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Abstract Book

ABSTRACT NUMBER 1

L-ARGININE SUPPLEMENTATION REDUCES FIBROSIS IN A MOUSE MODEL OF CHRONIC ARISTOLOCHIC ACID INDUCED NEPHROPATHY

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OBJECTIVE - Aristolochic Acid (AA) nephropathy (AAN) is a rapidly progressive tubulo-interstitial nephritis from toxic origin characterized by two interconnected phases: an early phase of acute kidney injury (AKI) leading to the later phase of chronic kidney disease (CKD) with progressive interstitial fibrosis. A reduced nitric oxide (NO) production in AAN has been demonstrated, which may contribute to renal function impairment. We previously established that sustaining NO bioavailability using L-Arginine (L-Arg) supplementation improves the outcome of AA-induced AKI. Since AKI contributes to the progression of renal disease towards CKD, we investigated in the present study the potential benefit of L-Arg supplementation in a chronic mouse model of AAN.

METHODS - To address this point, 8 weeks-old C57BL/6J male mice were subjected to daily i.p. injection of AA (3,5 mg/kg) for 4 days and L-Arg was supplemented in drinking water (5%) 7 days before first day of injection and all along the protocol Mice were euthanized 20 days after the first day of injection.

RESULTS - At day 20, we observed a significant reduction of NO bioavailability in AA-treated animals as measured by reduced urinary nitrate/nitrite and cGMP excretions. AA-treated mice displayed polyuria, proteinuria as well as increased levels of plasma creatinine and blood urea nitrogen. Histological analyses of AA-treated mice revealed numerous foci of tubular atrophy surrounded by severe interstitial fibrosis. Immunohistochemical staining of α-SMA revealed a significant increase of positive area staining. Moreover, mRNA expression of pro-fibrotic mediators like *TGF-β*, *CTGF*, *Periostin*, *ColI* and *ColIII* was also increased. L-Arg supplementation in AA-treated mice significantly decreased tubular atrophy as attested by reduced tubular injury score. L-Arg treatment also significantly limited development of interstitial fibrosis as attested by both reduced α-SMA immunohistological staining and collagens mRNA expressions. Finally, L-Arg treatment also decreased *TGF-β*, *CTGF* and *Periostin* mRNA expressions.

CONCLUSION - These results suggest that a preservation of NO bioavailibity may lead to a morpho-functionnal protection in AA-induced CKD. In the present mouse model of chronic AAN, NO seems to act as a key factor in protection of renal function and fibrosis development. In conclusion, restored NO bioavailability by L-Arg supplementation was demonstrated beneficial in improving renal injury in chronic AAN.

ABSTRACT NUMBER 2

ONLINE SURVEY EXPLORING OPINIONS OF EUROPEAN PEDIATRIC/ADULTS NE PHROLOGISTS AND GENETICISTS ABOUT DIAGNOSTIC TESTING OF ASYMPTOMATIC OFFSPRING FROM FAMILIES AFFECTED BY AUTOSOMAL DO MINANT POLYCYSTIC KIDNEY DISEASE

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BACKGROUND*:* Autosomal dominant polycystic kidney disease (ADPKD) is the most common monogenic cause of kidney failure with currently no cure. ADPKD is considered as an adult disease and until now, whether children in families with a positive history of ADPKD should be tested for the presence of the disease remains a matter of controversy. The main arguments against testing of children in families with ADPKD include (1) the current absence of effective treatment preventing cyst formation and cyst growth (2) the possible psychological stress and (3) the fear of being unable to obtain life or medical insurance. However, the attitudes of the caregivers regarding testing of offsprings of ADPKD has never been studied.

AIM*:* The aim of our study is to assess the attitudes and beliefs of the caregivers concerning testing of offspring in families with ADPKD and to identify the underlying arguments.

METHODS*:* We used an online questionnaire aimed for the paediatric and adult nephrologists and an adapted version for geneticists.

RESULTS*:* A total of 410 caregivers responded (53.4% male with a mean (SD) age of 48.3 (9.8) years) including 151 adult nephrologists, 216 pediatric nephrologists, and 43 geneticists. All three specialities similarly agreed that it was appropriate to “encourage clinical testing in adults” (group mean = 5.31, sd = 1.16). While all supported that doctors should “encourage clinical testing in minors” (group mean = 4.76, sd = 1.50), pediatric nephrologist demonstrated significantly stronger agreement ($t = 3.60$, $p < .001$) than geneticists. Regarding ethical concerns, although all specialities exhibited some disagreement with the statement that “prenatal genetic diagnosis is ethically justified” (group mean = 3.08, sd = 1.76), adult and pediatric nephrologists exhibited significantly higher levels of disagreement compared to geneticists ($t_{adult} = -2.10$, $p < .05$; $t_{pediatric} = -3.19$, $p < .01$). Similarly, all three specialities exhibited disagreement with the statement that “termination of pregnancy for ADPKD is ethically justified” (group mean = 2.78, sd = 1.67). Again, adult and pediatric nephrologists exhibited significantly higher levels of disagreement than geneticists ($t_{adult} = -2.967$, $p < .01$; $t_{pediatric} = -4.47$, $p < .001$). Finally, geneticists exhibited agreement with the statement that “pre-implantation genetic diagnosis is ethically justified” (geneticist mean = 4.48, sd = 1.63). This position was significantly different that of adult and pediatric nephrologists who exhibited disagreement ($t_{adult} = -2.51$, $p < .05$; $t_{pediatric} = -4.43$, $p < .001$).

CONCLUSION*:* Our survey demonstrated that most of the caregivers will support clinical testing of the offsprings of ADPKD families, however, there is no consensus on the value of genetic testing neither on the ethical issues of the family planning.

ABSTRACT NUMBER 3

3D-US WITH A CORRECTION FACTOR IS A GOOD ALTERNATIVE IN ESTIMATING TOTAL KIDNEY VOLUME IN CHILDREN WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

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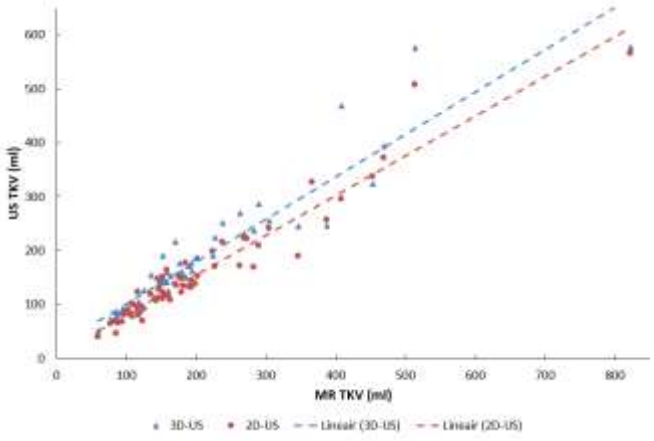
BACKGROUND: Total kidney volume (TKV) has been shown in adult Autosomal Dominant Polycystic Kidney Disease (ADPKD) to be an independent and strong predictor for disease progression. In the current interventional clinical trials, TKV measurement by magnetic resonance (MR) imaging has been shown to be more accurate, reproducible and able to detect small changes over a short period of time compared to ultrasound (US). Since future therapies in ADPKD could be extended to include children, we aimed to examine whether the high-resolution 3D-US TKV measurements might be used as an alternative method to MR measurements in ADPKD children.

METHODS: Prospective evaluations of renal MR, 2D- and 3D-US were performed, whereby TKV was calculated by means of manual delineations (MR, 3D-US) or by the ellipsoid method (2D-US). Correlations and differences between parameters were evaluated using Pearson r and Wilcoxon signed rank tests. After correction using the optimal linear regression, the variability of the measurements was examined using Bland-Altman plots.

RESULTS: We included 29 patients (17 male, 12 female) with a median age (SD) of 14.0 (3.4) years and eGFR 111 (17) ml/min/1.71m² leading to 58 evaluated kidneys. Although both US methods showed significantly lower TKV compared to MR (In ml, 3D-US: 181 (111); 2D-US 158 (101); MR 205 (132); all p<0.001), both showed a strong correlation to the MR TKV (2D-US: r=0.963; 3D-US: r=0.941). After correcting for the lower values in US, Bland-Altman plots showed slightly lower variability and error in 3D-US measurements compared to 2D-US in kidneys with a TKV below 200 ml (on average 15.5 ml error on 2D-US compared to 12.9 ml on 3D-US), although not reaching significance (p=0.23).

CONCLUSION: In children, 3D-US represents a good alternative for MR to measure small TKV in ADPKD. Compared with MR, US TKV was prone to underestimation. After correcting for these, 3D-US tended to be slightly more comparable to MR in small TKV (<200 ml) than 2D-US.

Figure: Correlations of 2D- and 3D-US with MR volumes in ADPKD patients



ABSTRACT NUMBER 4

BILATERAL RENAL VEIN THROMBOSIS IN THE NEWBORN

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OBJECTIVE : Neonatal renal vein thrombosis is a rare condition but is associated with significant renal morbidity. Its pathophysiological mechanisms remain elusive and our knowledge on the optimal therapeutic approaches is still deficient. There are no randomized controlled trials to guide management.

METHODS : We report a case of a full term male newborn with bilateral renal vein thrombosis (RVT). We describe the clinical presentation, the imaging modalities, the effects of various treatment options, the associated abnormalities and briefly discuss this rare syndrome.

RESULTS : A full term male neonate was admitted with a fast alteration of the general condition, macroscopic hematuria, thrombocytopenia and a palpable abdominal mass. Given the acute renal failure the diagnosis RVT was contemplated. A bilateral RVT was confirmed at abdominal doppler ultrasound. Intravenous administration of thrombolytic therapy was given but was unsuccessful. In a last attempt to preserve renal function surgical removal of the thrombus was performed, but unsuccessful. The clinical course was complicated by severe renal failure requiring renal dialysis. Spontaneous improvement of renal function was noted and the patient is currently free of dialysis but remains in chronic renal impairment. Unusually, this patient was shown to be heterozygous for factor V Leiden mutation and a specific point mutation in MTHFR (A1982C). Protein C and S levels were low at birth.

CONCLUSION : The present case of bilateral RVT in a newborn with both factor V mutation and a specific point mutation in MTHF (A1982C) suggest that the presence of an associated thrombophylic disorder shoud be looked for and that prolonged intensive therapy was eventually associated with partial recovery of renal function.

ABSTRACT NUMBER 5

OUTCOMES OF KIDNEY TRANSPLANTATION IN CHILDREN WEIGHING ≤15 KG

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Kidney transplantation (KT) in small children is challenging with a significant risk of complications. Aim: to describe data on early surgical complications, acute rejections (AR), patient and graft survival, in renal recipients weighing ≤15 Kg transplanted in the two main Belgian pediatric transplant centers. Two periods, before (period1) and since 2000 (period2) were compared. This reflects the introduction of new immunosuppression regimens (basiliximab and MMF) in 2000. Methods: A retrospective analysis was performed on 71 KTs (67 children) grafted between 1978 and 2015: 38 (54%) in period1 and 33 (46%) in period2. Results: The median age at KT was 3.2 yrs (range 1.3-11.3) and mean weight 12 ±1.9 Kg. KTs with living related donors were performed in 24 (34%) cases (39% in period1 and 27% in period2). For deceased donor kidneys median cold ischemia decreased significantly from 22 to 15 hrs during the successive periods ($p<0.03$). Twenty-three (32%) surgical complications were observed with no difference between the two periods, with 19 (27%) cases needing re-intervention. AR occurred in 24 (34%) KTs and the number decreased significantly over time: 20 (53%) in period1 and 4 (12%) in period2 ($p<0.001$). No difference in AR incidence was found between living and cadaveric donor KTs: 10 (42%) and 14 (30%) respectively. Transplantation survival free-of-AR increased significantly in period2 compared to period1: 97% versus 50% at 1 yr; 87% versus 50% at 10 yrs post-KT ($p=0.003$). Overall graft survival was 83% (95%CI 72-90%) at 1 yr and 74% (95%CI 61-83%) at 5 yrs post-KT. Graft survival tended to increase over time (period1: 74% and 63% at 1 and 5 yrs; period2: 94% and 86% at 1 and 5 yrs; $p=0.07$). Patient survival was 92% (95%CI 83-97%) at 1 yr, and 91% (95%CI 80-96%) at 5 yrs post-KT. Patient survival tended to increase over time (period1: 87% and 84% at 1 and 5 yrs; period2: 97% at 1 and 5 yrs; $p=0.2$). Conclusion: Kidney transplantation in children ≤15 Kg remains a challenging procedure. However, incidence of acute rejection as well as patient and graft survival are excellent and similar to adult recipients under current immunosuppressive regimens.

ABSTRACT NUMBER 6

EFFICACY OF THROMBOLYSIS WITH UROKINASE CONTAINING LOCKING SOLUTIONS FOR THROMBOTIC DYSFUNCTION OF TUNNELLED HEMODIALYSIS CATHETERS: A RETROSPECTIVE SINGLE-CENTRE COHORT STUDY

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OBJECTIVE : The use of tunnelled cuffed hemodialysis catheters (TCC) is complicated by the development of thrombosis and catheter-related bacteremia (CRB). The optimal regimen to treat thrombotic complications with thrombolytic locking solutions remains controversial.

METHODS: We retrospectively collected data on all thrombotic dysfunctions of TCC used between 2010 and 2014 at the UZ Brussel Hemodialysis Unit. We reviewed the efficacy of different treatment regimens with Urokinase thrombolytic catheter locks to restore adequate access blood flows and pump pressures. The advantage of multiple administrations of Urokinase locks between successive dialysis sessions was also investigated.

RESULTS: 148 patients had in total 773 thrombotic dysfunctions. In 80% of thrombotic dysfunctions treated with thrombolytic locking solution, Urokinase (50,000 IU in each catheter lumen) restored adequate access blood flow to more than 250 ml/min, with increases of mean blood flow by 54 ml/min. Normalisation of arterial and venous pump pressures occurred in 90% of dysfunctional catheters with a reduction of mean aspiration (arterial) pressure by 25 mmHg and mean outflow (venous) pressure by 32 mmHg (all $P<0.0001$). Mean catheter blood flow was significantly higher after administration of multiple doses as compared to a single dose of Urokinase (280 ±71 ml/min vs. 267 ±75 ml/min; $P=0.0153$). However, this beneficial effect depended on whether the catheter remained dysfunctional after the first treatment. If blood flow did not reach 250 ml/min after the first treatment subsequent Urokinase locks improved blood flow by a further 95 ml/min ($P<0.0001$) whereas only 8 ml/min were added in case blood flow had recovered normal values after the first dose ($P=0.1026$).
The overall incidence rate of catheter-related bloodstream infections was low in our cohort (0.23/1000 catheter days) and did not differ significantly in patients with (0.26/1000 catheter days) or without (0.1/1000 catheter days) thrombotic catheter dysfunction ($P=0.09$).

CONCLUSIONS: Urokinase was effective to treat TCC-related thrombotic dysfunction. Multiple administrations were more effective than one single administration
only if normal catheter function was not restored after the first thrombolytic treatment. Restricting thrombolytic therapy to one treatment in catheters with excellent
initial response might therefore be the most cost-effective treatment approach. The overall incidence of catheter-related bloodstream infections was low and not significantly associated with thrombotic TCC dysfunction.

ABSTRACT NUMBER 7

CITRATE-BASED LOCKING SOLUTIONS ARE MORE EFFICIENT THAN TAUROLIDINE-BASED LOCKING SOLUTIONS TO PREVENT THROMBOTIC DYSFUNCTION OF TUNNELLED HEMODIALYSIS CATHETERS: A RETROSPECTIVE COHORT STUDY

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OBJECTIVE : The optimal catheter lock to prevent thrombotic dysfunction of tunnelled cuffed hemodialysis catheters (TCC) remains controversial. The aim of the present study was to compare the incidence rate of thrombotic dysfunction and loss of TCC treated with citrate- or taurolidine-based locking solutions.

METHODS: Retrospective cohort analysis of incidence and treatment of thrombotic TCC dysfunction in adult hemodialysis patients. Data were prospectively collected since 01/05/2010. From 01/05/2010 until 31/07/2012 Cita-Lock™ 30% (Citra-L) was used as a locking solution and replaced since 01/08/2012 with TauroLock™-Hep5OO (Tauro-L). The observation period ended on 31/10/2014. .Thrombotic dysfunction was retrospectively defined as the use of Urokinase (Actosolv®) instillation. Catheter loss due to thrombosis was defined as thrombotic dysfunction unresponsive to thrombolytic therapy and requiring catheter replacement.

RESULTS: A total of 251 patients received hemodialysis using a total of 346 TCC. 236 (68.2%) TCC experienced 764 episodes of thrombotic dysfunction during the study period. Under Citra-L (70325 days at risk), 252 episodes of thrombotic dysfunction occured (3.58/1000 catheter days; 95% CI 3.17-4.05), whereas under Tauro-L (67140 days at risk), 512 episodes occurred (7.63/1000 catheter days; 95% CI 6.99-8.31). The rate ratio was 0.47 (95% CI 0.40-0.55; P<0.0001), corresponding to an incidence rate reduction of thrombotic dysfunctions by 53% with Citra-L. The rate of catheter loss due to thrombotic dysfunction was 0.15/1000 catheter days (95% CI 0.08-0.27) under Citra-L and 0.28/1000 catheter days (95% CI 0.18-0.43) under Tauro-L (rate ratio of 1.84 (0.89 to 3.81; P=0.1).
The rate of catheter-related bacteremia was 0.29/1000 catheter days with both locks (P=0.99).

CONCLUSIONS: The use of Citra-Lock™ 30% is associated with a 53% reduction in the incidence rate of thrombotic dysfunction of tunneled hemodialysis catheters as compared to Taurolock™-Hep500. There were no significant differences in the incidence rates of catheter loss and catheter related bacteremia

ABSTRACT NUMBER 8

HYPONATREMIA IS A MARKER OF SEVERITY OF HIV-DISEASE IN CART-NAÏVE PATIENTS: A RETROSPECTIVE COHORT STUDY

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OBJECTIVES*:* Hyponatremia is a frequent electrolyte disorder in HIV infected patients with a prevalence of up to 56% in the pre-cART era. Several studies have demonstrated that patients with hyponatremia are at an increased risk of death. We aimed to investigate the prevalence of hyponatremia in the recent cART-era and evaluate its association with mortality.

METHODS*:* Single-center retrospective cohort study. A total of 1196 cART-naïve patients followed at the AIDS Reference Center, St Pierre University Hospital in Brussels, Belgium, between 1 January 1998 and 31 December 2013 were included. Hyponatremia was defined as a baseline natremia lower than 135 mmol/l. The outcome of interest was the occurrence of death.

RESULTS*:* In this study 177 (14.8%) patients had hyponatremia at baseline with a median natremia of 132.0 mmol/l [interquartile range (IQR) 130.0-134.0 mmol/l]. Hyponatremic patients had a lower CD4 cell count (207.5±197.7/µl vs 400.4±277.0/µl), a higher prevalence of AIDS (50.3% vs 12.4%; P<0.0001), a shorter median time to a first hospitalization (2.0 IQR [0.0-12.0] months vs 13.0 IQR [2.0-29.0] months) and an increased incident hospitalization rate [785/1000 patient-years, 95% confidence interval (CI) 725 to 845 versus 370/1000 patient-years, 95% CI 352 to 388; P<0.0001]. A significantly higher proportion of patients with hyponatremia were hospitalized at first contact (72.3 % vs 20.0 %; P<0.0001).
The incident mortality rate was 28.3/1000 patient-years (95% CI 18.15-42.16) in patients with hyponatremia compared to 9.33/1000 patient-years (95% CI 6.63-12.75) in normonatremic patients (P<0.0001). Three-year cumulative survival rates were 85.8%±3.0% in hyponatremic patients and 96.3%±0.7% in normonatremic patients (log-rank P<0.0001).
However, in a multivariate Cox model adjusting for other risk factors such as AIDS, CD4 count and hepatitis C, hyponatremia was no longer a predictor for patient death (hazard ratio: 1.03, 95% CI 0.54-1.97; P=0.935).

CONCLUSIONS*:* Hyponatremia is a marker of severity of HIV-disease in cART-naïve patients but not an independent risk factor for mortality. HIV-patients with a low serum sodium at baseline might benefit from a close follow-up to improve outcomes.

ABSTRACT NUMBER 9

TITLE: KDRI IMPLEMENTATION: COULD THIS LEAD TO THE TRANSPLANTATION OF MORE AND HIGHER-QUALITY DONOR KIDNEYS?

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OBJECTIVE. The Kidney Donor Risk Index (KDRI) is a continuous risk score, which provides an estimate of the quality of the donor kidney and hence also its relative risk of graft failure after transplantation. The KDRI score is based on ten donor characteristics and should be a useful tool to improve the allocation of deceased donor kidneys. The score is already being used in the U.S.A. The reference donor (KDRI = 1) is set equal to the median donor of the previous calendar year. A low value of the KDRI is associated with a better long term outcome of the graft. This study investigates whether the implementation of the KDRI in our decision making process improved the acceptance rate and the quality of deceased donor kidneys in our centre.

METHODS. From April 1st till December 31st 2015, we performed a prospective single center study. For all single offered deceased donor kidneys from Eurotransplant to one of our patients on the transplant waiting list, the KDRI was calculated at the moment of an offer. We compared the number and the quality (based on the KDRI) of the transplanted kidneys in our study with a recent retrospective study performed in our centre (unpublished results), in which the KDRI had been calculated for all offered donor kidneys from 2010 till 2013. In the current study we also analyzed our motivation to decline an offer.

RESULTS. By implementing the KDRI in our decision making process, 26.7% of all offered donor kidneys (N=120) were transplanted, compared to 20.7% in the retrospective study (N=657) ($p = 0.033$). In addition, 57,1% of all offered high quality donor kidneys according to the KDRI (i.e. KDRI < 1) in our study were transplanted, compared with 38,7% previously ($p = 0.037$). The median KDRI in our trial was 1.18 compared to 1.09 in the retrospective performed study. Frequently cited reasons to decline a donor kidney were besides the KDRI: high donor age, a large difference in age between recipient and donor, smoking and high serum creatinine. The main reasons to decline a high quality donor kidney according to the KDRI were either not included in the KDRI calculation such as insufficient HLA matching or proteinuria. However, factors who were already included in the KDRI such as the fact of being a DCD donor, were also mentioned.

CONCLUSION. By the learning process of implementing the KDRI we transplanted more and higher quality donor kidneys. We suggest to think twice before declining an offered donor kidney with a KDRI < 1. Long term follow-up will show if transplantation of better quality kidney has an impact on graft and patient survival.

ABSTRACT NUMBER 10

ESTIMATED GFR POORLY REFLECTS THE CONCENTRATION OF VARIOUS UREMIC TOXINS IN PEDIATRIC CKD PATIENTS

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OBJECTIVE:
Glomerular Filtration Rate (GFR) is considered to be an overall index of kidney function in children with chronic kidney disease (CKD). As accurate measurement of GFR is time-consuming, labour-intensive and invasive in children, serum creatinine based equations such as the Schwartz formula are frequently used to estimate GFR (eGFR). When renal function deteriorates, uremic retention solutes, other than creatinine, accumulate and contribute to the uremic syndrome. We intended to evaluate whether eGFR is representative for various uremic toxin concentrations in children with different degrees of CKD.

METHODS
In 43 children (10.5±5.5 year, 79,1% boys) with CKD stage 1-5, the association between eGFR (Schwartz) and the natural logarithm of serum concentration of representative small solutes [uric acid (UA), urea, creatinine], middle molecules [$\beta_2$microglobuline (b2M), complement factor D (CfD)], and protein-bound solutes [p-cresylglucuronide (pCG), hippuric acid, indole acetic acid (IAA), indoxyl sulfate (IS), p-cresylsulfate (pCS), and 3-carboxy-4-methyl-5-propyl-furanpropionic acid (CMPF)] were evaluated using linear regression.

RESULTS
The mean eGFR was 45.07±23.98 mL/min/1.73m^2 (range 4.88 to 102.71). The explained variance (R^2) of eGFR was the highest (0.80) for creatinine and CfD, followed by b2M (0.68) and urea (0.63). In contrast, R^2 was low (0.20-0.40) for UA, total pCG, free and total HA, free and total IAA, free IS and free pCS. Even lower R^2 (<0.20) were found for free pCG, total IS, total pCS and CMPF.

CONCLUSIONS
The concentration of protein-bound uremic toxins were extremely poor related to eGFR. This is an important observation as protein-bound uremic toxins like total IS and total pCS have proven pathophysiological effects and exert important toxicity in adults with CKD. In contrast, eGFR seems to be a good indicator for urea and middle molecules such as b2M and CfD.

ABSTRACT NUMBER 11

CONCENTRATIONS OF REPRESENTATIVE UREMIC TOXINS IN A HEALTHY VERSUS UREMIC PEDIATRIC POPULATION

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OBJECTIVE
A myriad of different uremic toxins accumulate in the body in chronic kidney disease (CKD). In children, this accumulation is responsible for a complex multisystem disorder characterized by growth failure, protein-energy wasting, cardiovascular and mineral bone disease. We aimed at determining serum concentrations of representative uremic toxins in healthy and CKD children.

METHODS
In 25 healthy children (controls C) and 46 CKD children stage 1 to 5D (U), serum concentrations of representative small solutes [uric acid (UA), urea, creatinine], middle molecules ($\beta_2$microglobuline, complement factor D), and protein-bound solutes [p-cresylglucuronide, hippuric acid (HA), indole acetic acid (IAA), indoxyl sulfate (IS), p-cresylsulfate (pCS), and 3-carboxy-4-methyl-5-propyl-furanpropionic acid (CMPF)] were determined. For each uremic toxin, ratios of the medians ($M_{U/C}$) and of the interquartile ranges ($IQ_{U/C}$) were calculated.

RESULTS
The healthy and CKD children (of which 4 on dialysis) were 9.0±4.1 and 10.4±5.5 year (p=0.354), 52% and 78% boys (p=0.032), respectively. The CKD children not on dialysis had an estimated glomerular filtration rate of 46.0±23.4mL/min/1.73m^2 [range 10.6 to 102.7]. Concentrations of all studied uremic toxins were significantly higher in the U compared to the C group. $M_{U/C}$ ranged from 1.7 for UA to 23 for total IAA with values > 3 for total HA, total and free IS, free pCS, and total CMPF. All $IQ_{U/C}$ were larger than 1 (range from 2.4 for UA to 16.7 for free IS), indicating larger interindividual variability in the U versus C group.

CONCLUSIONS
This is the first study in the pediatric population revealing that in CKD versus healthy children concentrations of representative uremic toxins are 1.7-23 times higher. Further research is needed to evaluate associations between elevations of serum concentrations of the different toxins and clinically relevant outcomes.

ABSTRACT NUMBER 12

MYELOID HEME OXYGENASE-1 CONTROLS RENAL ISCHEMIA REPERFUSION INJURY

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OBJECTIVE. Renal ischemia reperfusion injury (IRI) is a leading cause of acute kidney injury. Compelling evidence exists that the stress-responsive enzyme heme oxygenase-1 (HO-1) mediates protection against IRI. HO-1 is ubiquitously inducible but the specific protection of myeloid HO-1 remains undefined. The aim of this study was to understand the role of the myeloid HO-1 in the natural control of renal IRI and after pharmacological induction of HO-1 by hemin.

MATERIALS AND METHODS. Myeloid HO-1 KO mice (HO-$1^{M\text{-}KO}$ mice), specifically deficient for HO-1 in myeloid cells, littermate (LT) control mice, and wild-type (WT) C57/Bl6 mice underwent bilateral renal IRI for 26 min. Mice were sacrificed 24h after surgery. WT mice were treated with hemin 5 mg/kg or saline 24h prior ischemia. Renal IRI was evaluated by plasma creatinine and histology. Renal inflammation, leukocytes influx and oxidative stress were assessed by ELISA, immunostaining and nitrotyrosine levels respectively. HO-1 expression in renal leukocytes was assessed by FACS.

RESULTS. Renal damages were worsened in HO-$1^{M\text{-}KO}$ compared to LT mice (i.e., higher creatinine levels and tubular necrosis). Intra-renal cytokine expression (i.e., IL-6, MCP-1 and KC), oxidative stress and neutrophil/macrophages influx were also enhanced. In WT mice, the protective effect of hemin pretreatment (i.e., plasma creatinine levels, tubular necrosis) was associated with a specific upregulation of HO-1 within myeloid $CD11b^{+}F4/80^{lo}$ renal cells before IRI and a higher proportion of these HO-1 producing myeloid cells upon IRI. A subsequent dampened renal inflammation was found in hemin-treated mice (i.e. IL-6, MCP-1 and KC).

CONCLUSION. Myeloid-derived HO-1 in $CD11b^{+}$ $F4/80^{lo}$ renal cells significantly controls the magnitude of renal IRI. Targeting myeloid HO-1 might represent a promising approach for preventing acute kidney injury in different clinical settings.

ABSTRACT NUMBER 13

THE UPTAKE OF 18F-FDG BY RENAL ALLOGRAFT IN KIDNEY TRANSPLANT RECIPIENTS IS NOT INFLUENCED BY RENAL FUNCTION

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OBJECTIVE. ^{18}F-Fluorodeoxyglucose (^{18}F-FDG) positron-emission tomography coupled with computed tomography (PET/CT) imaging has been recently proposed as a non-invasive tool for the diagnosis of renal allograft acute rejection (AR) in kidney transplant recipients (KTR). Still, the influence of kidney function on the renal graft uptake of ^{18}F-FDG remains debated.

METHODS. We retrospectively identified all KTR who underwent at least one ^{18}F-FDG PET/CT between January 2010 and December 2015. KTR with documented pyelonephritis or AR, as well as patients under chronic hemodialysis, were excluded. Medical, biological and technical parameters were extracted from a prospective database. Estimated glomerular filtration rate (eGFR) was assessed using chronic kidney disease (CKD)-EPI equation. Mean standardized uptake values (SUVmean) of renal graft cortex and aorta were measured in 4 and 1 volumes of interest, respectively. Spearman's rank correlation coefficient (ρ) and analysis of variance (ANOVA) were performed.

RESULTS. Eighty-two KTR aged of 58 ± 13 underwent ^{18}F-FDG PET/CT for tumor staging (n=46), suspected infection (n=11) or fever of unknown origin (n=25). Male-to-female ratio was 1.4. Mean eGFR was 50 ± 19 ml/min/1.73m² [range: 20.7; 94.4], including CKD stage 1 (n=3), stage 2 (n=21), stage 3a (n=20), stage 3b (n=29) and stage 4 (n=9). PET/CT imaging was performed within 67 ± 15 min following injection of 3.7 ± 0.6 MBq/kg of ^{18}F-FDG. Mean glycemia at the time of injection was 113 ± 34 mg/dl. Mean kidney and aorta SUVmean were 1.8 ± 0.2 and 1.7 ± 0.3, respectively. No significant correlation was observed between eGFR and kidney SUVmean (*ρ, 0.119; p, 0.28*) or aorta SUVmean (*ρ, -0.144; p, 0.20*) considering the whole cohort. ANOVA showed no difference of kidney (*p, 0.62*) and aorta (*p, 0.85*) SUVmean between CKD groups. Mean coefficient of variation (on the basis of kidney SUVmean of >3 consecutive ^{18}F-FDG PET/CT in 15 patients with no significant change of eGFR) reached 13.05%.

CONCLUSION. Our data suggest that the uptake of ^{18}F-FDG by renal allograft within an hour *post* injection is not significantly impacted by CKD.

ABSTRACT NUMBER 14

ADMINISTRATION OF THIRD-PARTY MESENCHYMAL STROMAL CELLS AT THE TIME OF KIDNEY TRANSPLANTATION: INTERIM SAFETY ANALYSIS AT ONE-YEAR FOLLOW-UP

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OBJECTIVE. Mesenchymal stromal cells (MSC) therapy has been suggested in kidney transplantation (KTx). We report on the 1-year follow-up of an open-label phase I trial using MSC at the time of KTx.

METHODS. On postoperative day 3 (D3), third-party MSC (~$2.0x10^6$/kg) were administered to 7 non-immunized first-transplant recipients from deceased donors, under standard immunosuppression (Basiliximab, Tacrolimus, MMF and steroids). No HLA matching was required for MSC donors. In parallel, 7 comparable KTx recipients were included as controls. Written informed consent was obtained from all participants.

RESULTS. No hemodynamic or immune-allergic side-effect was noted at the time of MSC injection. Still, 1 patient with a history of ischemic heart disease had a NSTEMI ~3h after MSC infusion. Four MSC patients presented with CMV reactivation within 165 ± 96 days *post* KTx, whereas 3 controls had positive polyoma-BK viremia within 92 ± 4d *post* KTx. Three MSC patients were affected by pneumonia within 269 ± 98d *post* KTx, whereas 3 controls had urinary infection within 48 ± 43d *post* KTx. No MSC engraftment syndrome was observed. At D14, eGFR in MSC and control groups was 47.1 ± 6.8 and 39.7 ± 5.9 ml/min, respectively (*p, 0.05*). At 1 year, eGFR in MSC and control groups was 43.1 ± 17.8 and 53.9 ± 13.4 ml/min, respectively (*p, 0.25*). At 3-month protocol biopsy, no rejection was evidenced in MSC or control patients. Later on, 1 acute rejection was diagnosed at D330 in 1 MSC patient. No biopsy-proven AR was noted in controls. Three patients developed anti-HLA antibodies against MSC (n=1) or shared kidney/MSC (n=2) mismatches.

CONCLUSIONS. MSC infusion was safe in all patients except one. Incidence of opportunist and non-opportunist infections was similar in both MSC and control groups. No MSC engraftment syndrome was documented. No difference in eGFR was found at 1 year *post* KTx. Putative immunization against MSC was observed in 3 patients.

ABSTRACT NUMBER 15

SMOKING HISTORY AND DELAYED GRAFT FUNCTION IN RENAL TRANSPLANT RECIPIENTS: AN OBSERVATIONAL COHORT STUDY.

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OBJECTIVE: Smoking is associated with unfavourable graft outcome in solid organ transplant recipients. It could possibly increase the risk of delayed graft function (DGF) through increased oxidative stress. We assessed whether a smoking history could affect the long term outcome in renal transplant recipients and whether there is an interaction with DGF.

METHODS: We included all consecutive adults undergoing a kidney transplantation between 1 January 2003 and 1 October 2015 at the Ghent University Hospital. We recorded outcomes until 31 October 2015. We used Kaplan-Meier and multivariate Cox proportional hazard analysis to examine the relationship between baseline smoking status and the incidence of 10-year graft loss with and without censoring for death. In a secondary analysis, we compared estimated glomerular filtration rate (eGFR) at year one, three and five after transplantation between adults with and without a previous smoking history.

RESULTS: Of all 1013 transplant recipients, the mean age was 52±13 years; 637 (63%) were male and 172 (17%) had diabetes mellitus at the time of transplantation. In comparison with non-smokers, former smokers had an 82% higher hazard of graft loss (aHR 1.82; 95%CI 1.33 to 2.48; p<0.001) and a 143% higher hazard of death-censored graft loss (aHR 2.43; 95%CI 1.48-3.96; p<0.001). The average eGFR in former smokers was 5 mL/min/1.73m^2 lower than in non-smokers three years (56±18 vs. 61±19; p=0.004) and 7 mL/min1.73m^2 lower five years after transplantation (55±19 vs. 62±19; p<0.001).

CONCLUSION: A history of smoking is associated with unfavourable graft outcome independent from DGF.

ABSTRACT NUMBER 16

EVOLUTION OF RENAL FUNCTION IN A LARGE COHORT OF HIV POSITIVE PATIENTS TREATED WITH HIGHLY ACTIVE ANTIRETROVIRAL THERAPY: A RETROSPECTIVE COHORT STUDY

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OBJECTIVE Patients infected with HIV have an increased risk to develop acute or chronic renal failure by direct pathogenic effects of the virus and nephrotoxicity of antiretroviral drugs.
The purpose of the present study was to investigate the evolution of the glomerular filtration rate (GFR) during long-term follow up in a large cohort of patients treated with highly active antiretroviral therapy and to determine the impact of renal insufficiency on mortality.

METHODS Retrospective cohort study of 2044 adult HIV positive patients with free access of highly active antiretroviral therapy followed at the Infectious Disease Department of the CHU-Saint Pierre in Brussels between 1/1/2005 and 27/02/2015. Prospectively collected routine clinical and laboratory data were extracted from a dedicated clinical database. Chronic renal failure was defined as a persistent reduction of MDRD GFR to less than 60ml/min/1.73m2. Evolution of renal function over time was assessed by calculating the slope of eGFR during follow-up. Patient survival was estimated by the Kaplan Meier method and modelled by Cox regression.

RESULTS Among the 2044 patient (average age 37.6 years, 63% male, 48% African, 47% Caucasian) 1651 (81%) had a baseline eGFR≥90, 352 (17%) between 60 and 90 and 41 (2%) <60 ml/min/1.73m2. A baseline eGFR <60 mL/min/1.73m2 was associated with older age, African race, diabetes, hyperlipidaemia, hypertension, highly viral load and lower number of CD4 positive cells. Baseline eGFR <60 mL/min/1.73m2 was associated with a mortality hazard ratio of 7.9 (95% CI 3.3 to 18.7; P<0.0001) as compared to normal renal function, but only 53 patients died during follow-up, precluding multivariate analysis. In the overall cohort eGFR decrease from 110.04±28 to 95.4 4± 22.7 ml/min/1.73m2 during the 10 year follow-up and the proportion of patients with eGFR 60 to 90 mL/min/1.73m2 increase from 17.2 to 39.6 %.
Distribution in the evolution of renal function was heterogeneous with approximately one third of patients improving renal function, one third having stable eGFR and one third with rapid loss of renal function and an overall decrease from 125 to 85 ml/min/1.73m2 during the 10-year follow-up.

CONCLUSION Chronic renal failure grade 3 to 5 is rare in HIV positive patients starting follow-up and associated with classical risk factors and more severe HIV infection.
Approximately one-third of patients experiences rapid loss of renal function with an average reduction of eGFR by 40 ml/min over 10 years. These patients should benefit from early diagnostic evaluation and targeted interventions to prevent irreversible renal injury.

ABSTRACT NUMBER 17

HEMODIAFILTRATION WITH ENDOGENOUS REINFUSION OF ULTRAFILTRATE (HFR) VS HIGH-FLUX HEMODIALYSIS: DISCREPANCIES IN DEPURATION OF MIDDLE MOLECULAR WEIGHT PROTEINS

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OBJECTIVE: HemodiaFiltration with endogenous Reinfusion of ultrafiltrate (HFR) is a technique combining convection, adsorption and diffusion. It aims to improve the plasma removal of middle molecular weight proteins (MMWP) in comparison with conventional hemodialysis (HD). The aim of this study was firstly, to compare the respective plasma removal performances of HFR vs high-flux polyphenylene HD regarding MMWP of MW ranging from 12 kDa to 50 kDa and secondly, to compare the performances of two HFR systems (HFR-SUPRA and HFR-SYNCLEAR) differing from each other by the molecular mass cut-off of the convective filter.

METHODS: In a first longitudinal study (6 months), 26 adult patients with end-stage renal disease treated by conventional HD since at least 3 months (thrice weekly sessions of 3 to 4 hours) were equally randomized into 2 groups: HFR-SUPRA (cut-off 42 kDa) and high-flux HD (cut-off 30 kDa). The respective removal performances of each technique were evaluated by measuring the concentrations of each MMWP in the plasma before and after one session and also at baseline after 6 months of treatment. A second study compared the performances of one session of HFR-SUPRA vs HFR-SYNCLEAR (cut-off 50 kDa) in 14 patients.

RESULTS: Statistically significant reductions of plasma levels of β2M (22 vs 11 µg/ml, p = 0.003), IL6 (13 vs 3 pg/ml, p = 0.04), IL33 (25 vs 9 pg/ml, p = 0.003), and leptin (271 vs 158 ng/ml, p = 0.006) were observed after one session of HFR-SUPRA. Reduction rate of IL33 was better with HFR-SUPRA vs high-flux HD (66% vs 26 %, p = 0.003). Any statistically significant reduction of β2M, IL18, leptin or PAI-1 baseline plasma levels was observed after 6 months of HFR-SUPRA. Extraction rate by convection process was better with HFR-SYNCLEAR vs HFR-SUPRA only for IL18 (44.5 % vs 0.9 %, p = 0.0002) and IL33 (110 % vs 40 %, p = 0.009), both ILs which have β trefoil structure. The adsorption capacity (median [min-max]) of the cartridge was excellent for β2M (99 [97-99] %, PAI-1 (80.5 [0-99] %) and IL6 (75 [22-96] %) but not significant for IL18 and IL33.

CONCLUSION: HFR allows a better depuration of IL33 in comparison with high-flux HD. The low extraction rate of some MMWP by the convective filter is likely explained by the binding of these MMWP to large molecules such as soluble receptors, leading to the formation of big complexes unable to be extracted by the convective filter. The variable depuration performance of HFR regarding molecules of comparable MW may be explained by factors other than the size, such as molecular conformation, ionic charge, polarization and diffusion gradient.

ABSTRACT NUMBER 18

OUTCOME AFTER ARTERIOVENOUS FISTULA CREATION: A SINGLE CENTER EXPERIENCE FROM BELGIUM.

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AIM OF THE STUDY: Investigate primary and secondary functional patency of AV accesses created at the CHU Brugmann (Brussels, Belgium).

METHODS: We retrospective reviewed all hemodialysis patients treated at the CHU Brugmann dialysis unit between 01/01/2010 and 31/12/2013 for AV accesses created between 01/01/2009 to 31/12/2012. Patient characteristics and access-related data were recorded in a dedicated database. Patency rates were estimated using the Kaplan Meier method.

RESULTS: 297 patients were reviewed. 50 patients with 58 AV accesses (57 fistulas and 1 graft) created during the study period were included. 80% of patients were dialyzed by a central venous catheter at the moment of AV access creation and 28% had their AV access created before starting hemodialysis. 7% of AV accesses needed surgical and 21 % angiographic revision before first use, in 83% of cases to correct venous stenosis. 78% of all created AV accesses were succesfully used for dialysis.
9% of AV accesses needed surgical revision and 41% at least one angiographic revision after first use (89% due to venous stenosis). Four (7%) accesses developed thrombosis during follow up, which was successfully reversed in 3 episodes by systemic thrombolysis with urokinase.
Functional primary patency was 60 % at 12 months and 50 % at 24 months. The Kaplan-Meier estimate of functional secondary patency was 90% at 3 years after AV access creation.

CONCLUSIONS: In this cohort nearly 80% of fistulas were successfully used as vascular access and primary patency was in line with currently published evidence. The excellent secondary functional patency of AV fistulas is probably due to a policy of systematic follow up and aggressive treatment of access complications.

ABSTRACT NUMBER 19

A CURIOUS CASE OF RECURRENT CULTURE NEGATIVE PD PERITONITIS

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CASE PRESENTATION

We present the case of a 39 year old Iraqi woman. Her medical history consisted of ESRD of unknown etiology (for which she was in chronic hemodialysis treatment since Nov. 2014), and tricuspid valve endocarditis (for which she had undergone surgery in Feb. 2015). She was admitted to our hospital after having missed several dialysis sessions on her way to Belgium. In the next few days, she was diagnosed with open pulmonary tuberculosis for which she received triple therapy (isoniazid/rifampicin/ethambutol) for 2 months, followed by isoniazid/rifampicin for an additional 7 months.

She was switched from hemodialysis to peritoneal dialysis in nov. 2015, after completion of tuberculostatic therapy. Shortly after starting PD, she complained of persisting malaise, with low-grade fever and nocturnal sweating. Initial clinical examination was normal and cultures (blood, PD catheter exit-site and PD effluent) remained negative. However, on repeat clinical examination, a palpable supraclavicular lymphadenopathy was found. PET-CT scan highlighted several mediastinal and upper gastro-intestinal adenopathies as well as an active lesion in L2. A surgical biopsy of the supraclavicular lymph node showed necrotizing granulomatous lymphadenitis. Staining, PCR and cultures for M. tuberculosis all remained negative. Hence, immune reconstitution inflammatory syndrome was suspected and she was treated symptomatically with NSAID.

In Feb. 2016, she was admitted for PD peritonitis. Ciprofloxacin was started for an exit-site infection with S. marcescens. PD effluent culture and PCR for M. tuberculosis remained negative. IP treatment with vancomycin/ceftazidime was continued for 2 weeks, with good clinical result. However, within two weeks after completion of treatment, she is readmitted with a recurrent episode of peritonitis. By now, initial PD effluent culture shows growth of M. tuberculosis complex (day 21). Quadruple anti-tuberculous treatment was started, the PD catheter was removed, and the patient was switched to hemodialysis.

TUBERCULOUS PD PERITONITIS

Mycobacterial peritonitis is an infrequent cause of PD-related peritonitis. Suspicion is warranted in patients with a previous history of Tuberculosis, in case of relapsing culture-negative peritonitis, and/or prolonged symptoms despite antibiotic therapy. Diagnosis is often difficult and sometimes requires laparoscopic biopsy of the peritoneum to confirm the presence of acid-fast staining bacteria. Treatment protocols are similar to those for extra-pulmonary tuberculosis. Ethambutol should be avoided in end-stage renal disease, given the risk of optic neuritis. Necessity to remove the catheter is still an uncertain issue.

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ABSTRACT NUMBER 20

PROTECTIVE EFFECTS OF PISTACIA LENTISCUS SEED EXTRACT AGAINST CALCIUM OXALATE MONOHYDRATE INDUCED PROXIMAL TUBULAR INJURY

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OBJECTIVE: Calcium oxalate monohydrate (COM) is the major crystalline component present in kidney stones and its adhesion / internalization into renal proximal tubular cells results in tubular injury. Its intrinsic tubulotoxicity remains unclear. In Algeria, Pistacia lentiscus (PL) is widely used in nephrolithiasis prevention. The present study aimed to in vitro assess the potential nephroprotective effect of Pistacia Lentiscus Ethanolic Seed extract (PLES) on proximal tubular cells in response to the adhesion of COM crystals.

METHODS: Human Kidney [HK]-2 cells were incubated with and without COM (200 µg/ml) in the presence or absence of PLES (35 and 70 µg/ml). Cell viability was measured by the resazurine assay. The number of surviving cells was examined by an automated counter cell (Bio-Rad) and their morphology was microscopically captured. The expression of E-cadherin, a marker of structural integrity, was analyzed by PCR. The extracellular production of H2O2 was measured by ROS-Glo™ H2O2 Assay. The concentration of IL-6, a proinflammatory cytokine released in the supernatant, was measured by with enzyme-linked immunosorbent assay (ELISA).

RESULTS: COM added to HK-2 cells significantly decreased the number of cells. The resazurine assay showed a toxicity of COM on HK-2 cells which exhibited internalized crystals on microscopic examination. At both concentrations, PLES incubated with COM was able to increase the number and the viability of cells. As compared to controls, there was a decrease in the expression of E-cadherin 24h after incubation with COM, which was counteracted by PLES. Overproduction of H2O2 and IL-6 induced by COM was also inhibited by PLES.
Conclusion: These data confirm the tubulotoxicity of COM on the proximal tubular epithelial cell. The modification of cell number, viability, E-cadherin expression, H2O2 and IL6 production can be significantly reversed by PLES. The highest concentration of PLES did not result in any increased beneficial effect. This traditional herbal remedy merits to be further investigated regarding its beneficial effect in limiting nephrolithiasis complications.

ABSTRACT NUMBER 21

PREDICTING DEATH IN ELDERLY PEOPLE WITH OR WITHOUT ADVANCED CHRONIC KIDNEY DISEASE: A SYSTEMATIC REVIEW OF RISK PREDICTION MODELS.

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OBJECTIVE Counselling older people with advanced chronic kidney disease (CKD) on renal replacement therapy versus conservative care requires reliable estimates of an individuals' risk of death within a given time-frame. We aimed to explore the quality and generalizability of existing risk prediction models (RPMs) for estimating risk of death in elderly and/or frail people with and without CKD.

METHODS We systematically searched for models predicting death in people >65 years with or without CKD. We built on two previous high-quality systematic reviews, updated the searches in Medline, including English-language papers published from 11/2011 through 02/2016. Two reviewers appraised development and validation quality guided by the Charms checklist.

RESULTS: We found 23 studies including 31 RPMs. 17 models targeted elderly people in general, two specifically targeted people with CKD 3-5, and 12 models people with end-stage kidney disease. Quality of model development and validation procedures were highly variable, reporting was generally poor. Only one model was externally validated with a report that included adequate information on predictive performance. It was developed for predicting 5-year risk of death without ESKD in non-frail community dwelling elderly people, and showed good calibration (Hosmer-Lemeshow p=0.9) with moderate discrimination upon external validation (c-statistic 0.69; 95% CI 0.64 to 0.74).

CONCLUSION: We found only one externally validated model for predicting death without ESKD in older non-frail people which showed only moderate discrimination. Other models lack external validation. Rather than building new models, further research should focus on external validation or recalibration of existing models.

ABSTRACT NUMBER 22

BALKAN ENDEMIC NEPHROPATHY STUDIED IN A METABONOMIC CONTEXT: PRELIMINARY RESULTS.

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OBJECTIVE. Aristolochic acid (AA), is the common term defining the mixture of structurally related nitrophenantrene carboxylic acid derivatives produced by plants from Aristolochiaceae family and currently used as traditional remedies worldwide. Even if severe adverse effects including chronic kidney disease and urothelial cancer have been recognized, leading to their official ban in many countries, they are still available over-the-counter and on the web. A few years ago, AA was recognized as the environmental causal factor of Balkan endemic nephropathy (BEN), a chronic interstitial nephropathy affecting thousands of individuals in Balkan countries. Besides 25,000 subjects diagnosed, more than 100,000 are suspected of being exposed to AA and at risk of developing the renal disease and related urothelial cancer.

METHODS. The spectroscopic analysis of small molecules fluctuating in biofluids according to the physiopathological status of an individual, is called “metabonomic”. Such analysis generates spectral profiles in which the subsets of metabolites constitute functional fingerprints. These ones can be further associated with specific pathologies and are very useful in many clinical applications. In this preliminary study, urine samples from BEN patients were analyzed by 1H nuclear magnetic resonance (1H NMR) in order to identify potential biomarkers of BEN.

RESULTS. The multivariate analysis of the 1H NMR spectra allowed us to classify patients according to the severity of renal failure. Moreover, the study of increased and decreased urinary metabolites suggested clues for the mechanism of disease development, including the most affected areas of the kidney. A higher urinary concentration of citrate, creatinine, glycine and hippurate were found as markers of a healthy profile. A decreased concentration of these metabolites in the presence of urinary phenylalanine was associated with a moderate stage of renal dysfunction, whereas the additional increased urinary concentration of glucose indicated a more severe stage. Taken together, these biomarkers could be easily and rapidly used to predict future “at risk” BEN patients. Such analyses performed on larger cohorts of « diseased » and « at risk » BEN individuals are now on the way.

CONCLUSION. The metabonomic analysis of urine samples from BEN subjects allowed to identify several urine biomarkers that can be useful to define early stages of the disease. The simplicity, safety and non-invasive collection of urine samples makes metabonomic approach a very interesting screening and diagnostic tool.