LONGITUDINAL EVALUATION OF CARDIOVASCULAR RISK AFTER PEDIATRIC KIDNEY TRANSPLANTATION

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Objective: Children with chronic kidney disease (CKD) carry an increased cardiovascular risk. Cardiovascular death is the second leading cause of death in children after renal transplantation. The 4C-T (Cardiovascular Comorbidity in Children with CKD and Transplantation) study evaluates cardiovascular target organ damage longitudinally in children prior to and after renal transplantation.

Design and method: The multicenter, prospective, observational 4C study enrolled 736 children aged 6 to 17 years with estimated GFR <40 ml/min/1.73 m² at 55 Pediatric Nephrology centres from 12 European countries. Of these, 226 have started renal replacement therapy (RRT) and entered the 4C-T sub-study. At annual study visits, the morphology and function of the heart and large arteries were monitored by noninvasive methods.

Results: 176 of the 226 patients on RRT had at least one visit after RRT start and were included in this analysis. 70 patients had started dialysis and 106 received a transplant. 62% of the patients were transplanted pre-emptively. Overall patients carried a higher cardiovascular risk compared to the age-matched general population as documented by elevated age-adjusted aortic pulse wave velocity (PWV) and carotid intima-media thickness (IMT). Factors determining PWV, IMT and left ventricular mass index (LVMi) were analysed using mixed longitudinal modelling (table).

Conclusions: Our data is consistent with the hypothesis that transplantation lowers cardiovascular risk. Mixed modeling allowed to decipher the positive effect of transplantation from interfering cardiovascular risk factors such as hypertension, hypercholesterolemia and PTH.

Table: Mixed longitudinal model for PWV, IMT and LVMi

<table>
<thead>
<tr>
<th>Effect</th>
<th>Dialysis</th>
<th>Tx after Dialysis</th>
<th>Preemptive vs Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP</td>
<td>0.04684</td>
<td>-0.0264</td>
<td>0.04684</td>
</tr>
<tr>
<td>PTH</td>
<td>0.009564</td>
<td>0.003614</td>
<td>0.009564</td>
</tr>
<tr>
<td>Male gender</td>
<td>-0.4157</td>
<td>0.0019</td>
<td>-0.3076</td>
</tr>
</tbody>
</table>

Conclusion: Our data is consistent with the hypothesis that transplantation lowers cardiovascular risk. Mixed modeling allowed to decipher the positive effect of transplantation from interfering cardiovascular risk factors such as hypertension, hypercholesterolemia and PTH.

LONGITUDINAL OUTCOME AFTER ANGIOPLASTY IN PATIENTS WITH RENAL ARTERY STENOSIS AND HIGH RESISTIVE INDEX

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Objective: The benefit of revascularization for renal artery stenosis is currently unclear. A number of prospective, randomised studies showed no advantage of revascularization compared with interference of pharmacological drugs. A predictor of a more positive response to interventional treatment is urgently needed. We have shown that patients with a high resistive index (RI > 80) by Doppler ultrasonography have inferior outcome after interventional revascularization for renal artery stenosis. Here we obtained long-term follow up data from the original study collective and compared this to a matched group of recent patients with high resistive index which did not undergo revascularization but had improved medical therapy.

Design and method: We measured the renal RI with Doppler ultrasonography in segmental arteries of both kidneys. 131 patients underwent renal angioplasty, 35 of these had renal RI values > 80. A further group of 31 patients with RI > 80 and renal artery stenosis > 65% did not undergo angioplasty. The combined endpoint was > 50 percent decrease in eGFR, end stage renal failure, or death. Mean (± SD) follow-up was 8.8 ± 4 years.

Results: In patients with high RI (> 80), a decrease in renal function occurred in 74% patients after PTA and 77% without PTA compared to 19% of those with PTA and low RI. 71% and 52% of patients, compared to 17%, required dialysis, and 89% and 48% compared to 31% died (p<0.001 high RI compared to low RI). A total of 94% and 90% with high RI reached the combined endpoint as compared to 39% of those with low RI (multivariate relative risk 16, CI 3.7 to 68; P<0.001 high RI vs low RI).

Conclusions: Patients with renal artery stenosis and a high renal resistive index do not benefit from angioplasty in long-term follow up for renal and patient survival. Patients with high resistive index continue to suffer a poor prognosis even under improved medical therapy.

EFFECT OF PA21, A NEW IRON-BASED PHOSPHATE BINDER ON FIBROBLAST GROWTH FACTOR 23 (FGF23) AND VASCULAR CALCIFICATIONS IN UREMIC RATS

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Objective: Cardiovascular disease is a major cause of mortality in patients with chronic kidney disease (CKD). Elevated serum phosphate and FGF23 are associated with cardiovascular disease in patients with CKD. Current therapy focuses on decreasing serum phosphorus using phosphate binders. PA21 is a new iron-based phosphate binder. Few studies have analysed how to suppress FGF23 up-regulation using phosphate binders.

To evaluate the effects of PA21 compared with other phosphate binders as lanthanum phosphate binder. Few studies have analysed how to suppress FGF23 up-regulation using phosphate binders.

Follow-up (yrs) 0 2 4 6 8 10 12 14
Event-free survival 0.0 0.2 0.4 0.6 0.8 1.0

Conclusion: Patients with renal artery stenosis and a high renal resistive index do not benefit from angioplasty in long-term follow up for renal and patient survival. Patients with high resistive index continue to suffer a poor prognosis even under improved medical therapy.
califications of thoracic aorta were significantly decreased by the three phosphate binders to a similar extent. PA21 was more efficient than lanthanum carbonate to prevent califications in the upper part of the thoracic aorta.

Conclusions: PA21 was as effective in the control of hyperphosphatemia, secondary hyperparathyroidism and vascular califications as La and Se. The role of FGF23 as a potential factor of calification needs to be confirmed.

1D.09 APPLICABILITY OF MEASUREMENT OF RENAL PERFUSION USING 1.5 TESLA MRI ARTERIAL SPIN LABELLING

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Objective: Renal perfusion is a key parameter of kidney function and the decrement of renal perfusion is a marker of target organ damage caused by hypertension. Detecting these changes in renal perfusion could help to manage antihypertensive therapy and evaluate patient prognosis. Measurement of renal perfusion by MRI with arterial spin labelling (ASL) is a non-invasive and non-time-consuming method without the need to inject any contrast agent. This study examined reproducibility of renal perfusion measured by 1.5 Tesla MRI.

Design and method: Renal perfusion was measured by ASL technique using an 1.5 Tesla MRI scanner. Subjects were scanned 3 times at two different days in an interval of two weeks to assess the test-retest reproducibility. Renal perfusion was automatically calculated for the cortex and medulla of the kidney by dedicated software.

Results: 14 patients were included with mean age 48.9 ± 12.7 and mean office blood pressure 132 ± 16/82 ± 10 mmHg and estimated glomerular filtration rate> 60 ml/min/1.73.m². The change of the mean total, cortical and medullary renal perfusion from the first examination to the second examination was 0.37 ± 130.62 ± 180.00.00 ± 12 ml/min/100 g kidney weight (p = 0.915) or 0.896 (p = 0.998), respectively. There was also no significant difference between the three renal perfusion measurements at one time point. For clinical trials these data indicate that to detect a 5% (10%) difference of cortical renal perfusion due to an intervention (vs placebo) only 38 (14) patients are required in face of the observed standard deviation for the change in renal perfusion.

Conclusions: The intra and inter-session reproducibility of cortical renal perfusion assessed by MRI ASL. 1.5 Tesla is excellent and small study cohorts can be used for examination of renal perfusion.

1D.10 PREDICTORS AND OUTCOMES OF CONTRAST-INDUCED ACUTE KIDNEY INJURY IN PATIENTS WITH PRIMARY PERCUTANEOUS INTERVENTION

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Objective: The incidence of contrast-induced acute kidney injury (CI-AKI) is rising due to increased use of coronary angiography and percutaneous coronary intervention (PCI). Patients undergoing primary PCI are at high risk of CI-AKI, a complication that negatively affects outcomes. The aim of the study was to evaluate the incidence, predictors and outcomes of CI-AKI in patients with ST-segment elevation myocardial infarction (STEMI) and primary PCI.

Design and method: 216 patients with STEMI and primary PCI (143 male, 64 ± 13 years (M ± SD), arterial hypertension 90%, previous myocardial infarction 27%, diabetes mellitus 21%, known chronic kidney disease 7%, anemia 14%, heart failure 62%, left ventricular ejection fraction (LV EF) 44 ± 15%) were examined. CI-AKI was defined using 2012 KDIGO Guidelines. Mann-Whitney test was performed. P < 0.05 was considered statistically significant.

Results: 20% of patients developed CI-AKI. Stages 1 and 2 of CI-AKI were found in 10 vs 41 patients, respectively. The incidence of contrast-induced acute kidney injury (CI-AKI) is significantly higher in patients with higher baseline serum creatinine (p < 0.05), higher contrast medium volume (p < 0.05), higher rate of hypertension (p < 0.05), higher rate of hyperphosphatemia (p < 0.05), higher rate of diabetes mellitus (p < 0.05), higher rate of heart failure (p < 0.05), higher rate of left ventricular dysfunction (p < 0.05) and higher rate of therapy with nephrotoxic antibiotics (p < 0.05). Patients with CI-AKI had higher risk of 30-days mortality (10 vs 3%, p < 0.05) and similar rate of 6 months rehospitalizations (66 vs 46%, p = 0.05).

Conclusions: CI-AKI in patients with STEMI and primary PCI developed in 20% of cases, predominantly in first 48 hours after PCI. CI-AKI was associated with higher rate of CKD, therapy with nephrotoxic drugs, multivessel coronary damage, higher baseline serum creatinine, CVA/GRF. CI-AKI had negative impact on 30-days mortality.

1D.11 RENAL MICROVASCULARITY AND RENIN SECRETION IN HUMANS WITH MULTIFOCAL RENAL ARTERY FIBROMUSCULAR DYSPLASIA

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Objective: Although fibromuscular dysplasia (FMD) is the second commonest cause of renovascular hypertension, knowledge on renal microvasculature and renin-angiotension system activity in kidneys with FMD are scarce. Given the fairly good results of revascularization, we hypothesized that renal microvasculature is intact in kidneys with FMD.

Design and method: In 58 patients with multifocal renal artery FMD (off medication) we selectively measured mean renal blood flow (MRBF) in both kidneys using the 153Xenon-washout-method. Blood samples were taken from the aorta and both renal veins to determine renin secretion rate (RSR) and creatinine-extraction (a proxy for glomerular filtration) for each kidney (both calculated as venous-arterial difference*renal plasma flow). Hypertensive patients without renovascular abnormalities (essential hypertension, EH, matched for age, gender, and dietary sodium intake (using 24 h urinary sodium excretion as a proxy) served as controls in a 1:2 ratio.

Results: MRBF was comparable between FMD and EH (Figure). In EH but not in FMD. MRBF was significantly lower in the left kidney as compared to the right (*p < 0.001). Although a wide variation was observed, we found that systemic renin levels were somewhat higher in FMD as compared to EH (median 19.6 (interquartile range 12.0-35.2) vs. 12.1 (8.4-19.9); p < 0.001), but without differences in RSR per kidney (Figure). Creatinine-extraction was also comparable between FMD and EH. In unilateral FMD, no differences were found between the affected and non-affected kidney with regard to MRBF, RSR, or creatinine-extraction (left column). MRBF was associated with 24 h urinary sodium excretion in FMD (Beta 0.357; p = 0.015), but not in EH.

Conclusions: MRBF and creatinine-extraction in kidneys with FMD is comparable to EH and to the unaffected kidney in patients with unilateral FMD, indicating that renal microvascular function is preserved in kidneys with FMD. The association between MRBF and sodium intake supports this hypothesis. Our findings that