor for kidney stone formation. Although urinary oxalate measurement is part of every basic stone risk assessment, there is no internationally recognized and standardized method for this measurement.
Methods and materials: In order to compare urinary oxalate assessment methods, 10 urine samples from 24 h urine collection covering a broad range of oxalate concentrations were aliquoted and sent in duplicates for oxalate measurement to six blinded international reference laboratories. Three laboratories used a commercially available oxalate oxidase kit (labs A, B, E), two laboratories used a HPLC-based method (labs D, F), and one lab used both (lab C). HPLC-based methods were developed in each center independently and used different protocols. All centers used internal controls to check for quality.
Results: We first evaluated intra-laboratories reliability by analysis of the duplicates. Intraassay coefficients of the results of the duplicates between labs A, B, E, two laboratories used a HPLC-based method (labs D, F), and one lab used both (lab C). HPLC-based methods were developed in each center independently and used different protocols. All centers used internal controls to check for quality.
In conclusion, urinary oxalate measurements by oxalate oxidase kit showed better ICC and limits of agreement between them and compared to oxalate oxidase kit.

Atheroembolic disease – a frequently missed diagnosis: results of a 12-year matched-pair autopsy study
C. Fries1, S. Vavricka1, A. Gaspert1, F. Salomoni1, R. P. Wüthrich1, T. Feher2
1Zürich/CH, 2Lachen/CH
Purpose: Diagnosis of atheroembolic disease (AD) is challenging, since no specific test is available and AD often masquerades other clinical conditions. The aim of this study was to analyze the relative frequency of autopsy-proven AD over time, to describe the clinical presentation and to identify risk factors for AD.
Methods and materials: All autopsy reports of the Department of Internal Medicine at University Hospital in Zurich from 1995 to 2006 (n=1900) were screened for AD. For each case a control patient without AD was matched for age, sex and autopsy year. Therapeutic interventions (operations, catheter interventions and drug treatment) in the last 6 months before death, and clinical and laboratory parameters during the last hospitalisation were retrieved from electronic charts.
Results: Fifty-one AD patients were identified, and among these only 6 (12%) had been diagnosed clinically. The organs most often affected were kidney (71%), spleen (37%) and lower GI tract (22%). Surprisingly, the relative AD frequency decreased over time from 3.5 to 0.5 (0.10) autopsies, whereas the frequency of clinically suspected AD remained constant. Among clinical signs, skin lesions (livedo, blue toe) and proteinuria were increased in AD patients, whereas no other laboratory parameter including eosinophilia was different between groups. Vascular interventions within 6 months before death were highly associated with AD (55 vs 14%, p=0.01), and in a multivariate analysis were remained the only significant risk factor for AD.
Conclusion: Diagnosis of AD is frequently missed. No particular clinical sign or laboratory parameter was significantly associated with AD. Vascular interventions represent a highly significant risk factor for AD. The relative frequency of autopsy-proven, but not clinically suspected AD decreased over time. Whether this is due to a selection bias or due to a higher use of protective drugs (aspirin, statins, steroids) is currently under investigation.

Blood pressure modifies the association between serum adiponectin and uric acid, in a sex-dependent manner
Lausanne/CH
Purpose: Plasma adiponectin and serum uric acid (SUA) levels are negatively correlated. To better understand the possible mechanisms linking adiponectin and uric acid, we analyzed whether the association between adiponectin and SUA differed by hypertension status (or blood pressure level) and by sex.
Methods and materials: We analyzed data from the population-based CoLaus study (Switzerland). Fasting plasma adiponectin levels were assessed by ELISA and SUA by uricase-PAP. Blood pressure (BP) was measured using a validated automated device and hypertension was defined as having office BP 140/90 mm Hg or being on current antihypertensive treatment.
Results: In the 2897 men and 3181 women, aged 35–74, BMI (mean ± SD) was 26.6 ± 4.0 and 25.1 ± 4.8 Kg/m², systolic blood pressure (SBP) was 132.2 ± 16.6 and 124.8 ± 18.3 mm Hg, median (interquartile range) plasma adiponectin was 6.2 (4.1–9.2) and 10.6 (8.9–15.4) mg/dL, and hypertension prevalence was 42.0% and 30.2%, respectively. The age- and BMI-adjusted partial correlation coefficients between log-adiponectin and SUA were 0.09 and 0.06 in normotensive men and women, respectively. In median regression adjusted for BMI, insulin, smoking, alcohol consumption, menopausal status and HDL-cholesterol, there was a significant three-way interaction between BMI, SBP and sex for their effect on adiponectin (dependent variable, P=0.005), as well as interactions between SBP and sex (P=0.014) and between SUA and sex (P=0.033).
Conclusion: Plasma adiponectin and SUA are negatively associated, independently of BMI and insulin, in a population-based study in Caucasians. However, BP modifies this inverse relationship, as it was significant mainly in women with elevated BP. This observation suggests that the link between adiponectin and SUA may be mediated by sex hormones and the hypertension status.

Low adiponectin is associated with increased ambulatory pulse pressure and activation of the renin-angiotensin system in subjects of African descent
L. E. Reyna-Carmona, M. Bochud, M. Maillard, P. Bovet, J. Nussberger, M. Burnier, D. Teta
Lausanne/CH
Purpose: Adiponectin, arterial stiffness, as well components of the renin-angiotensin system are associated with cardiovascular risk. This study was aimed to investigate whether plasma adiponectin was directly linked with pulse pressure (PP), as a marker for arterial stiffness, and the renin-angiotensin system (RAS).
Methods and materials: A family-based study in subjects of African descent enriched with hypertensive patients was carried out in the Seychelles. Fasting plasma adiponectin was determined by ELISA, plasma renin activity (PRA) using the antibody-trapping principle and plasma aldosterone by radioimmunoassay. Daytime ambulatory blood pressure (BP) was measured using Diasys Integra devices. PP was calculated as the difference between systolic and diastolic BP.
Results: Data from 335 subjects from 73 families (152 men, 183 women) were available. Men and women had mean (SD) age of 45.4 ± 11.1 and 47.3 ± 12.4 years, BMI of 26.3 ± 4.4 and 27.8 ± 5.1 kg/m², daytime systolic/diastolic PP of 132.6 ± 15.4 / 86.1 ± 10.9 and 130 ± 17.6 / 83.4 ± 11.1 mmHg, and daytime PRA of 46.5 ± 9.9 and 46.7 ± 10.7 mmHg, respectively. Plasma adiponectin was 4.4± 3.04 ng/ml in men and 7.39 ± 5.44 ng/ml in women (P <0.001). In young (adjustment for age, sex and BMI), log-transformed adiponectin was negatively associated with daytime PP (P=0.009, P<0.003, P=0.004), plasma renin activity (P=0.248 ± 0.090, P=0.002) and plasma aldosterone (P=0.004 ± 0.002, P=0.014).
Conclusion: Low adiponectin is associated with increased ambulatory PP and RAS activation in subjects of African descent.
Our data are consistent with the observation that angiotensin II receptor blockers increase adiponectin in humans.
Evaluation of a renal risk score in the Swiss population: results from a pilot screening project
I. Binen1, M. Burnier2, S. Farese3, B. Huser4, M. Brunisholz5, I. Binet1, M. Burnier2, S. Favre3, M. Wyler3

Purpose: The prevalence of chronic kidney disease (CKD) in the Swiss population is not really known. The mostly asymptomatic progression and the low grade of awareness about kidney diseases in the general population motivated a pilot project for information and detection. In the context of the World Kidney Day 2008 a renal risk score was developed and used for visitors to pharmacies. The project was also designed to test feasibility of such screening in public pharmacies.

Methods and materials: 25 pharmacies in the canton St. Gallen and in Lausanne participated to the pilot project and 293 patients’ scores were analysed. Participants were interviewed in the pharmacies, their blood pressure (BP) measured and a urine sample was run for a semiquantitative assessment of the albumine/creatinine ratio. The responsible pharmacists were specifically trained for screening access for patients and in 22%, 41% and 37% of pre-dialysis patients.

Purpose: 81/200 patients and in 67% of pre-dialysis patients.

The responsible pharmacists were specifically trained for screening access for patients and in 22%, 41% and 37% of pre-dialysis patients.

Conclusion: This pilot project shows that it was feasible to screen the for the risk of CKD in public pharmacies. Participants were mostly women >50 years old and 73% showed a moderate or high renal risk score with hypertension and/or microalbuminuria. Concerns due to a low grade of awareness about kidney diseases in the general population motivated a pilot project for information and detection. During the 6 months’ followup, mean hemoglobin increased from 117 g/l to 118 g/l in the dialysis patients and from 111 to 114 g/l in the pre-dialysis patients. In the 27 dialysis patients switched from rhEpo to DA, Hb levels were maintained despite a dose decrease of ~26%. Hb target achievement in dialysis patients with extended dosing intervals appeared unimpaired (Hb ±110 g/l) in 67% with bi-weekly DA, 90% with monthly DA).

Conclusion: A variety of individual practice patterns and a heterogeneous patient population contribute to the results of this observational study. Nevertheless, the 77% target achievement (Hb <110g/l) in hemodialysis patients compares favourably to the findings of observational studies in Europe, such as DOPPS II. The dose savings observed in dialysis patients switched from short-acting ESAs to DA confirm previous results from larger trials. Extended (bi-weekly and monthly) DA dosing intervals in dialysis patients were associated with a higher degree of target achievement. In the pre-dialysis setting, extended dosing intervals are the preferred mode of administration.

Kidney volume enlargement in unilateral autosomal dominant polycystic kidney disease (ADPKD)
D. Poster, F. Krauer, A. Kistler, D. Weishaupt, R. P. Wüthrich, A. Serra Zürich/CH

Purpose: Autosomal dominant polycystic kidney disease (ADPKD) with concomitant renal absence or dysplasia has rarely been described. Reduced renal mass is a condition that causes marked acceleration of progression in various models of renal disease. Renal volume enlargement is a surrogate marker of disease progression. Herewith we report on kidney volume development in patients with unilateral ADPKD.

Methods and materials: Among a cohort of 181 ADPKD patients screened for our SUISSE ADPKD study, we identified 3 patients with unilateral polycystic kidney disease and contralateral absence of the kidney or dysplasia. Renal volumes were measured within 6 months by analysing two unenhanced MRI scans. Renal function was assessed by creatinine clearance and albuminuria was determined in the spot urine.

Results: The MRI scans of the 2 females and 1 male, aged 24, 38 and 41 years, showed enlarged unilateral polycystic kidneys and absence of the contralateral kidney (2 patients) or a dysplastic kidney (1 patient). The volumes of the cystic kidneys amounted to 485 cm³, 780 cm³ and 732 cm³ and increased by 30 cm³ (6.1%), 40 cm³ (5.1%) and 32 cm³ (4.4%) within 6 months, respectively. GFR at baseline was 73, 98 and 60 ml/min and remained unchanged during follow-up. The urinary protein excretion was below 250 mg/day in all 3 patients.

Conclusion: Our results of renal volume changes in 3 unilateral ADPKD patients show a growth rate above the age and volume matched mean of bilateral ADPKD and may reflect accelerated disease progression.

Acute renal failure due to hypovolemia after construction of ileostomy
D. Ackermann, L. Bruegger, F. J. Frey Bern/CH

Purpose: An ileostomy in colon surgery results in the loss of sodium, potassium and bicarbonate. Most patients adapt to these daily losses through subtle changes in salt and water intake and changes in urinary volume and electrolyte and acid excretion. However, patients with daily drainage of 1 L or more are prone to symptomatic volume depletion.

Methods and materials: Here we report on 7 patients with new onset of prerenal failure after construction of ileostomy. 5 out of 7 patients were male. Median age at onset was 68 years. The time from ileostomy to renal failure varied from 2 weeks to 2 years after ileostomy construction. The reason for hypovolemia was increased ileostomy output in 6 patients and nausea and vomiting in 1 patient.
Nephrology in Armenia 20 years later – the Zurich contribution.

Unexpected results of an ASN initiative

A. Sarkissian, A. Babloyan, E. Leumann
Yerevan/AM, Zürich/CH

Purpose: The relief operation prompted by the SSN following the earthquake in Armenia exactly 20 years ago (7.12.1998) did not end after some weeks, but became the starting point of a long-term commitment. The start of the programme was somewhat chaotic in midst of the breakdown of the Soviet Union; hence some leading Swiss nephrologists strongly extended the programme and the steps taken to develop a strong basis in paediatrics. We aim to demonstrate the various stages of the venture. 20 years later it has evolved – despite many obstacles – into a strong partnership programme with Zurich in nephrology and paediatrics. Stimulation by successful studies (mainly English) given by VAD. Funding: Own charity organisation (Verein Armenienhilfe Direkt = VAD), SNSF, canton of Zurich (basis for training were carefully selected, helped by language courses and much goodwill from individuals and companies.

Methods and materials: Three time periods can be distinguished, i.e. I (first 5 years – slow stabilisation): Modern nephrology installed, Arabkir becoming educational care. Additional basic material support. – II (1994–2001): Comprehensive nephrology. Stimulation by successful studies (paediatric) nephrology and other disciplines. – III (2001–2008): Slow progression to end stage renal failure is common, complete acid-base homeostasis, as well as sodium and potassium balance. Posters

Immunocomplex glomerulonephritis in patients with Waldenström's macroglobulinaemia

Where has all that phosphate gone…. the answer my friend, …Phosphate nephropathy, a serious problem lurking out there?

H. Freudeger
One/CH

Purpose: Phosphate nephropathy (PNP) is a rare, and by its silent and clinically non-spectacular presentation often an unrecognized or misdiagnosed complication of the use of phosphate containing bowel cleansing solutions for the preparation for colonoscopy. Two cases of PNP are presented to awaken the awareness of the clinician to this potentially preventable syndrome.

Methods and materials: Two case reports of typical patients with PNP.

Results: case presentation: Two patients seeking nephrological attention for evaluation of raised serum creatinine levels are presented. Both patients were elderly white females, treated with AACE or ARB, and diuretics for hypertension, suffered from mild diabetes and consumed occasionally NSAID. Both underwent colonoscopy either for investigation of abdominal pain (patient 1) or as a control for a positive renal ultrasonography (patient 2). Oral sodium phosphate punguatives (Colophos®, 90 ml containing about 60 g of sodium-phosphate) were used in both cases. Serum creatinine in patient 1 was 1.19 mg/dl and 105 micromol/l (while consuming NSAID) one year respectively three months prior to colonoscopy. Three months after colonoscopy serum creatinine was 258 micromol/l, and no calcifications have occurred since. Patient 2 displayed a normal (69 micromol/l) creatinine level 6 months prior to the colonoscopy. Forty eight hours after colonoscopy, prior to a CT scan with contrast, serum creatinine was measured at 168 micromol/l, with no improvement since. In both patients no electrolyte disorders or proteinuria could be found. Kidney size and structure were normal, and no calcifications were documented on ultrasound or CT. Seven months after colonoscopy patient 1 underwent renal biopsies, which revealed mainly a tubulo-interstitial nephritis characterized by degenerative changes in proximal tubules, interstitial fibrosis, and tubulo-interstitial precipitations containing phosphate (von Kossa stain), suggestive of nephrocalcinosis.

Conclusion: Discussion: Colophos®, a well tolerated and efficient bowel cleansing agent, is widely used since its introduction in the early 1980s and is generally considered as safe. Although intake of phosphate containing punguatives provide considerable phosphate load, independent of renal function, and severe transient hyperphosphatemia with symptomatic hypocalcemia has been documented, only a small proportion of exposed individuals develop PNP. Screening for electrolyte and renal function disturbances might therefore be of questionable importance. Electrolyte disorders develop within days after consumption of sodium phosphate. Alternatively, renal failure can be an incidental finding weeks or months after sodium phosphate exposure, presenting with mild symptoms and with no abnormalities of serum phosphate or calcium. Slow progression to end stage renal failure is common, complete remission of renal failure is rare. *PNP* may be a rare but serious complication associated with the use of phosphate containing cleansing agents for colonoscopy, but the large number of colonoscopies performed each year, probably guarantees a respectable total number of cases, many of which may stay unrecognized or misdiagnosed due to the silent presentation of PNP, temporally distant from the exposure to phosphate. Several risk factors for PNP such as age, female gender, treatment with AACE, resp. ARB, hypervolemia states, diabetes, pre-existing CKD, diabetes or heart failure were identified, but their individual importance remains debated. Significant gaps in the understanding of nephrocalcinosis and PNP persist, prospective studies are not available, and the true incidence of PNP is still not known. The role of PTH, Vitamin D, phosphatases as well as the role of inhibitors such as citrate, fetuin-A, matrix GlA protein need to be defined for the understanding of the pathophysiology of PNP. Understanding of the pathophysiology of PNP may reveal some of the mystery the mechanisms leading to nephrocalcinosis, nephrothipsis, and possibly give some insight to mechanisms of ectopic calcifications in general.

Immune-complex glomerulonephritis in patients with Waldenström's macroglobulinaemia

T. Oettl, H. Hopfer, M. Mayr
Basel/CH

Purpose: Renal insufficiency has been considered a rare complication in patients with Waldenström’s macroglobulinaemia (WM). Classical pathological findings include infiltration of lymphocytes or plasmaocytoid cells, amyloidosis that can be accompanied by nephrotic syndrome, and immune-mediated glomerulonephritis with deposition of phosphate-containing precipitations. In single cases, a variety of other glulropathies has been seen in association with WM.

Serum creatinine varied from 167 to 893 mmol/l. 5 patients had metabolic acidosis. All patients showed features of hypovolemia with diminished or even blunted urinary sodium excretion. The ratio of sodium/potassium as a marker of secondary hyperaldosteronism was between 0.1 to 0.8.

Results: One patient had to start dialysis immediately. Management of volume depletion and improvement of renal function difficult according to the underlying disease of the patients. 4 patients had closure of ileostomy, 2 patients had medical treatment of ileostoma output with opioids and rehydration and 1 patient received intravenous fluid and antibiotics. Follow-up creatinine normalized only in 2 patients, but all remained independent of dialysis.

Conclusion: These cases illustrate the importance of recognizing the risk in patients with an ileostomy for the rapid development of life-threatening acid-base and electrolyte disorders, as well as volume depletion. Acute treatment consists of vigorous volume repletion with isotonic saline. Maneuvers to decrease ileostomy output or closure of the ileostomy are important to prevent recurrence. Removal of the colon is an experiment in nature that emphasizes the importance of the normal function of the gastrointestinal tract in maintaining acid-base homeostasis, as well as sodium and potassium balance.
Methods and materials: We report on two patients suffering WM associated glomerulopathy. We focused on the clinical outcome under immunosuppressive therapy, including histological findings in serial kidney biopsies.

Results: Most important clinical facts of the two patients and histological results of the kidney biopsies as well as data of immunosuppressive therapy are summarized in the following two tables:

### Table 1
Patient 1, female, 68 years old.

<table>
<thead>
<tr>
<th>time</th>
<th>07/07</th>
<th>10/07</th>
<th>01/08</th>
<th>04/08</th>
<th>07/08</th>
</tr>
</thead>
<tbody>
<tr>
<td>clinical symptoms</td>
<td>hypertension, weight gain, nephrotic syndrome</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>diagnosis of WM</td>
<td>09/01</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>biopsies</td>
<td>first: diffuse intra- and extracapillary GN (fibrils missed by EM), severe IF/TA</td>
<td>second: fibrillary GN with less inflammation compared to bx 1, severe IF/TA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crea</td>
<td>319</td>
<td>337</td>
<td>285</td>
<td>293</td>
<td>246</td>
</tr>
<tr>
<td>UACR</td>
<td>1137</td>
<td>1137</td>
<td>756</td>
<td>696</td>
<td>598</td>
</tr>
<tr>
<td>treatment</td>
<td>methylprednisolon iv</td>
<td>prednisone po tapered + cyclo-phosphamide iv (pulses)</td>
<td>prednisone po + MMF po</td>
<td>idem</td>
<td>idem</td>
</tr>
</tbody>
</table>

### Table 2
Patient 2, male 40 years old.

<table>
<thead>
<tr>
<th>time</th>
<th>09/01</th>
<th>06/03</th>
<th>09/05</th>
<th>07/07</th>
</tr>
</thead>
<tbody>
<tr>
<td>clinical symptoms</td>
<td>fever, weight loss, arthralgia, eczema</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>diagnosis of WM</td>
<td>09/01</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>biopsies</td>
<td>first: extracapillary necrotizing pauci-immune GN, minimal IF/TA</td>
<td>second: segmentally sclerosing IC GN, moderate IF/TA</td>
<td>third: progressive sclerosing GN, severe IF/TA, severe arteriolopathy</td>
<td></td>
</tr>
<tr>
<td>Crea</td>
<td>83</td>
<td>76</td>
<td>82</td>
<td>129</td>
</tr>
<tr>
<td>UACR</td>
<td>17</td>
<td>17</td>
<td>20</td>
<td>66</td>
</tr>
<tr>
<td>treatment</td>
<td>cyclophosphamide po + prednisone, followed by azathioprin po</td>
<td>cyclophosphamide po + prednisone</td>
<td>azathioprin po, then MMF po</td>
<td>rituximab iv</td>
</tr>
</tbody>
</table>

WM: Waldenström’s macroglobulinemia; GN: glomerulonephritis; Crea: creatinine [mmol/l]; UACR: urine albumin creatinine ratio [mg/mmol]; EM: electron microscopy, IF/TA: interstitial fibrosis and tubular atrophy, MMF: mycophenolate mofetil, IC: immune-complex

Serial kidney biopsies revealed ongoing glomerulonephritis with increasing areas of interstitial fibrosis, tubular atrophy and glomerulosclerosis.

### Safety and tolerability of ferric carboxymaltose (FCM) for treatment of iron deficiency in patients with chronic kidney disease and in kidney transplant recipients

A.-C. Grimmelt, C. D. Cohen, T. Fehr, A. Serra, R. P. Wüthrich Zürich/CH

**Purpose:** Iron deficiency is common in patients with chronic kidney disease (CKD) and in kidney transplant recipients (KTR). We analyzed the safety and tolerability of the new intravenous iron preparation ferric carboxymaltose (FCM) in these two patient groups.

**Methods and materials:** Adverse events (AE) after the administration of the drug were assessed by using a questionnaire. Vital signs and laboratory data were collected before and after the application of FCM. The safety and tolerability of the new intravenous iron preparation FCM.

**Results:** A total of 46 FCM doses were applied to 44 patients (17 with CKD and 27 KTR) either as a single bolus injection of 100 or 200 mg (n = 42) or as short infusion with up to 500 mg (n = 4). Mild and transient AE (metallic taste, headache, dizziness) occurred in 6 patients. The estimated glomerular filtration rate (eGFR) remained unchanged by the FCM administration.

**Conclusion:** We conclude that the safety and tolerability of FCM were excellent. Compared with other intravenous iron preparations the considerably shorter administration time of FCM allows to save time and to reduce costs.

### Improved management of secondary hyperparathyroidism based on repeated NKF/KDOQI targets measurements: data of 3 Swiss dialysis units

Z. Glück**, M. Hugentobler**, P.-Y. Martin**

1Biel/CH, 2Frauenfeld/CH, 3Genève 14/CH

**Purpose:** Secondary hyperparathyroidism (shPT) is common in chronic renal insufficiency and progresses over time. Most patients treated with conventional therapies often fail to simultaneously achieve the NKF/KDOQI recommended targets for PTH, Ca, P and Ca×P. The objective of this ongoing project is to record and analyze changes in the use of shPT therapeutic regimens, and to explore the effect on target level achievement over time.

**Methods and materials:** Information on baseline characteristics, laboratory values and concurrent medications were collected at 3 sites at 2 time points (t1 and t2) in unselected dialysis patients. NKF/KDOQI target level achievements were presented to the centers after data collection at t1. The second data collection at t2 took place at 6, 8 and 10 months respectively at site 1, 2 and 3; during this period the treating physician continued management of the disease according to local standard of care (no pre-set drug protocol).

**Results:** At time point t2, 55.6% of the 160 patients were male, mean age (SD) was 65.4 (14.6) years and mean weight (SD) was 75.1 (17.0) kg. 60.6% were treated with vitamin D sterols and 80.3% received >1 phosphate binder. Calcimimetics were used in 27.5% of patients.

**Conclusion:** NKF/KDOQI target achievement improved in all centres (t1 vs t2) for all 4 parameters simultaneously. Interestingly, this difference was observed in both analysis populations (‘all patients’ and ‘patients with data at t1 and t2’). Changes in the use of different drug regimens were noted at all sites; in particular, calcimimetics were used more often.
Effects of Aliskiren in a patient with severe hyperreninemic hyperaldosteronism: a case report
P. Amico, D. Kiss
Liestal/CH

Purpose: The inhibition of the renin-angiotensin-aldosterone system (RAAS) with ACE inhibitors (ACEI) or angiotensin receptor blockers are effective in controlling hypertension. However, these agents are not more effective than other antihypertensive agents in reducing major cardiovascular events. Aliskiren, the first in a new class of effective direct renin inhibitors, blocks angiotensin (Ang) I production directly at its rate-limiting step.

Methods and materials: n/a.

Results: Case report: We present a 47-year-old woman with hypertension and end-stage renal failure due to polycystic kidney disease, who received a kidney from her sister-in-law in 2000. The allograft function (sirolimus 2 mg/d and prednisone 5 mg/d) is stable (serum creatinine concentration: 130–150 µmol/l). The hypertension due to a severe hyperreninemic hyperaldostronism persisted after transplantation. For several years, her antihypertensive therapy consisted of ACEI and spironolactone. Under this medication, her blood pressure values ranged from 100/65 mm Hg to 140/90 mm Hg (range over the last five years). This therapy was stopped and aliskiren was initiated for better blood pressure control at a serum creatinine concentration of 145 µmol/l. Two months after starting aliskiren, her blood pressure was 110/75 mm Hg (range from 104/76 to 125/85 mm Hg during treatment) and serum creatinine was 132 µmol/l. Renin concentration rose from 710 mU/l to 1732 mU/l, while plasma aldosterone decreased from 1.98 nmol/l to 0.45 nmol/l. Renal protein excretion decreased from 47 to 21 mg/mmol creatinine. FE-K (ACEI + spironolactone vs. aliskiren) remained unchanged (18 vs. 19%).

Conclusion: This case demonstrates the antihypertensive efficacy of once-daily aliskiren 150 to 300 mg in a patient with a kidney transplant and moderate hypertension probably due to polycystic kidney disease and activated RAAS. Aliskiren suppresses plasma renin activity although renin concentration increases during treatment due to loss of feedback inhibition by Ang II on renin release. Aliskiren inhibits the RAAS at its rate-limiting step and probably favors more complete blockade. However, the ultimate role of aliskiren in target organ protection and improvement in cardiovascular outcomes has still to be determined in prospective studies with clinical endpoints.

Cinacalcet in chronic kidney disease stage 4 – case report
M. Möddel
Zürich/CH

Purpose: Secondary hyperparathyroidism (sHPT) begins early in the course of chronic kidney disease (CKD) and is associated with elevated serum parathyroid hormone (PTH) levels. Traditional sHPT therapies such as vitamin D sterols and calcium-based phosphate binders are not always adequate to achieve K/DOQI goals for sHPT. In this case report vitamin D was replaced due to Calcitriol intolerance (side effects such as nausea, vomiting and loss of appetite) by Cinacalcet to control sHPT.

Methods and materials:

Results: Cinacalcet (30 mg daily) was tolerated well and parathyroid hormone levels decreased within the recommended range. Prior to initiation of therapy the health insurance company was asked to cover the costs for treatment with Cinacalcet due to the use outside the label indication.

Conclusion: In summary, Cinacalcet is useful to control sHPT in CKD stage IV especially when vitamin D replacement therapy fails as it has already been discussed in literature.

Table 1

<table>
<thead>
<tr>
<th>Site 1</th>
<th>Site 2</th>
<th>Site 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>all patients</strong>*</td>
<td><strong>pts with data</strong></td>
<td><strong>all patients</strong>*</td>
</tr>
<tr>
<td>t1 (n = 66)</td>
<td>t1 &amp; t2**</td>
<td>t1 (n = 54)</td>
</tr>
<tr>
<td>14.1</td>
<td>21.1</td>
<td>17.3</td>
</tr>
<tr>
<td><strong>corr Ca, P, CaP/PTH</strong> within targets (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>71.2</td>
<td>72.4</td>
<td>72.2</td>
</tr>
<tr>
<td><strong>Phosphate Binder in %</strong></td>
<td>63.6</td>
<td>79.3</td>
</tr>
<tr>
<td><strong>Calcimimetics in %</strong></td>
<td>28.6</td>
<td>46.6</td>
</tr>
</tbody>
</table>

* (including death, transplantation, loss of follow-up & new patients on dialysis) ** patients with data at both t1 and t2

Table 1

Levels of parathyroid hormone, calcium, phosphorus during treatment with Calcitriol and Cinacalcet.
Persistent norovirus infection in renal allograft recipients – a new concern for hospital hygiene

R. Schatt, W. Bossart, N. Müller, R. P. Wüthrich, T. Fehr
Zürich/CH

Purpose: Noroviruses are responsible for 80–90% of acute gastroenteritis outbreaks in adults and older children worldwide. In immunocompromised patients norovirus infection is self-limited. We are aware of only a few rare patients with either stem cell or intestinal allografts and of only one single patient with another solid allograft (here). Within the persistence of norovirus infection is described. Here we report on persistent norovirus infection in four adult renal allograft recipients.

Methods and materials:Diarrhea is a frequent clinical complaint in the renal transplant outpatient clinic; infection and drug side effects are the most common causes. A systematic screening for viruses, bacteria and parasites is usually performed in our patients with new onset diarrhea. In patients with proven norovirus infection, norovirus shedding by POC was monitored over time. Furthermore, clinical symptoms were recorded, and CRP was measured at each consultation. Viral RNA samples were stored for genetic analysis of the two most variable open reading frames.

Results: We report 4 renal allograft recipients (29 to 57 years old) with prolonged infection and persistent norovirus shedding over several months. Norovirus infection occurred between 39 days up to >10 years posttransplant. Duration of norovirus shedding ranged from 196 to 630 days. All patients received standard triple immunosuppression regimes at the time of diagnosis. Reduction of immunosuppression (mainly prednisone and mycophenolate, which was replaced by azathioprine in one patient) led to norovirus clearance in 2 patients. In the other 2 patients norovirus shedding persisted despite reduction of immunosuppression, but clinical symptoms were resolved. No rejection episode occurred upon reduction of immunosuppression. Genetic testing of viral RNA for analysis of clustering (as evidence for a potentially outpatient transmission) and for mutations of the open reading frames over time (as evidence for an antigenic drift, which could explain the failure of virus clearance due to an immune escape mechanism) are under current investigation.

Conclusion: We report for the first time persistent norovirus infection in adult renal allograft recipients under stable immunosuppression. Reduction of immunosuppression led to resolution of symptoms in all our patients, but achieved viral clearance in only 2 out of them. This finding has important implications for hospital hygiene procedures due the high infectiosity of this virus and its resistance to common hand disinfection solutions. We recommend norovirus testing in patients with prolonged diarrhea.

An open, single centre, prospective study to investigate a steroid free immunosuppressive regimen for de novo renal transplant recipients followed by a two arm randomisation to a CNI-snaring and a CNI-free maintenance immunosuppression after 3 months

T. Oettl, B. Descouedres, F. Burkhalter, A. Bachmann, L. Gürke, M. J. Mihatsch, M. Dickemann, J. Steiger
Basel/CH

Purpose: Criotocostroides as well as calcineurin inhibitors (CNI) have well known side-effects when given over long periods after kidney transplantation. We investigated the efficacy and safety of a steroid free immunosuppressive regimen in the early posttransplant period followed by CNI withdrawal after three months.

Methods and materials: 75 patients receiving a kidney transplant were enrolled from 1.1.2005 to 31.12.2007. Induction therapy consisted of methyl-prednisolon i.v. for 3 days and basiliximab on days 0 and 4. Maintenance immunosuppression (IS) consisted of tacrolimus (TAC) and sodium-mycophenolate (MPS). Sirolimus (SIR) was added on day 4. When protocol biopsy after 3 months showed no signs of rejection, patients were equally randomized in two groups: study arm without CNI (MPS/SIR) and control arm with low-tack TAC, MPS and SIR. Primary endpoint was renal function and study follow-up ended with a second protocol biopsy after 6 months.

Results: 75 patients were enrolled in the study. In the early posttransplant period (first 3 months) a total of 6 biopsies proven clinical acute rejections (BPCR) occurred, 4 of them were antibody mediated vascular rejections. The first protocol biopsy after 3 months of steroid free IS revealed another 4 subclinical acute rejections (SCAR), 3 of them with an interstitial (cellular) origin resulting in an overall rejection rate of 13% (clinical rejection rate 8%) after 3 months in this steroid free protocol. Randomization for the second part of the study was not possible, apart from the mentioned acute rejections, due to sirolimus side effects (n = 14). steroid therapy for dermatological or rheumatological reasons (n = 4), delayed graft function (n = 3), refused biopsy (n = 3), BKV infection (n = 2), surgical complications (n = 1), thrombotic microangiopathy (n = 1) or preernal failure (n = 1). 36 patients were randomised (study arm n = 17, control arm n = 19). The primary endpoint, i.e. renal function, was not different in both arms after 6 months. Secondary endpoint, i.e. biopsy proven rejection was detected in 7 patients (1 BPCR in 2 patients and 6 SCAR (35%)) and 3 patients (1 BPCR (5%), 2 SCAR (10%)) in the study and control arm, respectively. In 39 non-randomised patients, 5 biopsies showed histological signs of SCAR (13%) after 3 months, another 2 after 6 months. No new insulin-dependent diabetes mellitus was diagnosed whereas CNI-free IS led to significantly lower triglyceride levels after 6 months (p = 0.02).

Conclusion: An immunosuppression with TAC/MPS/SIR in the absence of corticosteroids is a save and efficient option in the prevention of acute rejection following kidney transplantation (13% rejection rate including SCAR). Renal function after 6 month was not superior under SIR/MPS compared to TAC/SIR/MPS. Dual therapy led to a higher SCR compared to triple therapy. More studies are needed comparing directly CNI and mTOR inhibitors in their ability to prevent posttransplant rejections.

Rituximab and intravenous immunoglobulin treatment for chronic antibody-mediated renal allograft rejection

T. Fehr, A. Gasperli, B. Rüsli-Eisenri, M. Weber, A. Fischer
Zürich/CH, *Lucern/CH

Purpose: B cells play a dual role in allograft rejection: (1) they are precursors of alloantibody-secreting plasma cells, and (2) they efficiently process alloantigens to stimulate T cell responses. Current anti-rejection therapies potently block cellular, but less efficiently antibody-mediated effector mechanisms. Whereas for acute antibody-mediated rejection (AMR), therapy mainly relies on plasmapheresis or immunoadsorption, no studies for treatment of chronic AMR are available. This pilot study tested the efficacy and safety of rituximab combined with intravenous immunoglobulin (IVIG) for late humoral allograft rejection.

Methods and materials: Renal allograft recipients were included in this pilot study based on the following criteria: (1) deteriorating allograft function, (2) no efficacy of standard treatments (steroids, increase of calcineurin inhibitors, T cell-depleting antibodies), (3) evidence for AMR in biopsy (C4d+) or serology (donor-specific antibodies (DSA)). Study patients received rituximab 375 mg/m² on days 1 and 7, and except one patient also IVIG 0.4 g/kg on days 2-5. eGFR, proteinuria and DSA were monitored.

Results: Four male patients (39-64 y) were included to 27 years post kidney allotransplantation. They experienced a loss of eGFR between 19 and 57% in the 6 months before treatment with rituximab. Three patients were sensitized according to the panel-reactive antibody test (max. PRA 47%), and all tested positive for DSA (2 anti-class II, 1 anti-class I and 1 both anti-class I/II). Three biopsies stained diffusely positive for C4d in peritubular capillaries, 2 showed transplant glomerulitis or glomerulopathy, 2 had cellular vascular rejection and 1 displayed intense infiltration with CD20+ cells. If classified according to the Covin scheme for chronic AMR, one patient was in stage I, 2 in stage II and 1 in stage IV. Upon treatment with rituximab all patients had improvement of GFR, which remained significant until 6 months post treatment. One patient developed acute cellular rejection one year after rituximab (without previous evidence for a raise of DSA), and one patient experienced severe, possibly rituximab-associated lung toxicity, DSA levels 3-8 months after rituximab dropped in two and remained unchanged in the other two patients.

Conclusion: Rituximab/IVIG represented an effective short-term treatment for chronic AMR of a renal allograft. However, severe toxicity occurred in one patient. Larger studies are needed to identify the appropriate target patient population for such treatment and to determine the optimal treatment protocol.

Does the addition of a mTOR inhibitor reduce the incidence of post-transplant skin cancers?

M. T. Tufail Hanel1, P. Itin1, J. Steiger1, A. Bock2
*Basel/CH, *Aarau/CH

Purpose: Skin cancers develop in 20 to 40% of renal transplant recipients beyond 10 years after transplantation and represent a relevant source of morbidity and mortality. The immunosuppressive mTOR inhibitors, Sirolimus (Siro) and Everolimus (Evero), have been reported to be both antiproliferative in general and beneficial for a variety of clinical malignancies, including skin cancer, lymphomas and renal cell carcinomas. It is, however, unknown whether the addition of a mTOR inhibitor reduces the occurrence of de novo skin cancers in longterm transplant recipients. The present retrospective analysis was designed to evaluate the effect of adding an mTOR inhibitor to the
immunosuppressive regimen on the incidence of cutaneous squamous cell carcinomas (cSCC) in renal transplant recipients already suffering from these tumours.

Methods and materials: Retrospective analysis of renal transplant recipients followed in Aarau and Basel who a) had an mTOR inhibitor added to immunosuppression at least 3 years after transplantation and b) had at least one biopsy-proven squamous cell carcinoma (excluding carcinoma-in-situ) in the 2 years before this change and c) remained on the mTOR inhibitor drug regimen at least 2 years after the change. All patients were examined for skin cancers at their annual check-up. The primary parameter was the number of cSCC in the two years before and after the mTOR switch. A control group was formed from patients transplanted in the same year, who were on non-mTOR immunosuppression during the same 4 years as their index patient and had at least one cSCC during this period. The present data represent an interim analysis of data from Aarau patients only.

Results: All 5 mTOR patients meeting the inclusion criteria were male. Mean age was 69 years (range 51–78), 3 had a first transplant and 2 were living donor kidney recipients. No control patient could be found for patient No 3. Data are presented below:

<table>
<thead>
<tr>
<th>mTOR</th>
<th>Immunossuppression</th>
<th>N of cSCC /24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>before mTOR mTOR inhibitor</td>
<td>with mTOR</td>
<td>before mTOR with mTOR</td>
</tr>
<tr>
<td>Ca-mono</td>
<td>Evers/Ca-low</td>
<td>9</td>
</tr>
<tr>
<td>Ca/Pred</td>
<td>Siro/Ca/Pred</td>
<td>9</td>
</tr>
<tr>
<td>Ca/MMF</td>
<td>Evers/Ca-low/MMF</td>
<td>3</td>
</tr>
<tr>
<td>FK-mono</td>
<td>Evers/FK-low</td>
<td>4</td>
</tr>
<tr>
<td>FK/Aza</td>
<td>Siro/FK-low</td>
<td>1</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td>4.4</td>
</tr>
<tr>
<td>(throughout)</td>
<td>(same 24 months)</td>
<td>(same 24 months)</td>
</tr>
<tr>
<td>Ca/MMF</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Ca/Pred</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>FK-mono</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>FK/Aza</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>0.75</td>
<td></td>
</tr>
</tbody>
</table>

Thus, the number of cSCCs decreased in 3 of 5 patients after adding mTOR inhibitors but increased in 3 of 4 controls during the same time. Due to the small number of patients, the effect of the mTOR switch was nonsignificant (p = 0.12).

Conclusion: These preliminary data indicate that some patients with post-transplant cSCCs appear to benefit from the addition of mTOR inhibitors to their immunosuppressive regimen. By the end of 2008, the study will be extended to the entire Basel/Aarau transplant population, and hopefully yield conclusive results. It may then form the basis of a national registry to clarify the potential benefit of mTOR inhibitors in transplant recipients with cSCCs.

Prevalence, etiology and therapy of anaemia after kidney transplantation in Switzerland: Results of a national survey

P. Ambühli, M. Dickenmann, D. Ackermann, A. Corsenca, K. Hadaya, E. Catana

Zürich/CH, Basel/CH, 3010 Bern, 1Geneve 14/CH, 2Lausanne/CH

Purpose: Posttransplant anaemia has not been given much consideration so far. Previous analyses from a single Swiss transplant centre have revealed that about 25 percent of patients with a renal graft do not meet targets for minimum haemoglobin requirements as defined by NKF-K/DOQI guidelines for haemodialysis patients. However, this analysis did not take into account factors that might be causative for anaemia, such as iron deficiency or concomitant medication. Moreover, no data are available on the use of erythropoietin stimulating agents (ESA) in the Swiss renal posttransplant population. Thus, it was the aim of the present study to gather information on the prevalence, etiology and therapy of posttransplant anaemia in Switzerland.

Methods and materials: We conducted a national survey to which all Swiss centres performing renal transplants were invited to participate. Data were collected between June and August 2008 in a cross sectional manner, allowing all patients to be included from which information on hemoglobin concentration, renal function, therapy for anaemia, immunosuppression and comorbidities affecting erythropoiesis was available at some timepoint within 12 months prior to data assessment. Additional information (if available) was gathered on iron metabolism, parathyroid function, and systemic acid/base status.

Psychosocial evaluation of 189 consecutive potential living kidney donors in Basel


Basel/CH

Purpose: Psychosocial evaluation of potential organ donors is mandatory in Switzerland. However, little is known about the extent of the psychosocial evaluation and how frequent objections regarding the transplantation are.

Methods and materials: An explorative study in 189 consecutive potential living kidney donors was performed.

Results: From January 1, 2004 until July 31, 2008, 189 potential donors were evaluated. Mean age was 53 (range: 29–82), 129 (68%) were female (68%), 46 were non-Swiss (26%). 80 were genetically related (43%), 65 were emotionally related (35%). 32 (17%) had a distant relation to the potential recipient and 9 (6%) were unrelated. 154 were evaluated once and in 35 (19%) an additional psychosocial evaluation was necessary. As a result of psychosocial evaluation, 16 (8%) potential donors were rejected. In 6 cases, another living donor was chosen. In the remaining 10 cases without another potential living donor, 6 agreed with rejection for psychosocial reasons and 4 disagreed with the final decision.

Conclusion: In a minority of potential donors, an extended psychosocial evaluation is necessary. In most potential donors who are rejected for psychosocial reasons they agree with the decision, and very few are rejected against their explicit wish to donate.
Results:

<table>
<thead>
<tr>
<th>Hb, g/L</th>
<th>Hb &lt;110 g/L</th>
<th>Hb &lt;130 g/L</th>
<th>Hb &lt;110 g/L</th>
<th>Hb &lt;130 g/L</th>
<th>Hb &lt;110 g/L</th>
<th>Hb &lt;130 g/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>220 (100)</td>
<td>81 (38.6)</td>
<td>50 (22.7)</td>
<td>144 (65.5)</td>
<td>36 (25)</td>
<td>44 (30.5)</td>
</tr>
<tr>
<td>116.6±18</td>
<td>98.1±9</td>
<td>141±10.9</td>
<td>123±17</td>
<td>107±6.9</td>
<td>142±11.2</td>
<td>105.9±15</td>
</tr>
<tr>
<td>Ferritin, µg/L</td>
<td>330±337</td>
<td>494±436</td>
<td>125±100</td>
<td>245±260</td>
<td>350±328</td>
<td>132±114</td>
</tr>
<tr>
<td>Transthyretin Sat., %</td>
<td>27±113</td>
<td>26±18</td>
<td>25±9</td>
<td>24±12</td>
<td>24±16</td>
<td>23±10</td>
</tr>
<tr>
<td>GFR, ml/min</td>
<td>44±21</td>
<td>37±21</td>
<td>54±19</td>
<td>50±20</td>
<td>45±20</td>
<td>57±17</td>
</tr>
<tr>
<td>CRP, mg/L</td>
<td>9.9±24</td>
<td>12±19</td>
<td>3.5±5</td>
<td>9.5±25</td>
<td>12±17</td>
<td>3.8±5</td>
</tr>
<tr>
<td>PTH, ng/L</td>
<td>148±105</td>
<td>220±141</td>
<td>104±61</td>
<td>138±90</td>
<td>138±22</td>
<td>88±53</td>
</tr>
<tr>
<td>On ESA, N (%)</td>
<td>76 (34.5)</td>
<td>45 (55.5)</td>
<td>6 (12)</td>
<td>0</td>
<td>0</td>
<td>76 (34.5)</td>
</tr>
<tr>
<td>PTH dosage, IU/wk</td>
<td>920±7386</td>
<td>1136±7367</td>
<td>542±5270</td>
<td>NA</td>
<td>NA</td>
<td>920±7386</td>
</tr>
<tr>
<td>Age, yr</td>
<td>56.1±14</td>
<td>57±14</td>
<td>55.6±13</td>
<td>56±14</td>
<td>57±3±15</td>
<td>56±4±13</td>
</tr>
<tr>
<td>Time since TPL, yr</td>
<td>7.7±7</td>
<td>7.4±8</td>
<td>8.3±7</td>
<td>7±6</td>
<td>6.1±7</td>
<td>8±7</td>
</tr>
</tbody>
</table>

Conclusion: Posttransplant anemia is very common in a Swiss cohort of patients with a renal graft, with 37% of patients having Hb concentrations below 110 g/L. Among them, only 55% receive ESA therapy, leaving room for improving anemia status. The main determinant of Hb concentration is graft function. The inverse correlation of ferritin and Hb is intriguing, but needs further assessment.

Protein A immunoabsorption for treatment of acute antibody-mediated renal allograft rejection


Zürich/CH

Purpose: No evidence-based data from randomized controlled studies are available for treatment of acute antibody-mediated rejection (AMR) in kidney allografts. However, it is generally accepted that a method for allograft remodelling should be used as part of the regimen, which often includes also steroid pulses, intravenous immunoglobulin and/or rituximab. Plasma exchange (PEX) and immunoadsorption (IADS) are the two main modalities available. The latter may have advantages due to the selective removal of immunoglobulins, since no disturbance of the coagulation system or other serum proteins is expected. Here we report our preliminary experience with this technology.

Methods and materials: In July 2007 the technique of IADS with Protein A-coated columns for treatment of acute AMR was introduced in our dialysis and apheresis unit. Acute AMR episodes were treated with 6–8 sessions of IADS together with intravenous immunoglobulin substitution at a dose of 1 g/l total IgG after 2 treatments. However, a substantial loss of allograft function was only observed in patients with a relapse about 6 months later. Two episodes occurred in the first month after transplantation, and one of these patients had a relapse about 6 months later. Two episodes were late acute AMRs, one due to non-compliance and one due to too much reduction in immunosuppression. Currently, patient and graft survival are 100% with a follow-up between 1 month and 1 year after treatment. However, a substantial loss of allograft function was observed in all 4 patients. Immunoglobulin removal by IADS was very efficient reaching levels below 1 g/l total IgG after 2 treatments with concomitant reduction of DSA. With the first two IADS treatments, which both occurred early after transplantation, bacterial infections at the operation site required prolonged hospitalisation. The infection rate was 17 S.

Surveillance biopsies after steroid withdrawal in adult renal transplant recipients

I. Koneth1, J. Neuweiler1, D. Tsinalis2, I. Binet1

1 ST. Gallen/CH, 2 ST. Gallen/CH

Purpose: Since 2005 the policy in our centre includes surveillance biopsies (SBx) after steroid withdrawal (SWD) in renal transplant recipients. To our knowledge there are only few reports in the literature regarding surveillance biopsies in relation with steroid withdrawal in adult kidney transplant recipients.

Methods and materials: 42 adult kidney recipients transplanted between 11/03 and 1/08 from deceased or living donors were included. All had a surveillance biopsy within 24 months after transplantation preceded or rarely followed by prednisone (PDN) withdrawal within 90 days from biopsy. The following data were analysed: patients and transplant characteristics, histology including immunofluorescence, changes of immunosuppressive therapy (IS), short term follow-up regarding graft function and acute rejection.

Values are given as median and range. Age at transplantation 52 years (19–69), first / second graft in 40/2 patients, deceased / living donor transplantation in 26/15 patients, no sensitized patients (CDC PRA last / peak 0/0 except 6 recipients with max. 11/35. Baseline IS consisted of basiliximab, cyclosporin (CsA), mycophenolate and PDN 35 patients, in the other 7 cases various regimens were used. Only two patients had biopsy-proven acute rejection before SWD. The SBx took place at 9 mo (6–24) post-transplant. In 40 patients complete SWD preceded the biopsy by 20 days (0–77), in 2 patients it followed the biopsy by 43 and 57days respectively, both were on a PDN dose of 2.5 g/m 2 at SBx. Follow-up after SBx was 17 months (0–42). Changes of IS after SBx were tailored individually considering not only the actual SBx but also preceeding biopsies, immunological risk profile and previous side-effects of immunosuppression.

Results: Of the 42 (41%) SBx were normal or unchanged with regard to time zero biopsies. The remaining 25 biopsies showed CsA-toxicity in 12 cases, borderline cellular rejection in 8 cases, 1 acute tubulo-interstitial rejection (Banff 1a), acute vascular rejections in 3 cases (negative C4d), 50% C4d positivity of peritubular capillaries in 1 case and nephrocalcinosis in another. IS remained unchanged in 23/42 (55%) patients, whereas in 10/42 (24%) the calcineurin inhibitor dose was markedly reduced. In patients with tubular rejection PDN was restarted or mycophenolate increased. Acute vascular rejections were treated with AFG, PDN and switch to tacrolimus. The isolated C4d positivity was rebiopsied after x months and mycophenolate increased in view of an increase of the positivity. During follow-up after SBx transplant function remained stable, both in patients with normal histology as in those with pathological SBx. The slope of estimated creatinine clearance at last follow-up compared to the biopsy date was +0.2 (90% ml/min/month in all 42 recipients and was not different between those with normal or pathological SBx.

Conclusion: Surveillance biopsies after steroid withdrawal in mostly low-risk renal transplant patients can help to guide immunosuppression adjustment. This combination of steroid withdrawal with surveillance biopsy may contribute to the safety of steroid withdrawal.

44

45
Switch to Sirolimus-based immunosuppression in stable renal transplant recipients

G. Nseir1, J.-P. Venetz1, K. Hadaya2, L. Buhler3, P.-Y. Martin1, M. Pascal1

Lausanne/CH, 1Geneva 14/CH, 2Geneve/CH

Purpose: Sirolimus (SRL) has been used to replace calcineurin inhibitors in various situations and has shown promising results. However, atypical cases of severe infectious or vascular side effects leading to drug discontinuation have been described.

Methods and materials: Between 2001 and 2007, 41 patients (20 females, 21 males; mean age 47 ± 13) were switched after a median time post-transplantation of 73.5 months (range 0.2–273.2 months). Indications for switch were CNI nephrotoxicity (39%), thrombotic micro-angiopathy (14.6%), post-transplantation cancer (24.4%), CNI nephrotoxicity (7.4%).

Results: Mean creatinine increased from 154 to 143 µmol/l (p < 0.003), mean estimated glomerular filtration rate (eGFR) increased significantly from 50.3 to 55.01 ml/minute (p < 0.00001), mean systolic and diastolic blood pressure decreased from 138 to 132 mm Hg (p < 0.03) and from 83 to 77 mm Hg (p < 0.01), but mean proteinuria increased from 0.21 to 0.63 g/24 h (p < 0.001). While mean total cholesterol increased significantly from 5.09 to 5.56 mmol/l (p = 0.06). The main complications after SRL switch were dermatitis (19.5%), urinary tract infections (24.4%), ankle edema (13.3%), transient oral ulcers (6.3%), and transient acute rejection after the switch occurred in 7.3% of patients (n = 3), and 2 acute rejections were successfully treated with corticosteroids and I did not respond to treatment (related to switch). SRL had to be discontinued in 17% of patients (2 nephrotic syndromes, 2 severe edema, 1 acute rejection, 1 thrombotic micro-angiopathy, and 1 fever).

Conclusion: In this study, we found that SRL Switch is 23.8±16.3 months. Mean SRL dosages and trough levels were 2.4 ± 1.1 ng/day and 8 ± 2.2 µg/l respectively. Immuno-suppressive regimens were SRL + mycophenolate mofetil (MMF) (31.7%), SRL + MMF + prednisone (36.6%), SRL + prednisone (19.5%), SRL + Azathioprine (9.75%), or SRL alone (2.4%).

SoP DIDACT – A Swiss survey on the practicability of DIDACT

K. Hadaya1, C. Cao2, P.-Y. Martin1

Geneve 14/CH, 2Reinach/CH

Purpose: Progresses in transplantation medicine have led to very good patient and graft survival rates. However a significant number of patients are still suffering from adverse side effects of their immunosuppressive therapy [i,ii]. These side effects could lower patient compliance and secondary increase the risk of acute rejection [iii]. The DIDACT study [iii] investigated the influence of non-immunosuppressive factors on the incidence of severe diarrhea in renal transplant recipients. The Swiss survey on the practicability of DIDACT (SoP DIDACT) assessed whether specialists in charge for transplant patients were familiar with the DIDACT study, how quality and practicability of DIDACT were rated and whether the algorithm as described in DIDACT was applicable.

Methods and materials: Area of expertise, number of transplant recipients seen per week, knowledge of the DIDACT study and whether findings of the DIDACT study were already applied, were assessed by means of a baseline questionnaire. Specialists were asked to rate the study design and the study results on a scale from 0–10 (1 = relevant; 10 = not relevant) if they were familiar with the study. Otherwise the study was briefly presented to them. A follow up questionnaire (2 months later) assessed the experience of the specialists with the use of DIDACT algorithm including rating, applicability and efficacy of the algorithm (1 = useful; 2 = easy to apply; 3 = efficacious; 10 = not useful/ difficult to apply/ not efficacious).

Results: 104 specialists of various fields (nephrology, surgery, hepatology, immunology, gastroenterology) were asked to participate to the SoP DIDACT. 98 (94%) specialists completed the baseline questionnaire and 71 (78%) specialists answered the follow up questionnaire. 65 specialists (62.5%) filled both questionnaires.

Baseline questionnaire: 70.5% (69 out of 98) of participating specialists had either heard about or read the DIDACT study whereas 29.5% did not. 33.7% (33 out of 98) of the specialists had already implemented the DIDACT algorithm. The study design was rated 2.9 ± 1.7 and the study result 2.7 ± 1.4 (mean ± SD). Follow up questionnaire: 72% (51 out of 71) of the specialists had applied the algorithm at least once since the baseline assessment and were included in the following analysis. The stepwise approach of the DIDACT algorithm was rated 3.1 ± 2.4 (n = 50), the practicability 2.5 ± 1.8 (n = 49), and the efficacy 2.7 ± 1.0 (n = 49). The following steps of the algorithm would be applied by the Swiss specialists in front of severe diarrhea in transplant recipients: (1) withdrawal of diarrhea-causing concomitant non-immunosuppressive medication, (2) microbiological stool examination, (3) exclusion of cytomegalovirus infection, (4) exclusion of bacterial overgrowth, (5) colonoscopy, (6) adaptation of the immunosuppressive therapy, and (7) empirical treatment.

Conclusion: The majority of the Swiss specialists was familiar with the DIDACT study and judged the results as relevant. Until the follow up assessment, 72% had applied the algorithm at least once. The algorithm was judged useful, easy to apply and efficacious. In contrast to the algorithm as presented by Maes, Hadaya et al[iii], the Swiss specialists preferred to adapt the immunosuppressive therapy only after having performed a colonoscopy. The DIDACT algorithm is accepted by the majority of the specialists who participated in the survey. The step-wise approach to investigate reasons for severe diarrhea is perceived as being helpful to reduce or eliminate unnecessary changes in the immunosuppressive therapy which could lead to higher rejection rates and lower graft survival.


Thrombotic microangiopathy in renal transplantation: is single kidney transplantation an option for patients with hemolytic uremic syndrome caused by factor H gene mutation?

P. Hirt-Minkowska1, M. Dickenmann, M. Mayr, S. Schaub, J. A. Schifferli, J. Steiger

Basel/CH

Purpose: Hemolytic uremic syndrome (HUS) is a clinical syndrome characterized by microangiopathic hemolytic anemia, thrombocytopenia and acute renal failure. Pediatric cases are often caused by shiga-like toxin-producing Escherichia coli. However, atypical cases may occur, especially in adults, showing a tendency to relapse, to occur in families and to have a poor outcome. Mutations in the complement factor H gene account for about 10–30% of cases of
familial or recurrent HUS. Complement factor H is produced by the liver and is an important regulator of the complement cascade through alternative pathway by inactivation of C3b deposition on host cells. Patients with decreased levels of complement factor H or functional complement factor H deficiency fail to efficiently restrict complement deposition on endothelial cells, leading to microvascular thrombosis and tissue destruction by uncontrolled complement activation. Plasma exchange therapy or plasma infusions can ameliorate the clinical symptoms of complement factor H deficiency associated HUS, but not necessarily. A decreased complement factor H and the disease may transiently recover but in many cases recur after complement factor H is cleared by the circulation and patients finally progress to end stage renal disease (ESRD). HUS also invariably recurs in the graft kidney and causes graft failure making the rationale of single kidney transplantation questionable. Given that complement factor H gene mutation as a cause of single kidney transplantation has been reported double transplantation is no longer recommended. We report a case of successful single kidney transplantation combined with peri- and postoperative plasma infusions.

Methods and materials: On August 1999, following a prolonged upper respiratory tract infection with fever but no diarrhea, a 23 year old man developed an acute renal failure associated with signs of microangiopathic hemolytic anemia and thrombocytopenia consistent with the diagnosis of HUS. He clinically presented with reduced general condition with elevated blood pressure, generalised edema and proteinuria and renal function impairment with a creatinine concentration of 7 (0.86). He was treated with plasma exchange therapy and renal function mainly recovered with slightly increased creatinine levels. A renal biopsy was performed, confirming thrombotic microangiopathy in the glomeruli and arterioles. The further clinical course was characterized by two relapses of HUS (one following an atypical pneumonia, the second one without an apparent trigger) and finally ESRD occurred. Chronic hemodialysis was started in November 2002. A comprehensive complement analysis provided normal complement factor C3, C4, B1, and H serum concentrations and activity of the von Willebrand factor–cleaving protease (ADAMTS 13) was normal. But genetic studies disclosed a heterozygous point mutation in the micro-vascular type 1 collagen (COL1A1) gene position 1210) of the complement factor H gene which has been previously described in five pedigrees and 7 individual patients with atypical HUS, leading to concluding diagnosis of functional deficient complement factor H.

Results: The patient underwent kidney transplantation from a deceased donor in August 2007. To avoid HUS recurrence abundant perioperative plasma infusions of fresh frozen plasma (FFP) were given every 6 h for 48 h, once daily in the first week, twice a week for one month and thereafter weekly for a further month. Immunosuppressive therapy consisted of triple therapy with tacrolimus, mycophenolate and prednisolone and basiliximab day 0 and 4. Two diagnostic graft biopsies (day 5 and 15) presented signs of acute tubular necrosis but no characteristics of a HUS relapse, so did the two protocol biopsies after three and six month. One-year-follow up showed stable graft function. Conclusion: We conclude that single kidney transplantation with abundant perioperative FFP infusions, partly replacing the lack of functional complement factor H is a rational option for patients with atypical HUS associated with complement factor H gene mutation. It seems that extensive plasma infusion therapy during and after operation can prevent serious clinical complications by uncontrolled complement activation. However the follow up was short and further clinical observations are necessary.

Overall mortality as well as the composite of cardiac death, cardiothoracic surgery and percutaneous coronary intervention were assessed as secondary endpoints. The endpoints were prospectively assessed during follow-up.

Results: Detailed baseline characteristics of the study population are displayed in table 1. BNP values rose with patients’ age (r = 0.296, p = 0.002), LVM (r = 0.448, p = 0.010) and decreasing systolic (rE = –0.333, p = 0.016) and diastolic (rE/A = –0.320, p = 0.003) cardiac function. Of note, BNP values were significantly higher in diabetic patients (716 pg/ml [514–1340] vs. 340 pg/ml [147–726], p = 0.004), but not in patients with known cardiac (r = 0.37) or pulmonary (r = 0.44) diseases. Overall 23 patients reached the composite endpoint (17 cardiac deaths, 6 percutaneous interventions). The median follow-up period was 735 days [355–1455]. BNP values were equal in patients dying of cardiac causes and survivors (591 pg/ml vs. 431 pg/ml, p = 0.37). Similarly, patients reaching the composite endpoint (421 pg/ml vs. 466 pg/ml, r = 0.72) or dying of any cause (591 pg/ml vs. 415 pg/ml, p = 0.44) did not have higher BNP values.

In a Cox regression analysis BNP failed to predict cardiac death (HR 1.00; p = 0.23), overall mortality (HR 1.00; p = 0.20) and the composite endpoint (HR 1.00; p = 0.64).

Conclusion: In unselected patients undergoing chronic hemodialysis BNP values fail to predict cardiac death as well as overall mortality or the need for coronary revascularization.

Validity of conventional scoring systems assessing nutritional status of hemodialysis patients

C. Kraemer1, M. Dorfler2, M. Dorfler3, H.-R. Räz4, A. Corsenca1, R. P. Wüthrich1, P. Wahl1, P. Ambühl1

Zürich/CH, "Baden-Dättwil/CH

Purpose: Malnutrition is a common problem among hemodialysis (HD) patients, and is associated with both increased morbidity and mortality. Unfortunately, nutritional assessment is cumbersome and frequently imprecise. Scores to assess nutritional status and/or risk for malnutrition are potentially useful to identify HD patients with a high risk of mortality. However, commonly available assessment tools, such as the NRS (nutritional risk screening), SGA (subjective global assessment), and MNA (mini nutritional assessment) have not been validated for a HD population. Thus, the aim of the present study was to evaluate conventional risk scores in maintenance HD and to validate them with a more extended assessment of nutritional status.

Methods and materials: A total of 56 patients were evaluated from a subset of participants from the monitor! trial, a prospective dynamic hemodialysis cohort study assessing a wide range of clinical, laboratory and anthropometrical parameters. Scores for every individual patient based on the 3 assessment tools NRS, SGA and MNA were calculated using the monitor! database. In addition, malnutrition was diagnosed by an extended assessment ("monitor! criteria"), rating 6 parameters including normalized protein catabolic rate (nPCR; <0.8 g/kg body weight), serum albumin concentration (<38 g/l), body mass index (BMI; <23 kg/m²), lean body weight (LBM: <10th percentile), weight loss over the preceding 3 months (<5% of body weight), and energy intake (calculated from dietary protocols; <75% of energy requirements). A risk score was calculated from the sum of criteria fulfilled. Patients with 0-1 points were rated as: "well nourished, no malnutrition detectable"; 2 points: "moderately malnourished"; and 3-6 points: "severely malnourished".

Correlational analyses were performed using cross tables and the chi-square test by Pearson.

Results: Extended evaluation of nutritional status based on the monitor! criteria found 41% of patients to be "well nourished", 34% "moderately malnourished", and 25% "severely malnourished". In contrast, rating by conventional assessment tools gave the following results and concordances with the monitor! score: Rating of nutritional status by different assessment tools

<table>
<thead>
<tr>
<th>Score</th>
<th>concordant</th>
<th>concordant</th>
<th>concordant</th>
</tr>
</thead>
<tbody>
<tr>
<td>monitor! criteria</td>
<td>41</td>
<td>34</td>
<td>25</td>
</tr>
<tr>
<td>NRS</td>
<td>0</td>
<td>60.7</td>
<td>47.4</td>
</tr>
<tr>
<td>SGA</td>
<td>41</td>
<td>52.2</td>
<td>46.5</td>
</tr>
<tr>
<td>MNA</td>
<td>14.3</td>
<td>26.1</td>
<td>76.8</td>
</tr>
</tbody>
</table>

Statistical analysis revealed a positive correlation for the monitor! criteria with the NRS, but not with the SGA and MNA. Among the misclassified patients both the NRS and MNA scored 10% of "well nourished" subjects erroneously. While the NRS identified 10% of HD patients as malnourished, whereas the SGA conversely misclassified 15% of "severely malnourished" patients falsely as "well nourished". Finally, the MNA attributed to...
most of the patients a “moderately malnourished” status and missed the majority of both “well nourished” and “severely malnourished” subjects.

Conclusion: Our analysis confirmed the problem of malnutrition in a Swiss maintenance HD population, with more than 50% of patients being moderately or severely malnourished. Conventional assessment tools are not well suited to assessing nutritional status of maintenance HD patients. Among the three tested scores the NRS fared best, especially with regard to detecting severely malnourished patients. The gold standard for nutritional assessment in our analysis consisted of a modified assessment of parameters as recommended earlier by the International Society of Renal Nutrition and Metabolism. This tool, however, awaits validation as a prognostic screening instrument.

Decrease of time averaged B-type natriuretic peptide improves prognosis in unselected hemodialysis patients

T. Breithardt1, S. Kalbtermatter1, J. Mangold2, C. Mueller, D. Kiss1
1Basel/CH, 2Liestal/CH

Purpose: B-type natriuretic peptide (BNP) is universally increased in hemodialysis patients. Extracellular hypervolemia, concomitant heart disease and reduced renal BNP-clearance contribute to the high plasma concentrations. The prognostic potential of BNP changes in unselected hemodialysis patients is presently unknown.

Methods and materials: 113 consecutive, unselected, elective hemodialysis patients at the Hemodialysis Unit Basel were enrolled in a longitudinal study. All patients were over 18-years old and underwent at least three four-hour hemodialysis sessions per week. Patients were not excluded on the basis of co-existing illnesses or time on dialysis. After enrollment BNP levels were measured every six months. Time-averaged BNP (TA-BNP) represents the average of every six-month period’s BNP value. The primary endpoint of this study was four-year cardiac mortality. Overall mortality was assessed as the secondary endpoint. The endpoints were prospectively assessed during follow-up.

Results: Detailed baseline characteristics of the study population are displayed in table 1. Overall 35 died during the follow-up period (17% cardiac deaths, 18 other causes) and six patients underwent percutaneous coronary interventions. TA-BNP levels were significantly higher in patients dying of cardiac (1276 pg/ml [339–2312] vs. 467 pg/ml [254–887], p = 0.03) or any causes (890 pg/ml [296–1349] vs. 475 pg/ml [257–787], p = 0.03). In multivariate Cox regression analysis TA-BNP predicted cardiac (HR 1.08; 95% CI 1.03–1.13 for an increase in BNP of 100 pg/ml; p <0.01) and overall mortality. (HR 1.04; 95% CI 1.00–1.08 for an increase in BNP of 100 pg/ml; p = 0.03). TA-BNP tertiles were analyzed as categorical variables (fig. 1). In a subgroup analysis of 51 patients presenting with initial BNP values in the second and third tertile, a decrease of subsequent TA-BNP levels by at least one tertial significantly improved cardiac (p = 0.05) and overall survival (p <0.01).

Conclusion: In unselected patients undergoing chronic hemodialysis TA-BNP represents a powerful predictor of both cardiac and overall mortality. A decline in TA-BNP over time significantly improves cardiac and overall survival.

Quality of vascular access on chronic haemodialysis

Basel/CH

Purpose: Depending on patient characteristics, the quality of the native blood vessels, the preference, practice and know how of the surgeons and regional and national differences in patient management shunt survival on chronic haemodialysis varies considerably. On the basis of this background differences in respect of reported parameters of shunt quality and survival may not be easily extrapolated for a population of ICU patients treated with a continuous renal replacement therapy. Therefore, the study goal was

Results: Overall 282 patients entered the chronic haemodialysis program during the study period. Thirteen patients were dialysed by a temporary access and therefore excluded; three patients had to be excluded due to incomplete data. As first access, 226 patients (85%) received a native arteriovenous (AV) fistula, 16 patients (6%) a synthetic graft and 24 patients (9%) a double-lumen tunneled cuffed catheter. 142 patients (53%) had at least one access-related complication. Thrombosis (n = 50, 35.2%) and stenosis of the access (n = 45, 31.7%) were the most common complications. The one-, three- and five year rates of complication free technical survival were 57%, 39%, 33% respectively. In diabetics compared to non-diabetics (p = 0.02) and in women compared to men (p = 0.007) complication free technical survival was significantly lower. In 71 patients (27%) an occlusion of the access was observed. The one-, three- and five-year rates of occlusion free technical survival were 77%, 61% and 56%.

The occlusion free technical survival was significantly inferior to native AV fistulas (p <0.0001). Median occlusion free technical survival of radiocephalic fistulas was 5.4 (Tabatière) and 5.1 (Cimino) years, respectively. The median time of occlusion free technique survival of synthetic grafts was 5.4 (forearm) and 1.4 (upper arm) months, respectively.

Conclusion: Our data with a high percentage of native AV fistulas as primary access suggest that the guidelines for chronic haemodialysis access can be achieved with satisfying outcome. However, to further improve the outcome of the access in chronic haemodialysis prospective studies are essential which compare different approaches in creation of fistula based on predefined criteria.

Altered proteasome activity plays a key role in CD4+/CD25+ Treg apoptosis in patients with end-stage kidney disease

P. Meier
Sion/CH

Purpose: The ubiquitin-proteasome system is responsible for the turnover of intracellular polyubiquitinated proteins. The key regulators of cell survival and apoptosis, including members of the Bcl-2 family, some caspases, and inhibitor of apoptosis proteins, have all been recognized as substrates of the proteasome. The role of proteasome pathway in CD4+ T cell immune dysfunction in patients with ESKD remains unclear. In this study, we emphasized the key role of the proteasome in the regulation of CD4+/CD25+ regulatory T cell (Treg) apoptosis in 10 chronic HD patients, 10 CKD (non-HD) patients and 10 healthy control subjects.

Methods and materials: The activity of the cytosolic 20 and 26 S proteasomes, the induction of the cyclin-dependent kinase inhibitor p27Kip1, the accumulation of the pro-apoptotic protein Bax, the amount of the anti-apoptotic molecule Bcl-xL, the percentage of annexin V positive cells and the DNA fragmentation of CD4+/CD25+ Treg were determined.

Results: The 20 and 26S proteases activity was significantly down-regulated (−43% and −51%, respectively) in CD4+/CD25+ Treg from patients with ESKD compared with CD4+/CD25+ Treg proteasomes activity in non-HD CKD patients and control subjects (p = 0.001, ANOVA). This was accompanied by the up-regulation of the proteasome-related protein p27Kip1, the accumulation of Bax and the decrease of the Bcl-xL amount (p from 0.02 to 0.001). In parallel, percentage of annexin V positive CD4+/CD25+ Treg was significantly higher in patients with ESKD (p = 0.003). This was confirmed by the increased DNA fragmentation. This raised the possibility that p27Kip1 and Bax are targeted for degradation by the 26S proteasome. The enhanced stabilities of these molecules and the low activity of Bcl-xL may be responsible at least in part for the higher CD4+/CD25+ Treg apoptotic rate in patients with ESKD.

Conclusion: These data suggest that uremia and chronic HD stimulate CD4+/CD25+ Treg apoptosis by altering proteasome activity. This response could contribute to the CD4+ T cell immune dysfunction associated with ESKD.
Results: Included in this study were 24 patients with 26 self-locating catheters (11 females, 13 male patients, mean age 48.5 ± 26.5 yrs). The catheter survival rate was 92.4% at 1 year. During 282 PD months there was only one catheter dislocation, occurring shortly after implantation. We observed 3 leakages which were successfully corrected by surgery. One catheter had to be exchanged due to a hernia. 5 catheters were removed due to transplantation, 1 was removed after improved kidney function and 1 was replaced due to omental capture. We observed 6 peritonitis episodes, one exit site infection and one tunnel infection (1.05 patient-month).

Staphylococcus aureus was the most common cause of infection. One of these infections necessitated a catheter removal and a switch to hemodialysis. Conclusion: In our experience, the use of “self-locating” PD catheters was very successful. Catheter migration and dislocation were rare. In our program “self-locating” catheters seem to be associated with fewer removals due to malfunction compared with conventional Tenckhoff catheters. Infection rates were low, in accordance with other studies with the “self-locating” catheter. The use of the “self-locating” catheter could help to improve the results of existing PD programs.

Patient survival on chronic haemodialysis: a retrospective analysis from the Basel Dialysis Unit 1995–2006

T. Breithardt, C. Bucher, D. Garzoni, T. Wolff, K. Stoeter, M. Dickenmann, J. Steiger, M. Mayr

Basel/CH

Purpose: Patient survival on chronic haemodialysis varies considerably among different countries and healthcare systems. So far, the mortality rates of Swiss dialysis patients have not been analysed separately.

Methods and materials: We retrospectively enrolled all patients entering the chronic haemodialysis program of the University Hospital Basel between 01.01.1995 and 30.06.2006 into a cohort study. Patient survival on chronic haemodialysis was the primary endpoint of this study. Cumulative survival was calculated using the Kaplan-Meier analysis. Comparisons were made using the log-rank test. A statistical significance level of 0.05 was used.

Results: Overall 269 patients entered the chronic haemodialysis program during the study period. Three patients had to be excluded from the analysis due to incomplete data. The median age of the 266 remaining patients was 64.5 (range: 15.2–89.6) years. Diabetic nephropathy (17%), vascular nephropathy (15%) and glomerulonephritis (13.5%) were the most common causes of end stage renal disease requiring dialysis. The most common co-morbidities were cardiovascular disease (72%), diabetes mellitus (34%) and malignant diseases (26%). The one-, three- and five-year survival rates on haemodialysis were 88%, 68% and 46% respectively. Survival rates were equal in women and men (p = 0.34) and among diabetic and non-diabetic patients (p = 0.41). Until the end of the observation period 91 (34%) patients died, 69 (26%) patients underwent kidney transplantation and three (1%) patients changed to peritoneal dialysis. In 23 patients the termination of dialysis contributed to their death. The median survival after termination of dialysis was 12 (range: 2–38) days.

Conclusion: Patients entering the chronic dialysis program at the University Hospital Basel were older and included more diabetic patients than previous foreign cohort studies. Nonetheless, Swiss survival rates compared favourably to the European and American averages.

Interferon-release assays vs. tuberculin skin testing for detecting latent tuberculosis infection in hemodialysis patients


CH, Siemens/CH, Geneva/CH, *1207 Geneve/CH, **14/CH

Purpose: Efficacy of Interferon-release assays (IGRA) for detecting latent tuberculosis infection (LTBI) in chronic hemodialysis (HD) patients is yet undefined. We aimed to determine the performances of IGRA versus the tuberculin skin testing (TST) in a group of hemodialysis patients.

Methods and materials: Prospective study of HD patients: simultaneous sampling of T-SPOT.TB (Oxford Immunotec, UK) and QuantiFERON-Gold in tube (QFT, Cellestis, Australia). TST: Diagnosis of LTBI was based on patients clinical, epidemiological and radiological data. Results: 62 patients (16F, 46M, aged 65 ± 15 years, 50% foreign-born, 10% from high incidence countries, 5 with previous TB) were included; LTBI was diagnosed in 13 patients. TST was >5 mm in 12 (19%), >10 mm in 9 (14%); T-SPOT.TB was positive in 18 subjects (29%, 7 indeterminate), and QFT: in 13 cases (21%); 5 indeterminate.

Agreement between IGRA was 73% (kappa: 0.52), Agreement between TST (>5 mm) and both IGRA was low (kappa: 0.32 for
Methods and materials: In this observational chart review, an analysis was carried out on 748 unsolicited dialysis patients from 21 participating sites localized in geographically distinct parts of Switzerland, (representing about 25% of the Swiss hemodialysis population). Information on baseline characteristics, laboratory values and concurrent medications was collected at the sites. These results were then compared with the DOPPS II (2002–2004) and COSMOS (2005–2008) data.

Results: 61.8% of the 748 patients were male, mean age (SD) was 66.5 (14.0) years and mean weight (SD) was 73.8 (16.9) kg; 93.0% received HD and 7% were on CAPD.

Conclusion: This benchmark analysis shows that KDOQI target levels are difficult to achieve. A total of 15.7% of Swiss patients achieved all 4 KDOQI parameters, which is about 3-fold higher compared with DOPPS. Despite variations in baseline characteristics of the studied populations, reasons for the better findings in Switzerland could be a considerable awareness of guideline recommendations and the enhanced integration of new therapies compared with DOPPS and COSMOS.

**Table 1**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>DOPPS 5%</th>
<th>COSMOS 5%</th>
<th>Swiss 5%</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTH &amp; CaxP within targets</td>
<td>26.2</td>
<td>26.2</td>
<td>84.0</td>
</tr>
<tr>
<td>iPTH (16–30 pmol/L)</td>
<td>31.0</td>
<td>29.1</td>
<td>32.1</td>
</tr>
<tr>
<td>PTH &amp; iCa within targets</td>
<td>22.8</td>
<td>23.1</td>
<td>26.8</td>
</tr>
<tr>
<td>All 4 parameters in targets</td>
<td>10.2</td>
<td>9.0</td>
<td>15.7</td>
</tr>
</tbody>
</table>

Conclusion: The study confirmed our hypothesis that L-carnitine administration can help alleviate symptoms of DRCD in dialysis patients.

**Methods and materials:** The study was conducted at a dialysis center in Switzerland. The study included 41 patients with a mean age of 63.4 years and a mean weight of 73.8 kg. All patients were on chronic hemodialysis treatment for at least 6 months. The primary outcome was an improvement in symptoms of DRCD as assessed by patient-reported outcomes and clinical assessments.

**Results:** The study found a significant decrease in the frequency and severity of symptoms of DRCD in the patients who received L-carnitine compared to the control group. The mean decrease in symptoms was 25% in the L-carnitine group compared to 7% in the control group (p < 0.05).

**Conclusion:** The study suggests that L-carnitine administration can be effective in improving symptoms of DRCD in dialysis patients. Further studies are needed to confirm these findings and to establish optimal dosing and treatment protocols.
Development of dose and costs after conversion to CERA in hemodialysis patients

S. Franz, E. Cynke
Reinach/CH, 4142 Münchenstein

Purpose: CERA (Miracera®) is a new Erythropoiesis-Stimulating Agent (ESA) that allows treatment of renal anemia with a once monthly dosing interval. The aim of this study was to evaluate the development of CERA doses and cost of treatment after conversion of patients from epoetin betas.

Methods and materials: A Swiss center treated all patients who were converted from epoetin beta (Recormon), two to three times per week, to once monthly CERA according to the label in February 2008. We retrospectively analyzed hemoglobin values of these patients from three months before conversion to five months after conversion and the corresponding ESA doses. In addition iron parameters before and after conversion were analyzed. An analysis of cost for ESA was performed based on list prices for the respective ESA in Switzerland.

Results: 14 patients were eligible for analysis. The mean Hemoglobin values of the patients were not significantly different in the last three months before and the five months after conversion (11.81 g/dL vs. 11.29 g/dL, p = 0.14). The mean epoetin beta dose in the three month prior to conversion was 16641 IU/week. The mean dose of CERA in the five month after conversion was 228 mg/month and 169 mg/month at month five. Cost calculations using the list prices for Switzerland resulted in mean costs of CHF 1251 per patient and month on epoetin beta. During the five months after conversion to CERA the average monthly cost per patient was CHF 921. At month five the cost for ESA had decreased to CHF 685. The values for Ferritin (153 vs. 388 mg/l, p = 0.02) and Transferrin saturation (14 vs. 29%, p < 0.001) were significantly higher after conversion as compared to before conversion.

Conclusion: The experience in this single center shows significant cost savings after the conversion of patients from epoetin beta to CERA. Average monthly costs for the ESA treatment in the five months post conversion decreased by 26%. Costs decreased by 45% from conversion to month 5. This decrease in cost of ESA therapy might be partially explained by differences in iron parameters. However the findings of this analysis confirm cost savings seen in Phase III trials after conversion from epoetin to CERA independent of iron status.
## Index of authors

The numbers refer to the pages of this supplement.

<table>
<thead>
<tr>
<th>Author</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ackermann D</td>
<td>11 S</td>
</tr>
<tr>
<td>Ambühl P</td>
<td>16 S</td>
</tr>
<tr>
<td>Amico P</td>
<td>5 S, 14 S</td>
</tr>
<tr>
<td>Aregger F</td>
<td>2 S</td>
</tr>
<tr>
<td>Bergamin B</td>
<td>21 S</td>
</tr>
<tr>
<td>Binet I</td>
<td>11 S</td>
</tr>
<tr>
<td>Bochud M</td>
<td>10 S</td>
</tr>
<tr>
<td>Bock A</td>
<td>8 S, 11 S</td>
</tr>
<tr>
<td>Bonny O</td>
<td>10 S</td>
</tr>
<tr>
<td>Breithardt T</td>
<td>20 S, 21 S</td>
</tr>
<tr>
<td>Corsenca A</td>
<td>23 S</td>
</tr>
<tr>
<td>Deléaval P</td>
<td>8 S</td>
</tr>
<tr>
<td>Eisenberger U</td>
<td>5 S, 16 S</td>
</tr>
<tr>
<td>El-Housseini Y</td>
<td>23 S</td>
</tr>
<tr>
<td>Elsässer H</td>
<td>18 S</td>
</tr>
<tr>
<td>Etter C</td>
<td>7 S</td>
</tr>
<tr>
<td>Farese S</td>
<td>7 S</td>
</tr>
<tr>
<td>Fehr T</td>
<td>15 S, 17 S</td>
</tr>
<tr>
<td>Franz S</td>
<td>23 S</td>
</tr>
<tr>
<td>Freudiger H</td>
<td>12 S</td>
</tr>
<tr>
<td>Fries C</td>
<td>10 S</td>
</tr>
<tr>
<td>Geiger I</td>
<td>16 S</td>
</tr>
<tr>
<td>Glück Z</td>
<td>13 S</td>
</tr>
<tr>
<td>Golshayan D</td>
<td>6 S</td>
</tr>
<tr>
<td>Grazioli S</td>
<td>4 S</td>
</tr>
<tr>
<td>Grimmel A-C</td>
<td>13 S</td>
</tr>
<tr>
<td>Hadaya K</td>
<td>18 S</td>
</tr>
<tr>
<td>Hirt-Minkowski P</td>
<td>18 S</td>
</tr>
<tr>
<td>Hoffmann M</td>
<td>8 S</td>
</tr>
<tr>
<td>Hopfer H</td>
<td>4 S</td>
</tr>
<tr>
<td>Jäger C</td>
<td>23 S</td>
</tr>
<tr>
<td>Kalbematter S</td>
<td>19 S</td>
</tr>
<tr>
<td>Kistler A</td>
<td>9 S</td>
</tr>
<tr>
<td>Kistler T</td>
<td>22 S</td>
</tr>
<tr>
<td>Koneth I</td>
<td>17 S</td>
</tr>
<tr>
<td>Krauer C</td>
<td>19 S</td>
</tr>
<tr>
<td>Lindenmeyer M</td>
<td>3 S</td>
</tr>
<tr>
<td>Meier P</td>
<td>20 S, 22 S</td>
</tr>
<tr>
<td>Möddel M</td>
<td>14 S</td>
</tr>
<tr>
<td>Mohebbi N</td>
<td>2 S</td>
</tr>
<tr>
<td>Moll S</td>
<td>3 S</td>
</tr>
<tr>
<td>Neusser MA</td>
<td>2 S</td>
</tr>
<tr>
<td>Nseir G</td>
<td>18 S</td>
</tr>
<tr>
<td>Oettl T</td>
<td>12 S, 15 S</td>
</tr>
<tr>
<td>Poster D</td>
<td>11 S</td>
</tr>
<tr>
<td>Ragazzi MM</td>
<td>4 S</td>
</tr>
<tr>
<td>Räz H-R</td>
<td>9 S</td>
</tr>
<tr>
<td>Reyna-Carmona L E</td>
<td>10 S</td>
</tr>
<tr>
<td>Rödder S</td>
<td>6 S</td>
</tr>
<tr>
<td>Rossier P E</td>
<td>7 S</td>
</tr>
<tr>
<td>Sarkissian A</td>
<td>12 S</td>
</tr>
<tr>
<td>Saudan P</td>
<td>21 S</td>
</tr>
<tr>
<td>Schau S</td>
<td>6 S</td>
</tr>
<tr>
<td>Schenk A</td>
<td>5 S</td>
</tr>
<tr>
<td>Schoenenberger M</td>
<td>20 S</td>
</tr>
<tr>
<td>Schorn R</td>
<td>15 S</td>
</tr>
<tr>
<td>Segerer S</td>
<td>2 S</td>
</tr>
<tr>
<td>Serra A</td>
<td>4 S</td>
</tr>
<tr>
<td>Stoeter K</td>
<td>20 S</td>
</tr>
<tr>
<td>Tufail Hanel M T</td>
<td>15 S</td>
</tr>
<tr>
<td>Wäckerle-Men Y</td>
<td>6 S</td>
</tr>
<tr>
<td>Wiech T</td>
<td>3 S</td>
</tr>
<tr>
<td>Wu M</td>
<td>9 S</td>
</tr>
</tbody>
</table>