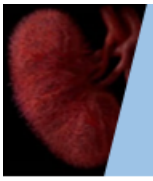

Belgian Society of Nephrology

S
BVN
N

ABSTRACT BOOK

ANNUAL MEETING

APRIL 2018

LIVING TOMORROW VILVOORDE

Bioimpedance spectroscopy in patients with end stage renal disease

S. Dejongh, P. Evenepoel, B. Meijers

Objective
Bioimpedance spectroscopy (BIS) has been developed as a non-invasive measure for body composition, including volume status. For patients with end stage renal disease, devices employing this technology provide estimates of overhydration and target dry weight. Comparative studies on such devices for hemodialysis patients are scarce. We performed a prospective study on maintenance dialysis patients.

Methods
Patients were measured with two BIS devices (Bodystat Multiscan (BSM) 5000; EuroMedix and Body Composition Monitor (BCM); Fresenius) both before and after their midweek hemodialysis session. All patients were measured on the right side of the body, unless an AV-fistula was present. The primary endpoint was overhydration. Other parameters included extracellular water (ECW), intracellular water (ICW), total body water (TBW), as well as impedance at several (5 kHz, 200 kHz, 500 kHz and 1000 kHz) frequencies. Results were analysed used Deming regression. We enrolled 50 hemodialysis patients.

Results
Excessive (> 3 l UF) overhydration was detected in 64% of patients by BSM and 10% by BCM. After dialysis, significant overhydration (> 1 L) was detected in 76% of patients by BSM and 22% by BCM. The primary endpoint differed significantly between devices. The BSM had a constant difference of 2,07 l (proportional bias (P= 0,06), constant bias (P <0,0001) more overhydration as compared to the BCM. In contrast, estimates for ECW, ICW and TBW measured by BCM exceeded those measured by BSM. Finally, raw impedance data measured by both devices were similar.

Conclusion
We observed a clinically meaningful difference in estimated overhydration, exceeding 2 l. This difference can neither be explained by measured impedance values, nor by estimate values for ECW, ICW or TBW. Presumably, this points to major differences in the algorithms used. These findings rule out using both devices interchangeably on a single ward.

Is higher potassium concentration in the dialysis bath safe for patients chronically treated by hemodialysis ?

F. Krzesinski, P. Lancellotti, B. Dubois, A. Delcour, J-M. Krzesinski, P. Delanaye

Background: The mortality, especially cardiovascular, of the hemodialysis patients is significantly higher than that observed in the general population. Sudden death is one of the main causes accounting for 27% of deaths. The role of the variations of potassium (K^+) induced during dialysis and the accumulation of K^+ in the inter-dialytic period are one of the explanations for this excess mortality. Our work sought 1) to test the safety of a 1 mmol / l elevation of the dialysis bath concentration in K^+ on pre- and post-dialytic potassium levels of the patient; 2) to assess the interest of these changes on electrical myocardial repolarization modifications

Methods: We included 27 chronic hemodialysis patients (3X4h / week), stable. We performed K+ assays before and after dialysis for 15 days under the usual conditions of dialysis with electrocardiographic (ECG) recordings before and after dialysis at the first dialysis session of the week. We then increased the K + dialysis bath concentration by 1 mmol / l and compared the induced changes in K+ concentration and electrocardiographic parameters before and after the sessions.

Results: Before bath changes, QTc measurements and QT dispersion were significantly increased at the end of dialysis compared to those obtained before the session (444 vs. 459, p = 0.0097 and 38 vs. 41.5, p <0, 0001, respectively). On the other hand, after the use of a bath enriched in K +, although the QTc remained higher at the end of dialysis (441 vs. 453, p = 0.0033), the dispersion of QT was no longer significantly modified. End-of-dialysis ECG analysis before and after the bath change showed no significant change in QTc with even a significant improvement in QT dispersion (41.5 vs. 38). No patient developed pre-dialysis hyperkalaemia > 5.5 mmol / l while the variations of K + in post-dialysis were significantly less important with the new baths. On the other hand, there were no significant changes in cardiac heart rates and other ionic changes.

Conclusions: Higher K + concentration in the dialysis baths is associated with less QTc modifications at the end of dialysis and no variations in QT dispersion. It remains to be shown that either arrhythmia or sudden death will be reduced by longer-term analysis in larger populations.

Acute kidney dysfunction with no rejection » is associated with poor renal outcomes at 2 years post kidney transplantation

F. Paquot, L. Weekers, C. Bonvoisin, H. Pottel, F. Jouret

OBJECTIVE: “Acute kidney dysfunction with no rejection” (ADNR) corresponds to acute kidney injury without histological evidence of acute rejection (AR) in kidney transplant recipients (KTR). ADNR prognosis is unknown.

METHODS: From 2007 to 2015, we retrospectively categorized all KTRs with a for-cause kidney biopsy within 12 months post-kidney transplantation (KTx) into 2 groups: ADNR and biopsy-proven AR. Control group (C) included KTR with no ADNR or AR within 24 months post-KTx. BK virus nephropathy and primary nonfunction were excluded. Estimated glomerular filtration rate (eGFR) was determined using the Modification of Diet in Renal Disease (MDRD) equation. Linear mixed models established intercepts and slopes of eGFR decline from 6 to 24 months post-KTx. Cubic spline analysis calculated the percentage of patients with a ≥30% reduction of eGFR from 6 to 24 months post- KTx.

RESULTS: The mean age (years) at KTx was 50.2±14.2, 47.9±17.8 and 53.6±12.4 for ADNR (n=93), AR (n=22) and C (n=135), respectively. The female/male ratio was 39.8% (ADNR), 45.5% (AR) et 34.1 (C). The rate of delayed graft function was not significantly different among groups, and reached 26.9% (ADNR), 22.7% (AR) and 14.1% (C). The median time for for-cause graft biopsy was 22 [10-70] and 13 [7-43] days post-KTx for ADNR and AR, respectively. Of note, ADNR included 21 (22.6%) patients with "borderline" histology. At 6 months post-KTx, eGFR was higher in C (55.2±1.6 mL/min) vs. ADNR (45.5±1.9 mL/min; $p<0.05$) and vs. AR (48.6±3.9 mL/min; p, 0.13). The eGFR slope from 6 to 24 months post-Tx was positive in C (0.16±0.06mL/min/month) compared to negative slopes in ADNR (-0.05±0.08mL/min/month, $p<0.05$) and in AR (-0,04±0.16mL/min/month, p, 0.26). The proportion of KTR presenting with a ≥30% reduction of eGFR from 6 to 24 months post-KTx reached 7.4% in C vs. 25.8% in ADNR ($p<0.05$) and 19% in AR ($p<0.05$).

CONCLUSION: In the present monocentric cohort, ADNR occurs frequently and early post KTx, and is associated with a significantly lower eGFR at 6 months and a significantly faster eGFR decline from 6 to 24 months post-KTx, in comparison to controls.

Evolution of protein bound uremic toxins Indoxyl sulfate and p-Cresyl sulfate in Acute Kidney Injury

L. Veldeman, J.Vanmassenhove, W. Van Biesen, R.Vanholder, G.Glorieux

Objective:
Indoxyl sulfate (IxS) and p-Cresyl sulfate (pCS) are the most investigated protein-bound colon-derived uremic toxins. There is a gradual and significant increase in serum concentrations of both IxS and pCS as chronic kidney disease (CKD) progresses. Although the retention pattern of protein-bound uremic toxins has been thoroughly studied in chronic kidney disease, there is, up till now, no such data in acute kidney injury (AKI).

Methods
In this study, 194 adult patients admitted with sepsis to the intensive care unit were included. Uremic solutes (IxS, pCS and creatinine (sCrea)) were quantified at inclusion (D0) and four days after inclusion, unless follow-up ended before day 4 because of death, start of RRT, discharge from the ICU or refusal of further blood sampling. In the latter case, the last sample collected before drop-out was analyzed (D_{end}).
AKI and its severity were defined according to the RIFLE classification (Risk, Injury, Failure, Loss of kidney function, and End stage renal disease), at D0. In a sub-analysis, patients were grouped according to the evolution of AKI class from D0 to D_{end}. Finally, we compared the concentrations of IxS and pCS in AKI with those in CKD patients matched for serum sCrea.

Results
Serum levels of sCrea (1.20 mg/dL [0.79-2.12] vs 0.73 [0.52-0.89], p<0.001), IxS (64.0 µg/dL [25.2-180.2] vs 25.8 [9.7-61.0], p<0.001) and pCS (250.0 µg/dL [64.3-593.3] vs 151.7 [27.4-308.1], p<0.05) were higher in patients with AKI vs no AKI at D0.
When subdividing AKI into R, I and F RIFLE stages, a stepwise increase in the levels of sCrea was observed at D0 between each stage. In contrast, IxS and pCS levels only increased from stage I (IxS) and F (pCS) on. When grouped according to evolution in RIFLE class from D0 to D_{end}, all solute concentrations were higher (p<0.001) in the group with negative (unfavourable) evolution of AKI stages. Comparing D_{end} to D0, there was a decrease (p<0.001) of all solute concentrations in the group with favourable evolution, but percentwise this decline was more important for pCS (-62%) and IxS (-55%) than for sCrea (-24%). In the group with the negative evolution, there was a marked rise in sCrea (p<0.001), a moderate one for pCS (p<0.05), but no change at all for IxS (p=0.112). Comparing AKI with CKD patients matched for serum creatinine (1.86 [1.40-2.50] vs 1.87 mg/dL [1.42-2.53], NS), total levels of both IxS (249.5 [161.1-370.8] vs 113.0 µg/dL [35.3-227.1], p<0.001) and pCS (881.5 [470.8-1467.8] vs 266.1 µg/dL [70.4-600.9], p<0.001) were higher in patients with CKD.

Conclusion
Although concentrations of IxS and pCS both tend to rise in sepsis patients with AKI, their evolution is not conform with that of sCrea.
IxS and pCS concentrations are lower in AKI compared with CKD patients for the same level of sCrea.

Sclerostin: a master regulator in the bone-vascular axis?

A. De Maré, B. Opdebeeck, E. Neven, P.C. D'Haese, A. Verhulst

Objectives:
The Wnt/β-catenin signaling, one of the most important bone anabolic pathways, might also be a major player in the crosstalk within the bone-vascular-axis. When pathologically disturbed, this axis results in the concomitant occurrence of disturbed bone metabolism and vascular calcification (VC). A hallmark of these VCs is the transdifferentiation of vascular smooth muscle cells (VSMCs) towards bone-forming (osteochondrogenic) cells. In the current study we investigated parameters related to the Wnt/β-catenin signaling cascade and its inhibitor sclerostin.

Methods:
Rats were given 0.3mg warfarin/g diet to induce VC. Rats not receiving warfarin were included as controls. Rats were sacrificed at different time-points, i.e. after 4, 6, 8 and 10 weeks of warfarin treatment, to follow up the development of VC. At sacrifice; VC, aortic mRNA expression and immunohistochemistry, bone status and serum biochemistry were analyzed.

Results:
Results showed a time-dependent increase in VC in warfarin-treated rats. Aortic calcium concentration significantly differed from controls in 4-wk treated rats ($p=0.0286$), reaching a 50-fold increase in 10-wk treated rats ($p=0.0061$). Furthermore, aortic mRNA levels of osteochondrogenic transdifferentiation markers (Sox9, $p=0.0317$ and Cbfa1, $p=0.0635$) and β -catenin (regulating target gene transcription, $p=0.0159$) were upregulated. Interestingly, aortic mRNA ($p=0.0159$) and protein levels of sclerostin, and also serum levels ($p=0.0381$) of this protein, were significantly upregulated in 10-wk treated rats compared to control rats. Finally, a mild but significant decrease in bone formation parameters was observed in 10-wk treated warfarin rats.

Conclusion:
Our results support the hypothesis that VSMCs transdifferentiate towards osteochondrogenic cells and thereby also express genes/proteins associated with the Wnt/β-catenin signaling, including its inhibitor sclerostin. The latter thereby may act as a negative feedback protein to prevent excessive (vascular) calcifications, similar to its function in bone. Sclerostin might also spillover from the vessels to the circulation (high serum sclerostin levels) causing mild inhibition of bone formation.

Atypical presentation of Goodpasture's syndrome in a Syrian war refugee

C. Milea, H. Germanos, L. Bienfait, N. Frusch, J. Nortier

Objective. Goodpasture's syndrome (GS) is a rare but severe disorder that may occur without prodrome and be life-threatening. The course of the disease is quite variable and the triad of findings consisting of pulmonary hemorrhage, glomerulonephritis and antibody to glomerular basement membrane antigens (anti-GBM) is not so often present at the time of presentation, causing some delay in the diagnosis.

Methods. We report the case of a 45 year old Syrian man, active smoker, arriving in Belgium as a war refugee and sheltered in a refugee center. After a few weeks, he was admitted for fluid overload and oliguria without any pulmonary manifestation. Chest x-ray was normal but acute kidney failure with heavy proteinuria (9 g/L) was found. Diagnosis of GS was confirmed by the detection of anti-GBM antibodies in the serum as well as in the linear IgG deposits upon immunofluorescence performed on the renal biopsy material. Extensive extracapillary proliferation (crescents) was observed in all the 17 glomeruli examined on the renal tissue sample. Hemodialysis (HD) was started and intensive daily plasma exchanges were performed. Despite immunosuppressive therapy (oral cyclophosphamide 50 mg twice a day and methylprednisolone boluses 1g/day for 3 days, 250 mg the 3 days after and followed by oral 32 mg/day), the patient remained HD dependent.

Results. One month after admission, the patient experienced a severe hemoptysis. Lung fibroscopy confirmed intraalveolar hemorrhage, suggesting a re-activation of the systemic disease. Increasing immunosuppressive drugs resulted in the remission of clinical symptoms. Due to severe thrombocytopenia, cyclophosphamide had to be replaced by azathioprine. Up to now, the patient is currently on regular HD and registered on Eurotransplant waiting list for a kidney transplant.

Conclusions. The absence of pulmonary involvement at initial presentation does not exclude GS diagnosis. Any delayed management can lead to irreversible kidney damage. As shown in the present case, the renal disease may be fulminant. Language barrier and economic precarity of war refugees in Belgium and other European countries may be two significant factors resulting in a delayed diagnosis of such a renal emergency.

Atypical presentation of systemic lupus erythematosus and ANCA-associated vasculitis overlap syndrome

F. Touzani, G. Gambino, C. Catalano, A. Pozdzik

Objective: Diagnosis of systemic lupus erythematosus (SLE) can be considered in presence of lupus nephropathy characterized by glomerular immune-complex deposits, typically in a full house immunofluorescence pattern together with ANA or anti-dsDNA antibodies. In contrast, glomerulonephritis in ANCA-associated vasculitis (AAV) is classically pauci-immune. Patients fulfilling both SLE and AAV classification criteria, defining "SLE/AAV overlap syndrome", have been only rarely reported.

Case report: A 40-year-old man presented to the emergency because of haemoptysis and macroscopic haematuria. We found acute kidney injury (plasma creatinine 5.16 mg/dL) with active urinary sediment. Chest tomography showed intra-alveolar diffuse haemorrhage confirming pulmonary-renal syndrome. High titers of anti-MPO ANCA in the absence of ANA strongly correlated with microscopic polyangiitis. Kidney biopsy confirmed crescentic glomerulonephritis, however full house immunofluorescence pattern corresponded to lupus-like nephropathy. Despite plasma exchanges associated to steroids and rituximab, kidney function declined and haemodialysis was initiated. During 12 months of follow-up on azathioprine-low dose steroids treatment, he remains still asymptomatic. However, considering the appearance of ANA, existence of antiphospholipid antibodies and fluctuating low complement level, we considered the diagnosis of SLE/AAV overlap syndrome.

Conclusion: Lupus-like nephropathy associated to AAV has a very poor kidney outcome. As in our case the delayed appearance of ANA in association to other immunological SLE parameters correlated with SLE/AAV overlap syndrome diagnosis, we propose a regular screening for clinical and biological SLE criteria even in their absence at initial presentation.

ADPedKD: an international web-based database for longitudinal data registry of children with Autosomal Dominant Polycystic Kidney Disease (ADPKD)

S. De Rechter, F. Schaefer, M. Liebau, D. Mekahli

Objective: Although literature on Autosomal Dominant Polycystic Kidney Disease (ADPKD) is merging over the last decades, data on paediatric ADPKD are still scarce. Moreover, unified diagnostic, follow-up and treatment approaches regarding modifiable disease factors in order to slow down disease progression are currently lacking for ADPKD children. We therefore aim to build the largest international multicentre cohort, named ADPedKD, from which we will generate data on the incidence and presentation of ADPKD in childhood. Furthermore, we intent to define a paediatric patient risk stratification score, after identification of progression factors.

Methods: Patients diagnosed with ADPKD, based on genetic analysis or a positive familial history and imaging, before the age of 19 years are eligible for inclusion in this observational register study. Ethical committee approval is organized per country as regulations differ internationally. After written informed consent, clinical patient data are pseudonymously introduced in our secured web-based database (www.adpedkd.org), both retrospectively and prospectively, from all participating centres throughout the world. Our main focus consists of the initial presentation, pre- and perinatal history, genetic analysis, renal function and longitudinal follow-up.

Results: We currently have 31 centres registered in ADPedKD, from 14 different countries: Belgium, Czech Republic, France, Germany, Italy, Luxembourg, Poland, Portugal, Romania, Russian Federation, Serbia, Spain, Turkey and United Kingdom. Twenty-for centres are in the patient recruitment phase; while the others are already actively entering patient data, resulting in 113 registered paediatric ADPKD patients.

Conclusion: The ADPedKD initiative is the first and the largest international paediatric ADPKD registry that will provide evidence for a paediatric patient risk stratification scoring system from an early disease stage.

Protein-bound uremic toxins promote vascular calcification by glucose mediated activation of inflammation and coagulation pathways

B. Opdebeeck, S. Maudsley, A. Azmi, A. De Maré, W. De Leger, B. Meijers, A. Verhulst, P. Evenepoe, P. D'Haese, E. Neven

Objective
Protein-bound uremic toxins indoxyl sulfate (IS) and p-cresyl sulfate (PCS) have been associated with cardiovascular morbidity and mortality in patients with chronic kidney disease (CKD). We aimed to provide direct evidence for a role of these toxins in CKD-related vascular calcification.

Methods
To induce CKD, rats were orally dosed with adenine sulfate for 10 days and continuously exposed to either vehicle, IS or PCS (150 mg/kg/day) until 7 weeks after CKD induction. Vascular calcification was assessed by measurement of arterial calcium content and through histochemical evaluation. Quantitative mass spectrometric proteomics was further employed to investigate the mechanistic pathways underlying IS and PCS-mediated vascular calcification.

Results
IS and PCS exposure did not worsen renal function, fibrosis, or inflammation. Calcification in the aorta, carotid and femoral arteries was significantly increased by exposure to both toxins, for which serum levels similar to CKD patients were reached. Arterial calcification was not associated with changes in bone metabolism inherent to CKD. Unbiased proteomic analyses of arterial samples coupled to functional bioinformatics annotation analysis revealed that calcification events were likely associated with acute phase response signaling, coagulation and glucometabolic signaling pathways, while escape from calcification was linked with liver X receptors and farnesoid X/liver X receptor signaling pathways. Further metabolic linkage to these pathways also revealed that IS/PCS exposure engendered a pro-diabetic state, evidenced by elevated resting glucose and reduced glucose transporter (Glut1) transcript expression.

Conclusion
We demonstrate that both IS and PCS directly promote vascular calcification via activation of inflammation and coagulation pathways in the arterial wall which was strongly associated with impaired glucose homeostasis.

Treatment with a TNAP inhibitor prevents the development of vascular calcification in a rat model with warfarin-induced vascular calcification.

B. Opdebeeck, A. Verhulst, P. D'Haese, E. Neven

Objective
Vascular media calcification significantly contributes to cardiovascular morbidity and mortality in elderly and patients with diabetes and chronic kidney disease. Pyrophosphate (PPi) is a well-known calcification inhibitor that binds to nascent hydroxyapatite crystals and prevents further incorporation of inorganic phosphate into these crystals. However, the enzyme tissue non-specific alkaline phosphatase (TNAP), which is highly expressed in calcified arteries, degrades extracellular PPi into phosphate ions, by which PPi loses its ability to block vascular calcification. Here, we aimed to evaluate whether a TNAP-inhibitor is able to prevent the development of arterial calcification in a rat model of warfarin-induced vascular calcification.

Methods
To induce vascular calcification, rats received a diet containing 0.30% warfarin and 0.15% vitamin K1 throughout the entire study and were subjected to the following daily treatments: (i) vehicle (n=10) or (ii) 10 mg/kg/day TNAP-inhibitor (n=10) administered via an intraperitoneal catheter from start of the study until sacrifice at week 7. Calcium and phosphorus levels were determined in serum and urine samples as these are important determinants of vascular calcification. The mRNA expression of osteo/chondrogenic marker genes (runx2, TNAP, SOX9, collagen 1 and collagen 2) was analyzed in the aorta by qPCR to verify whether vascular smooth muscle cells underwent reprogramming towards bone-like cells. At sacrifice, vascular calcification was evaluated by measurement of the total calcium content in the arteries and quantification of the area % calcification on Von Kossa stained sections of the aorta.

Results
No differences in serum calcium and phosphorus levels was observed between both study groups. Warfarin exposure resulted in distinct calcification in the aorta and peripheral arteries in vehicle treated rats. Importantly, daily treatment with a TNAP-inhibitor significantly reduced vascular calcification as indicated by a significant decrease in calcium content in the aorta and peripheral arteries and a distinct reduction in area % calcification on Von Kossa stained aortic sections as compared to vehicle treated controls. Treatment with a TNAP-inhibitor did not modulate the mRNA expression of osteo/chondrogenic marker genes runx2, TNAP, SOX9, collagen 1 and 2.

Conclusion
Treatment with a TNAP-inhibitor significantly reduced the development of vascular calcification in the aorta and peripheral vessels of warfarin exposed rats. Further research will explore the signaling pathways by which this TNAP-inhibitor inhibits calcifications in the arterial wall.

Poor vitamin K status associates with inflammation and low areal bone mineral density and predicts fractures in de novo renal transplant recipients

P. Evenepoel, K. Claes, B. Meijers, M. Laurent, B. Bammens, M. Naesens, B. Sprangers, H. Pottel, E. Cavalier, D. Kuypers

Background & Objective: Vitamin K deficiency is prevalent among patients with end stage renal disease (ESRD). A poor vitamin K status associates with accelerated vascular calcification. Preliminary data indicate that poor vitamin K status may compromise bone health and that increased inflammation may be in the causal pathway. We investigated the association between vitamin K status, inflammation, bone mineral density and incident clinical fractures in a cohort of patients with ESRD, referred for single kidney transplantation.

Methods: Parameters of mineral metabolism (including biointact PTH and FGF23, sclerostin, calcidiol, calcitriol), inflammatory (CRP and il6), osteoprotegerin, bone turnover markers (P1NP, BsAP, and TRAP5B) and desphosphorylated-uncarboxylated Matrix Gla Protein (dp-ucMGP), were assessed on blood samples collected immediately prior to kidney transplantation in 468 patients. Areal bone mineral density (aBMD) was measured at lumbar spine and femoral neck by dual energy x-ray absorptiometry within 14 days posttransplant.

Results: Poor vitamin K status, defined by dp-ucMGP >500 nmol/L, was highly prevalent (90%). High dp-ucMGP levels independently associated with elevated inflammatory markers and low aBMD. No associations were observed between vitamin K status and bone turnover markers. During a median follow-up of 5.1 years, 33 patients sustained a fragility fracture. In Cox-proportional hazards analysis, a dp-ucMGP above median associated with incident fractures, even after adjustment for classical determinants, including age, gender, aBMD, and history of previous fracture (HR 2.21 [1.00-4.91], $p<0.05$).

Conclusion: Poor vitamin K status associates with inflammation and low aBMD in patients with ESRD and predicts incident fractures in *de novo* renal transplant recipients.

REMODELING ACTIVTY IS THE MAIN DRIVER OF BONE MINERAL DENSITY CHANGES IN DE NOVO RENAL TRANSPLANT RECIPIENTS

P. Evenepoel, K. Claes, B; Meijers, M. Laurent, B. Bammens, M. Naesens, B. Sprangers, E. Cavalier, D. Kuypers

Background & Objective: Corticosteroids are traditionally thought to be the major culprit of bone mineral density loss in renal transplant recipients. In recent decades, steroid minimization immunosuppression protocols rapidly gained popularity. The present study aimed to investigate bone mass changes and correlates in contemporaneous de novo renal transplant recipients.

Methods: Between 2006 and 2012, we enrolled 157 adult recipients of a single kidney transplant into a 5-year follow-up study. Areal bone mineral density (aBMD), as assessed by dual energy x-ray absorptiometry at various skeletal sites (forearm, lumbar spine and hip), mineral metabolism parameters (including PTH, FGF23, sclerostin, calcidiol and calcitriol), and bone remodeling activity, as reflected by bone turnover markers (trimeric P1NP, BsAP, and TRAP5B), were monitored at time of transplantation, and 1 and 5 years post-transplantation. Only patients with available DXA at the time of transplantation, Yr 1 and 5, and free of bisphosphonates were included in the present analysis (n=69). Cumulative methylprednisolone exposure amounted to 2.5 ad 5.6 g, at Yr1 and Yr5 respectively.

Results: Posttransplant aBMD changes, overall, were minimal and were significant only at the ultradistal radius during the first postoperative year (-2.2% decline, p=0.01) and at the lumbar spine between Yr1 and Yr5 (+ 2.6% increase, p=0.009). Important inter-individual differences were noted. In regression analysis, bone remodeling activity, as opposed to mineral metabolism parameters and cumulative corticosteroid exposure, associated consistently with aBMD changes, both in the early and late posttransplant period. In agreement with previous histomorphometric data, we observed declining levels of TRAP5B, a biomarker of bone resorption, early after renal transplantation. Markers of bone formation also decreased, but not consistently and less prominently. Again, inter-individual variability was high.

In **conclusion**, with current steroid minimization immunosuppressive protocols, aBMD changes after renal transplantation are limited and related to bone remodeling activity rather that corticosteroid exposure. Our data suggest that monitoring bone remodeling activity may help to identify renal transplant recipients who will benefit most from bone preserving measures.

A multi-center study to evaluate which socio-economic and psychosocial factors interfere with medication adherence in ESRD.

S. Boesmans, O. Boey, E. Mahieu, C. Vanfraechem, J. Vanuytsel, T. D'Hondt, Y. De Groote, R. Buyl, A.M. Bogaert

Objectives: Medication nonadherence averts patients from gaining the full benefit of the prescribed medications and is associated with poor outcome and increased mortality. Compliancy to therapy is a key component of the effective management of all patients, including those with ESRD. In the literature nonadherence among hemodialysis patients varies widely from 12.5% to 98.6%. Patients with ESRD have complex medication and dietary regimens and in addition are challenged with requirements for renal replacement therapy. We aimed to evaluate the prevalence of self-reported medication adherence in our institution, as well as to evaluate which socio-economic and psychosocial factors could affect their compliancy.

Methods: We assessed barriers to medication adherence in 143 patients on chronic dialysis. The majority of the patients in this study undergo hemodialysis (88%), 14 of them are on peritoneal dialysis regimen (10%) and 3 patients are on home-hemodialysis (2%). Socio-economic factors that might interfere with compliancy were analyzed with a simple question survey. Compliancy was assessed by self-reported measures using the validated Morisky 8-item Medication Adherence Scale (MMAS-8). Depression was screened using the Patient Health Questionnaire (PHQ-9), a widely used depression screening instrument in nonpsychiatric setting.

Results: In the studied population 66% of the subjects were male versus 34% females. The mean age was 74 years (±11 SD) and the mean BMI was 26.1 (± 5SD). ESRD was associated with diabetes mellitus in 41% of our patients. We divided our study population in three groups according to their medication adherence depending on their score on the MMAS-8; 65% of our patients have a high medication adherence whereas 30% have a moderate and 5% have a low therapeutic adherence. There is an almost statistic significant relationship between having financial difficulties and low compliance (p 0.054). Among our patients 17% reported having financial issues; Within those subjects, 48% have a high medication adherence whereas 52% have a moderate/low adherence. In comparison 70% of our patients who didn't report having financial problems have a high medication adherence and 30% have a moderate/low therapeutic adherence. We found a negative correlation between the educational grade of the patient and medication intake. The higher the education, the worse the adherence; however those results were not of statistical significance due to the small number of patients having a degree in our population. There was also a trend for unemployed or disabled patients for being less compliant in comparison with patients having a job or being retired, but again the amount of patients are too small to be statistically significant. Surprisingly we did not find a significant correlation between depression and compliancy, this could be explained by the fact that only 4% of our population is struggling with depression. Medication dispensation by a nurse didn't have an impact on therapeutic adherence. We did not find any correlation between therapeutic adherence and gender, race, marital state, overweight or diabetes.

Conclusion: We can conclude that our sustained efforts to motivate our patients about therapeutic adherence have paid off since the compliance in our institution is satisfying with 65% of our patients having a high medication adherence. Medication intake tend to be worse in patients having financial issues, a higher educational grade and in unemployed or disabled.
We emphasize the need to study a larger population of patient with ESRD to analyze if the trends we did find could be of statistical significance when transferred to a larger group.

Risk factors for peritoneal dialysis related complications: a single-center, retrospective cohort study

P-J Van Gaal, C. Simons, K. Wouters, V. Kovacic, A. Bernaerts, R. Hellemans, D. Abramowicz, K. De Greef, V. Hartman, B. Bracke, M. Couttenye

Background

Peritonitis and catheter-related problems are important complications of peritoneal dialysis (PD). Identifying risk factors of peritonitis and catheter dysfunction may help in patient selection and improve outcomes on PD.

Methods

We conducted a single-center, retrospective cohort study to identify risk factors for peritonitis, for the need to undergo a reintervention to the PD-catheter and for catheter dislocation over an 8-year study period.

Results

We included 111 PD-patients, with a mean age of 50.6 years, 56% males, who experienced a total of 76 episodes of peritonitis, 123 surgical interventions on a PD-catheter and 86 catheter dislocations. After multivariable analysis, significant risk factors of peritonitis were body-mass-index (BMI) (hazard ratio [HR] 1.06 per increasing unit of BMI of 1 kg/m²; 95% confidence interval [CI] 1.01 – 1.11; p = 0.01) and heart failure with reduced ejection fraction (HFrEF)(HR 2.22 – 95% CI 1.23 – 4.04; p = 0.009). Risk factors to undergo a surgical reintervention to the PD-catheter are higher BMI (HR 1.05 per unit of BMI of 1 kg/m²; 95% CI 1.01 – 1.08; p = 0.01) and undergoing a surgical reintervention itself (HR 1.53; 95% CI 1.00 – 2.34; p = 0.047). We could not identify significant risk factors for catheter dislocation. Patients with hypertensive nephropathy or glomerulonephritis have a lower risk for a surgical reintervention (HR 0.50; 95% CI 0.32 – 0.78; p = 0.002).

Conclusion

PD-patients with a higher BMI or heart failure (HFREF) have a higher risk of PD-peritonitis. A higher BMI is also a risk factor for a surgical reintervention to the PD catheter during the time on PD.

PREVENTION OF TUNNELED CUFFED CATHETER MALFUNCTION WITH PROPHYLACTIC USE OF TAUROLIDINE LOCKING SOLUTION CONTAINING UROKINASE: A PROSPECTIVE AND RANDOMIZED PLACEBO-CONTROLLED TRIAL

F. Bonkain, F. Van Hulle, J.C. Stolear, Ph. Madhoun, Ph. Durieux, C. Catalano, M. Allamani, D. Vandervelde, S. Treille, M.M. Couttenye, A. Van Craenenbroeck, A. Dhondt, W. Van Biesen, M. Libertalis, Ch. Tielemans, K.M. Wissing

Objectives: Prospective clinical trial to test the hypothesis that prophylactic weekly use of urokinase locks in tunneled cuffed hemodialysis catheters with a history of multiple thrombotic dysfunctions reduces the incidence of recurring thrombotic dysfunction by at least 50%.

Design: Prospective, multi-center, randomized, double-blinded, placebo-controlled trial. Patients were allocated using block randomization with permuted blocks of 4, stratified for the participating centers.

Setting: Eight Belgian hemodialysis high care and low care units.

Participants: Adult prevalent patients undergoing hemodialysis at least 3 times a week via a tunneled cuffed catheter and having presented at least 2 separate thrombotic dysfunctions during the 6 months preceding inclusion.

Intervention: Taurolock™ U 25,000 once a week and Taurolock™HEP500 after the two other dialysis sessions in the TauroU group versus Taurolock™ HEP500 3 times a week in the Control group. The Control group received the standard lock as a placebo indistinguishable from the Taurolock U™ 25,000 once a week. Follow-up 6 months.

Main outcome measures Incidence rate of thrombotic catheter dysfunction requiring urokinase as primary outcome. Catheter removal for thrombosis and overall treatment failure (catheter removal, systemic fibrinolysis and refractory thrombosis with impossibility of catheter removal or systemic thrombolysis) as secondary outcomes.

Results 68 patients were randomized (N=36 in the TauroU group, N=32 in the Control group) and followed for a total of 9821 catheter days at risk. 15/36 (42%) catheters in the TauroU group required at least one therapeutic lock *vs* 23/32 (72%) in the Control group (P=0.012). A total of 24 urokinase locks (4.8/1000 catheter-days) were administered in the TauroU group *vs* 59 (12.3/1000 catheter-days) in the Control group (Rate ratio 0.39; 95%CI 0.23 to 0.63; P<0.0001). 2 catheters were removed for resistant thrombosis in the Control group *vs* 0 in the TauroU group without significant difference in the overall incidence of treatment failure. No bleeding complications occurred during the study.

Conclusions Taurolock U 25,000 once a week is highly efficient in preventing recurring thrombotic dysfunction of tunneled cuffed catheters.

Trial registration: Clinical trials NCT02036255

No funding

Towards optimised dialysis removal of protein-bound uremic toxins

O. Deltombe, D. Schneditz, R. Masereeuw, G. Glorieux, S. Eloot

Objective Patients with renal failure retain a large variety of solutes, of which the protein-bound uremic toxins (PBUTs) are known to exert damage to the (cardio)vascular system. Their removal during haemodialysis (HD) is strongly hampered due to their binding to proteins, such that different studies already focused on interfering with this binding to improve dialyser clearances. Kinetics of PBUTs are, however, known to be even more complex than can be explained based on their protein binding alone. We therefore studied potential PBUT distribution in the erythrocytes and transport through the erythrocyte cell membrane.

Methods Blood samples of 6 HD patients were analysed to check intracellular concentrations of four anionic PBUTs in erythrocytes: hippuric acid (HA), indole-3-acetic acid (IAA), indoxyl sulfate (IS), and *p*-cresyl sulfate (PCS). To quantify cellular transport, loading and unloading tests were performed *in vitro* with blood from 8 healthy subjects and 8 HD patients, respectively. Experimental data were further used in a kinetic model to derive transport characteristics of the studied PBUTs. Erythrocyte transmembrane transport was also explored by checking the impact of an inhibitor of anion exchange by Band 3 proteins.

Results All four studied PBUTs were detected in erythrocytes from HD patients. For each of them, erythrocyte transmembrane transport was more enhanced in the subsequent order HA<IS<PCS<IAA, independent of their percentage protein binding. Remarkably, an uneven partition of intra- and extracellular concentrations was found at equilibrium, with relatively higher intracellular concentrations for HA and PCS, and even more increased for IAA and IS, suggesting that these solutes might bind to intracellular and/or membrane structures. Finally, inhibiting Band 3 protein affected the erythrocyte transmembrane transport of IS and PCS and, to a lesser extent, of IAA, while no impact was found for HA, all underlining the different kinetics of these solutes.

Conclusion By further exploring the erythrocyte transmembrane transport of PBUTs, their kinetics can be better understood, and new strategies to increase their removal during haemodialysis can be developed.

Calciphylaxis: case series of rare presentations

A. Colson, E. Papakrivopoulou, L. Kubasiewicz, T. Keersmaekers, J. Vanparys, A. Derwa

Objective

Calcific uremic arteriopathy (CUA) or calciphylaxis is a disease predominantly affecting patients with end-stage renal disease (ESRD) and associated with high mortality. Most lesions occur on the lower extremities. We report 4 cases of CUA over a period of 3 years in our centre, affecting less common locations-the breast, penis and lower abdomen.

Case Series

Four patients have been treated for CUA in our centre from 2015 until now. Median patient age was 65 (range 54-81), 75% females and all of white ethnic background. The main demographic, laboratory and risk factor data for CUA is summarised below:

Case	Age (years)	Gen-der	Race	ESRD duration (months)	HD Efficacy (average kT/V)	Ca x PO4 product (normal <4,40)	Serum PTH (pg/ml)	Albu-min	Warfa-rin	Cause of death
1	68	F	White (Turkish)	19	1,5	4,1525	735	27	Y	general decline
2	62	F	White (North African)	3	1,3	4,446	116	24	N	general decline
3	54	M	White (North African)	15	1,6	4,8314	594	22	N	N/A
5	81	F	White (Caucasian)	24	1,1	3,479	223	27	N	aspiration pneumonia

All female cases were obese and cases 1-3 had multiple diabetic complications (vasculopathy, retinopathy, neuropathy). The breast and lower abdominal lesions presented as painful, erythematous nodules with overlying skin ulceration and necrosis. Mammography demonstrated extensive vascular calcifications and scattered micro-calcifications in each breast. Punch biopsy of the breast tissue in case 2 showed skin and subcutaneous tissue with mild acute and chronic inflammation, fibrosis and focal necrosis but no evidence of calcium deposits. Case 3 presented with painful leg and penile lesions with extensive ulceration and skin necrosis. Leg x-ray showed vascular calcification and diagnosis was confirmed by biopsy showing calcium deposits around vascular structures. Sodium thiosulfate, intensive wound care and O2 therapy were instigated (median start time from admission 13 days; range 10-54). Only case 3 showed any improvement and survived; case 4 showed improvement but did not survive.

Conclusion

CUA carries a high mortality and a high index of suspicion is required in atypical locations in dialysis patients as biopsy is not always diagnostic. Symptomatic treatment shows some promise for controlling disease progression but more effective therapies are necessary.

Exploring Metabolic Changes with Potential Treatment Implications in TSC Patients: A Multicenter Pilot Study

P. Janssens, K. Thedieck, L. De Waele, A. Jansen, D. Mekahli, F. Jouret

Objectives: Tuberous sclerosis complex (TSC) is an inherited multisystemic disease caused by inactivating mutations of *TSC1* or *TSC2* genes, which respectively encode the TSC proteins, hamartin and tuberin. When cells functionally lose one of the TSC proteins, the mTOR pathway becomes activated, and cells start to proliferate, eventually leading to tumor growth. Concomitantly, cells become more vulnerable to changes in nutrients given these intracellular metabolic alterations. Hence, in both cellular and animal models of TSC, important alterations in glucose, lipid and amino acid metabolism have been reported. Currently, the best therapeutic option for TSC is mTOR inhibition (e.g. everolimus), which slows tumor growth. However, these agents do not kill the tumor cells. Consequently, when mTOR inhibitors are withdrawn, TSC tumors grow again. Note also that treatment with mTOR inhibitors corrects TSC-associated metabolic alterations, thereby restoring the potential metabolic vulnerabilities of tumor-forming cells. No studies have been performed thus far on the metabolism of TSC patients, except for the beneficial impact of the ketogenic diet based on low glucose, high fat and limited protein diet on the epilepsy.

Methods: We plan to study the metabolism of 25 TSC patients aged between 12 and 60 years old, as well as of 25 matched healthy controls. These patients will be recruited from 2 university TSC centers (Leuven, Brussels). We will measure standard clinical parameters of glucose metabolism (e.g. insulin, c-peptide, HbA1C) and perform a broad and detailed metabolic screening combining non-targeted nuclear magnetic resonance spectroscopy and mass spectrometry in two specialized centers (Liège and Groningen).

Results: The inclusions have started, and we aim to complete recruitment by the end of the year.

Conclusion: With the present project, we aim to study metabolic changes in glucose, lipids and amino acids in a limited but well-characterized cohort of TSC patients with a known *TSC1* or *TSC2* mutation, in comparison to matched healthy controls. We hypothesize that we will find specific metabolic alterations in glucose, lipid or amino acid metabolism in TSC patients that will pinpoint metabolic vulnerabilities of tumor-forming cells that could be specifically targeted by drugs and/or nutritional measures. This study presents an original approach which may generate novel pathophysiological and therapeutic hypotheses in a rare (kidney) disease.

Sarcoidoisis recurring neurologically after kidney transplantation

N. Hanset, A. Ivanoiu, T. Duprez, A. Devresse, N. Demoulin, N. Kanaan

A 27 year-old man transplanted with a kidney one year ago was admitted for behavioural disorder and weight loss. His past history was relevant for sarcoidosis, presenting at the age of 16 with acute renal failure, bilateral anterior uveitis and hypercalcemia. At that time, kidney biopsy was not performed because of a congenital solitary right kidney. Corticosteroids were administered for 9 months with normalization of creatinine. He was subsequently lost for follow-up. Nine years later, he was admitted for end-stage renal disease, hypercalcemia, and hilar adenopathies. Lymph node biopsy revealed non-necrotising granulomatosis leading to a diagnosis of sarcoidosis. The patient was treated with corticosteroids and hemodialysed for 18 months until he was transplanted with a kidney from a deceased donor. His immunosuppressive regimen included tacrolimus, mycophenolate mofetil (MMF) and low-dose methylprednisolone (MP). Evolution was uneventful until his family noticed aggressive behaviour and social withdrawal for the past three months, accompanied by a significant weight loss.

Physical examination was normal except for nasal and malar reddish rash. Laboratory investigations showed normal CRP, creatinine, albumin and calcemia levels. Serum PTH level, 1,25(OH)²vitaminD3, TSH, T4, ACE and lysozyme levels were in the normal range. Urinalysis showed an increased calcium/creatinine ratio (0.82 mM/mM (N < 0.4)), with normal proteinuria. Tacrolimus through level was in the range. Serum PCR for CMV, EBV and HSV were negative. Chest x-ray was normal. Gadolinium enhanced brain MRI showed multiple, diffuse microlesions with blood-brain barrier breaches. Lumbar puncture displayed increased white blood cells count (98% lymphocytes), with negative PCR for Mycobacterium tuberculosis. A diagnosis of sterile lymphocytic meningitides secondary to neurosarcoidosis was made. Cutaneous lesions were retrospectively evocative of lupus pernio.

The patient was treated with oral MP (32 mg daily for four weeks, tapered by 4 mg every 2 weeks). He experienced a first relapse under 12 mg of MP/day. Despite increasing MMF doses and resuming MP at 32 mg/day with a slower tapering, a new relapse occurred under MP 8 mg/day, leading to resume doses of MP to 32 mg/day. Slower tapering of MP (4 mg/month) is currently ongoing.
In conclusion, our patient experienced a neurological recurrence of sarcoidosis one year after kidney transplantation, highlighting (1) the need to consider the diagnosis in patients with a history of sarcoidosis and (2) that immunosuppressive maintenance therapy may not be effective to prevent neurosarcoidosis after transplantation.

Towards an animal model of chronic kidney disease with a tuneable degree of renal dysfunction

L. Moonen, C. Cuesta-Apausa, P. D'Haese, C. Martínez-Salgado, F. López-Hernandez, B. Vervaet

Objective: An important feature of the clinical course of CKD is the graded decline in renal function, which, based on measurement of GFR, can be divided in 5 stages ranging from CKD1 (normal function) to CKD5 (end stage renal failure). Extrapolating data from animal studies to the clinical situation requires a good functional correlate between the target population and the experimental model. Based on the facts that 1) an acutely injured kidney persistently loses renal mass in the presence of its healthy counterpart and 2) an early nephrectomy (Nx) of the healthy kidney rescues the decay of the injured kidney, we hypothesized that a sufficiently delayed Nx would not be able to efficiently induce renal recovery of the injured kidney and that by varying the Nx delay time, one would be able to predefine the eventual degree of remnant renal function correlating with the different clinically relevant CKD stages.

Methods: Acute kidney injury was induced in 29 male Wister rats by left ischemia/reperfusion (UIRI) for 60 min at 35°C after which contralateral Nx was performed 3, 10 or 20 days later (n=8/group). Control rats (n=5) underwent mock-I/R and mock-Nx surgery. In addition to serum and urine creatinine, renal function was assessed by transcutaneous measurement of GFR 24 and 72 hours after Nx and weekly thereafter. Rats were euthanized 11 weeks after Nx. Kidneys were weighed and PAS stain was used to microscopically evaluate histopathology.

Results: In all groups 24h after Nx renal function was impaired as evidenced by reduced GFR and increased levels of serum creatinine. However, when Nx was performed early after UIRI (3 days), renal function completely recovered between week 3 and 5 after Nx. Nx on day 10 and 20 led to a persistent significant decrease in renal function of 20.3% (p=0.007) compared to sham animals. No significant difference in decline in renal function was detected between both groups (day 10 and 20). Nx induced compensatory renal hypertrophy/repair in all groups as shown by an increase in renal mass. However, when Nx was performed 20 days after UIRI renal hypertrophy/repair was significantly reduced. On a histological level, Nx on day 3 and 10 after UIRI led to little morphologic alterations compared to control animals. However, renal histopathological alterations were more severe when Nx was performed 20 days after UIRI. Animals in this group showed loss of brush border, cast formation, inflammation and tubular atrophy.

Conclusion: In the UIRI model, early Nx (i.e. day 3) rescues renal function, whereas a sufficiently delayed Nx (day 10, 20) is not able to induce a full functional recovery of the injured kidney, thereby mimicking CKD2 in the current setting. Varying Nx delay time after UIRI thus can provide an experimental method to induce renal dysfunction of different but tunable severity. Further optimization towards more severe degrees of renal dysfunction can be achieved by increasing the Nx delay time to more than 20 days or, more preferably, increase the severity of ischemic injury (by increasing the ischemia time) in order to keep total study duration within a considerable experimental time frame.

Unilateral nephrectomy attenuates progression from acute to chronic kidney injury by downregulating immune response pathways

L. Moonen, B. Cuypers, P. Meysman, K. Laukens, P. D'Haese, B. Vervaet

Objective:
Enhanced renal repair is defined as the remarkable repair of an acutely injured kidney upon removal of the healthy contralateral kidney. If the latter kidney is left in place, repair is only marginal and the injured kidney turns fibrotic. It is yet unclear to which extent and by which molecular mechanism a nephrectomy is able to alter the fate of injured kidney cells.

Methods:
Acute kidney injury was induced by left ischemia/reperfusion (I/R) after which either right nephrectomy (Nx) or mock-Nx was performed 3 days later. Wild type C57BL/6J mice underwent 21 min of ischemia at 36°C. Control mice underwent mock-I/R and mock-Nx surgery. Mice were euthanized at either 7 days or 6 weeks after I/R. Kidneys were weighed and qPCR analysis of the profibrotic genes Col1, Col4, TGFbeta and CCN2 was performed. Masson/H&E stain was used to microscopically evaluate histopathology and the extent of collagen deposition. RNA-sequencing was used to compare differential gene expression.

Results:
In the I/R without Nx group the median left kidney-to-body weight ratio (mg/g) at week 6 was 2.8 (range 2.1-3.1), whereas that of its right healthy kidney was 6.7 (range 6.4-7.0), indicating severe atrophy in the injured left kidney. In the Nx group, left kidney-to-body ratio was 6.9 (range 6.0-7.3) and that of its right kidney at the time of Nx 6.5 (range 5.9-7.5). When no Nx was performed, Col1, Col4, TGFbeta and CCN2 were upregulated 18-, 5-, 7- and 3-fold compared to controls at week 6, respectively. In case of Nx, this decreased to 5-, 2-, 2-, and 0-fold upregulation. On a histological level, Nx strongly attenuated cortical atrophy and tubulo-interstitial fibrosis. Preliminary whole transcriptome RNA-seq analysis at day 7 showed differential expression of 534 genes (257 up, 277 down) of which immune response and MAPK pathways were most significantly downregulated upon Nx.

Conclusion:
In conclusion, Nx performed 3 days after I/R has an early immunosuppressive action and attenuates renal atrophy and fibrosis in C57BL/6J mice. This murine model is a useful alternate tool to further study the mechanism of physiology-driven enhanced renal recovery.

Cytomegalovirus colitis in a hemodialysis patient, a rare presentation but significantly improved with ganciclovir therapy

F. Valente, I. Simon, I. Houem, L. Verset, A. Hadefi, J. Nortier

Objective. Morbi-mortality associated with cytomegalovirus (CMV) infection in immunosuppressed patients is well known, in particular in HIV-infected patients and transplant recipients. Although regular hemodialysis (HD) patients represent a high-risk population for developing CMV infection because of their compromised immunity, clinical manifestations are unusual (1, 2). We present the case of a HD patient who presented with severe acute colitis due to CMV infection and rapidly recovered after ganciclovir therapy.

Methods and Results. A 88-years old woman, on regular HD for end-stage diabetic nephropathy, was admitted for aqueous diarrhea and diffuse abdominal pain for 3 days, without fever. Laboratory examination revealed a significant inflammatory syndrome (CRP 340 mg/l). Abdominal computed scan described a thickening of the descending colon and rectum-sigmoid walls with hyperaemia of the mucosa, indicating a rectocolitis supposed to be of infectious origin. Blood cultures were negative, and culture of the faeces was unfortunately not obtained. An empirical treatment based on ceftriaxone and metronidazole was given for 5 days, with improvement of the clinical symptoms and decrease of the CRP level. The patient was discharged and a colonoscopy was planned.
After 10 days, the patient was readmitted for further deterioration of the general status and persistence of non-bloody, aqueous diarrhea. Physical examination revealed abdominal distension without tenderness. Laboratory analyses showed again an increase of the CRP (160 mg/l). Blood cultures and culture of faeces were negative after 48 hours. On the 2nd day of admission, after a peak of temperature above 38° C, ceftazidim and vancomycin were started. The day after, colonoscopy described colic mucosal bleeding at the contact, suggestive of ischemic colitis or ulcero-hemorrhagic rectocolitis. Histopathological examination found ulcerations and inflammatory granulation tissue with marked endothelial hyperplasia. Immunohistochemical staining specific for CMV was positive, leading to the diagnosis of primary CMV colitis. However, an ischemic colitis superinfected by CMV could not be excluded. Subsequently, Polymerase Chain Reaction (PCR) testing confirmed CMV viremia (4,650 copies/ml of viral DNA). Treatment was started with ganciclovir (loading dose of 5mg/kg followed by 1.25 mg/kg 3 times a week, after each HD session). One week later, the patient was asymptomatic. The treatment was maintained for 3 weeks. PCR CMV testing at the 2nd and 3rd weeks of treatment returned negative. A follow-up colonoscopy will be planned 2 weeks after the end of the treatment.

Conclusion. The present case describes clinically significant symptoms of colitis associated with CMV infection in a HD patient, rapidly recovering after specific antiviral therapy with ganciclovir. As chronic uremia is known to induce compromised immunity, CMV colitis should be considered as a differential diagnosis of colitis in HD patients.

References

(1) Kim SH et al, Hemodial Int 2011, 15(2): 297-300.
(2) Tabernero G et al, Nefrologia 2004, 24(3): 279-282

Tunneled hemodialysis vascular access-related bacteremia complicated by pacemaker probes infection required cardiac surgery

C. David, M. Taghavi, H. Mertes, M. Kianda, D. De Bels. Sanoussi, A. Pozdzik

Objective: The concomitant presence of a central venous catheter and cardiovascular implantable devices (CID) creates a high risk circumstance for endocardial infection. CID related endocarditis secondary to vascular access-related bacteremia is associated with high mortality in hemodialysis patients. Staphylococci are the most frequently reported (68-93%). The main documented risk factors are diabetes mellitus, black race, obesity and repetitive endocardial injuries.

Case report: We report the case of a 63-year-old African woman under hemodialysis for end stage renal diseases probably secondary to arterial hypertension. Main history included diabetes mellitus, hypertensive heart disease, complete atrio-ventricular bloc (triple chamber pacemaker implanted in 2003), atrial flutter, bronchopulmonary obstructive disease and obesity. She presented recurrent septicaemia (2 episodes due to *S. marescens* and the 3 episodes due to *S. aureus* during the last 12 months). Despite well conducted antibiotic treatment, central venous catheter was replaced several times. During the last episode the two-dimensional transoesophageal cardiac echography displayed an image of endocarditis associated with strands accolated to persistent floating. P*ositron-emission tomography* (PET) confirmed proximal parts of PM probes infection so we introduced rifampicine and cefazoline. When bloodstream infection cleared PM devices were removed by cardiotomy and replaced by epicardial devices. All removed probes were positive for *S. aureus*. Meantime she presented ventricular tachycardia and a subcutaneous defibrillator was placed. No further bacteremia was documented. Femoral vein is the only accessible vascular access for hemodialysis. Actually, she is not eligible combined heart-kidney transplantation because of obesity and comorbidity.

Conclusion: Our patient presented all classically described risk factors for CID infection that was triggered probably by recurrent central venous catheter implantation. Appropriate antibiotic therapy need to be combined with ICD removal because of high recurrence rate of infection like in our patient, and higher mortality rate if ICD is left in place. Unfortunately, some patients (3-15%) are unsuitable for CDI removal given a high risk profile of post-procedural complications. This is why a multidisciplinary approach for these patients is crucial for an optimal management.

Preimplantation genetic testing for polycystic kidney disease is an option for affected families.

V. Berckmoes, P. Verdyck, P. De Becker, A. De Vos, G. Verheyen, P. Van der Niepen, W. Verpoest, I. Liebaers, M. Bonduelle, M. De Rycke

Objective: In this study, the strategies and clinical outcome of a large cohort of preimplantation genetic testing (PGT) cycles for PKD performed at one centre for medical genetics between 2005 and 2016 are reported. As males affected with autosomal dominant PKD (ADPKD) may present with reproductive system abnormalities and infertility, the clinical outcome was compared between couples with the female partner affected with ADPKD and couples with the male partner affected with ADPKD.

Methods: Sixteen single-cell clinical tests for PKD based on multiplex PCR of STR markers were applied for 91 PGT cycles for 43 couples (33 couples for polycystic kidney disease 1 (PKD1), 2 couples for polycystic kidney disease 2 (PKD2) and 8 couples for autosomal recessive polycystic kidney disease (ARPKD)). In 18 couples, the male partner was affected with ADPKD and 12 of them had a documented infertility status. This group underwent 52 cycles to oocyte retrieval (OR). For 18 other couples, the female partner was affected with ADPKD and 4 male partners from this group had a documented history of infertility. This group underwent 31 cycles to OR.

Results: Blastomere biopsy was performed on 584 day 3 cleavage stage embryos. A diagnosis was obtained for 93.3% of the analysed embryos of which 36.8% were genetically transferable. Transfer of 74 embryos in 53 fresh cycles and transfer of 34 cryopreserved embryos in 33 frozen-warmed embryo transfer cycles resulted in a live birth delivery rate of 38.4% per transfer with 31 singleton live births, 2 twin live births and 1 ongoing pregnancy. The observed cumulative delivery rate was 57.8% per couple after five treatment cycles. The clinical pregnancy rate and live birth delivery rate was significantly lower for couples with the male partner affected with ADPKD compared with couples with the female partner affected with ADPKD. However, female age, which is a well-established determinant factor for treatment outcome, was the only variable significantly associated with live birth delivery rate.

Conclusion: This study shows that PGT for PKD performed in our centre offers good reproductive outcomes from both fresh and frozen embryo transfers. Our results can be a valuable tool for physicians to counsel PKD patients about their reproductive options. Males affected with ADPKD who suffer from infertility should be advised to seek treatment on time to improve their chances of conceiving a child.

Kidney progenitor cells with podocyte differentiation capacity found in urine of cystinosis patients

F. Oliveira Arcolino, K. Veys, L. van den Heuvel, E. Levtchenko

Cystinosis is a lysosomal storage disorder characterized by the pathological accumulation and crystallization of cystine in different cell types. If not treated, renal failure invariably develops within the first decade of life. We have shown that cystinosis patients void excessive number of podocytes and proximal tubular cells in urine. We hypothesized that in compensation for cell loss, ongoing regeneration might happen, and it could be reflected by the presence of kidney progenitor cells in urine of the patients.

We quantified the total number of cells and the number of kidney progenitor cells in urine using qPCR analysis of mRNA extracted of fresh urine samples of healthy donors (n = 10, age range 4-12 years old) and cystinosis patients (n = 8, age range 4-15 years old). None of cystinosis patients had kidney graft. The expression of vimentin was correlated to calibration curves derived from known numbers of adult kidney progenitor cells and normalized to volume of urine. We have cultured urinary cystinosis progenitor cells and characterized them by qPCR, FACS and immunofluorescent analysis.

We demonstrate a significant increased excretion of kidney progenitor cells in cystinosis patients (progenituria), while in controls no progenitors were found in urine. FACS analysis showed that the progenitor cells isolated from cystinotic urine expressed mesenchymal stem cell proteins as CD73, CD44, CD105, CD29, did not express hematopoietic stem cell markers and were positive for the kidney proteins CD24 and CD133. The clones were positive for nephron progenitor markers, such as Vimentin, NCAM, *PAX2* and *CITED1* and were able to differentiate either into functional podocytes or proximal tubular cells.

Our data demonstrate the presence of kidney progenitor cells in urine of cystinotic patients, which might indicate a fast turnover of cells and the attempt of tissue regeneration to compensate cell loss. Urinary cystinotic progenitor cells might have a therapeutic application in regenerative medicine once the correction of the genetic defect and consequent phenotype are successful.

Haemodialyser fiber blocking: the inner counts

F. Vanommeslaeghe, W. Van Biesen, M. Dierick, M. Boone, A. Dhondt, S. Eloot

Coagulation in the haemodialysis (HD) circuit decreases treatment efficiency and can result in substantial blood loss. So far, multiple surrogate markers are used during or after haemodialysis, to estimate the activation of coagulation. None of these tools is able to quantify fiber patency in the entire dialyser, and validation against a gold standard is lacking. Being able to objectively determine the number of patent fibers would overcome this important barrier in comparative studies in different dialysers and different anticoagulation strategies.

We therefore developed a novel technique based on micro-CT scanning to quantify coagulation in fibers of haemodialysers. To illustrate the potential of this technique, different machine parameters and visual scoring were evaluated during HD.

Twenty stable HD patients were treated with post dilution haemodiafiltration for 245±20min with an FX600 haemodialyser on a 5008 dialysis machine (both Fresenius, Germany) using low molecular weight heparin anticoagulation according to body weight. Every 30min, ultrafiltration and substitution flows and volumes, venous and arterial pressure, transmembrane pressure, blood volume monitoring and online clearance monitoring, all as indicated by the machine, were registered. After dialysis, haemodialyser and venous chamber and line were scored with colour coding, and clot sizes were visually estimated. Next, in an *in vitro* setting, continuous mild positive pressure ventilation was applied in the dialyser for 24h after which dialyser dry mass was measured. The 20 used and 3 fresh non-used dialysers were, as a gold standard, scanned (resolution 25µm) in HECTOR (an in-house developed High-Energy CT scanner Optimised for Research). After image reconstruction, the open, non-coagulated fibers were counted in a representative cross-section at the dialyser outlet (ImageJ, Fiji).

In non-used *versus* used FX600 dialysers, 10748±2 *versus* 8930±2465 [range 534-10692] open fibers were counted, witnessing the very high accuracy of the method. In used dialysers, the number of open fibers did not correlate with any of the measured machine parameters. Furthermore, the associations with the visual scoring of the dialyser (R^2=0.41) and venous chamber (R^2=0.34), and with the post-dialysis dialyser dry mass (R^2=0.62) substantially suffered from disappointing point prevalence predictive power, making these parameters unreliable at the level of the individual patient.

Although an important issue in clinical practice, dialysis machines do not provide any online parameter to accurately predict fiber blocking in haemodialysis. The described micro-CT scanning technique is a feasible, objective, non-invasive, accurate and reproducible tool for quantification of the degree of fiber blocking in a haemodialyser after use, making it a potential gold standard for use in studies on fiber blocking during renal replacement therapy.

What we should know when prescribing teicoplanin in peritoneal dialysis patients

S. Eloot, J. Vanmassenhove, W. Van Biesen

Objective Although there are clear guidelines on how to administer vancomycin intraperitoneally, there is less experience with the use of teicoplanin in case of PD peritonitis caused by methicillin resistant gram positives. We studied teicoplanin kinetics during IV and IP administration in order to optimise antibiotic therapy in a patient with MRSE peritonitis.

Methods A PD patient (male, residual eGFR 10mL/min, 88kg) was diagnosed with MRSE peritonitis. Because of documented vestibulotoxicity, most likely caused by previous vancomycin administration, it was decided to treat the patient with teicoplanin instead. After three days of IV teicoplanin administration (800mg on day 1 and 600mg on days 2 & 3), 20mg teicoplanin was added to each of the four 2L dwells per day, i.e. tree times Bicavera 1.5% (Fresenius Medical Care) and one Extraneal (Baxter), during 15 consecutive days. Blood and PD fluid were sampled after the long dwell before the start of IP treatment (d0), and at the outflow of day 3 (d3) and 7 (d7). Total and free teicoplanin levels were determined with an in-house developed ultra-high performance liquid chromatography-high resolution mass spectrometry (UHPLC-HRMS) method, and percentage protein binding was calculated. A two-pool model (pool 1 equal to dwell volume and pool 2 the distribution volume for teicoplanin being 0.68L/kg body weight, i.e. 60L) was calibrated for the clearance among both pools (K_{12}) by fitting on the measured plasma and dialysate concentrations.

Results The low dialysate teicoplanin concentration at d0 (i.e. only 2.6mg/dL) illustrates the hampered teicoplanin transport from plasma into dialysate. This can be attributed to the high protein binding of 92±1% and is also reflected in a negligible clearance K_{12} between plasma and dialysate in the calibrated kinetic model. The limited renal and dialysis removal also led to much higher plasma concentrations at d0 (i.e. 28.8mg/L) than would be expected theoretically from dose and distribution volume (i.e. 10mg/L). From d0 on, the patient got into a kind of steady state dialysis regime with teicoplanin TAC concentrations in dialysate of 8.4mg/L (max 10mg/L at inflow → min 6.6±1.2mg/L at outflow), while total plasma concentrations were 24.8±3.6mg/L as mainly uploaded by the previous IV administrations. After switching to teicoplanin IP (instead of IV), the patient's clinical condition improved dramatically and CRP levels dropped over the next few days. Unfortunately, after stopping the antibiotic treatment, patient relapsed to colonisation of the PD catheter with MRSE. The PD catheter was thus removed and patient was switched to haemodialysis.

Conclusion Due to teicoplanin's high protein binding which hampers transperitoneal transport, and its long half-life, IV administration is not a feasible option to treat peritoneal related infections caused by methicillin resistant gram positives. To avoid nephrotoxic blood levels as well as sub-therapeutic dialysate levels, low dose IP teicoplanin administration is recommended in each dwell.

Atypical granulomatous pattern of tubulointerstitial nephritis and uveitis syndrome: case report and literature review

M. Taghavi, C. David, C. Fosso, M. Depierreux, A. Pozdzik

Background : Tubulointerstitial nephritis and uveitis (TINU) syndrome is a rare disease in which the underlying physiopathology is to date poorly understood though some hypothesize that infection and autoimmunity are involved. It occurs more often in young woman and renal impairment usually precedes uveitis. Renal biopsy findings vary considerably, however tubulointerstitial nephritis is always found as a constant. However, granulomas are rare. TINU remains a diagnosis of exclusion. Because of a delay up to several months between the occurrence of renal and ophthalmologic features, TINU is certainly underdiagnosed and the prognosis can worsen especially in the absence of follow-up.

Case report: We report a 31-years-old African woman who came to our center with fatigue, headache, fever, ophthalmic pain, weight loss and acute kidney injury (AKI) (plasma creatinine (PCr) 2 mg/dL). She had no medical condition except for a recent history of peripartum hypertension treated by nifedipin. The renal biopsy showed tubulointerstitial nephritis and several, small non-necrotizing granulomas. Concomitantly, bilateral anterior uveitis with several, small granulomas was found by ophthalmologist. Laboratory tests showed high levels of C-reactive protein and hypokalemia (3.2 mmol/L). Infectious serology and autoimmune screening were negative. Nifedipin was discontinued for more than 2 weeks regarding the possibility of drug-induced interstitial nephritis without, however, improvement of the renal function. Patient was therefore diagnosed with TINU syndrome after excluding other differential diagnosis such as tuberculosis, sarcoidosis and drug-induced interstitial nephritis. As renal function declined (PCr 3.7 mg/dL), we started steroid therapy (methylprednisolone 750 mg daily pulses for 3 days followed by daily oral progressive tapering). After 3 months of corticoids her renal function improved (PCr 1.3 mg/dL) and ophthalmic pain disappeared.

Conclusions: Here we report a case with atypical clinical and histological presentation: 1) clinical symptom such as fever occurs in up to 40% of cases and 2) histological granulomas pattern of tubulointerstitial nephritis on kidney biopsy has been only rarely reported. We therefore suggest that TINU should be actively searched in patients who only manifest either uveitis or tubulointerstitial nephritis, and assessment should be made in collaboration with nephrologists, ophthalmologists, internists infectiologists and renal pathologists. There is no evidence-based guidelines regarding TINU treatment. Renal function declines is a key indication for systemic treatment further to which the renal outcome is usually good as in our case.