

Evaluation of Kidney Injury Markers in Children, Undergoing Open Heart Surgery

*Jekabs Krastins¹, Karina Mahlina², Mikelis Birznieks³,
Dagne Gravele⁴, Diana Amerika⁵, Aigars Petersons⁶,
Aivars Petersons⁷, Renars Erts⁸*

¹ Children's Clinical University Hospital, Clinic of Anesthesiology and Intensive Care, Latvia

² Rīga Stradiņš University, Department of Paediatrics, Latvia

³ University of Latvia, Faculty of Medicine

⁴ Children's Clinical University Hospital, Clinical and Biochemical Laboratory, Latvia

⁵ Pauls Stradins Clinical University Hospital, Renal Transplants Centre, Latvia

⁶ Rīga Stradiņš University, Department of Paediatric Surgery, Latvia

⁷ Rīga Stradiņš University, Department of Internal Diseases, Latvia

⁸ Rīga Stradiņš University, Department of Physics, Latvia

Introduction. Acute kidney injury (AKI) is a serious complication in the perioperative period, and is consistently associated with increased morbidity and case fatality rate. This has been best researched in the cardiac surgery setting where it has been shown that up to 52% of patients exposed to cardiopulmonary bypass (CPB) will develop AKI, with 2–18.9% requiring renal replacement therapy (RRT). Depending on the criteria used to define AKI and the postoperative period studied, mortality ranges from 1% to 30% although this is consistently higher, approaching 80%, if RRT is required.

Aim, Material and Methods. The aim of the study was to evaluate perioperative expression of various kidney injury markers and to establish their sensitivity, specificity and cut-off values for AKI in children after open heart surgery. During 2012–2015, we conducted prospective uncontrolled cohort study, 92 children with various congenital heart lesions undergoing CPB were enrolled. Serum creatinine (SCr) level was determined by Jaffé's method (Cobas 6000 analyser, Roche), serum Cystatin C (CysC) was determined by particle-enhanced nephelometric immunoassay, urine NGAL was determined by ARCHITECT system (Abbott Diagnostics, Illinois, USA).

Results. AKI developed in 42 patients (45.6%) by meeting at least KDIGO stage I criteria (with SCr rise by more than 50% from the baseline). 38 patients comply with the first stage of AKI, 2 with second stage AKI, and 2 patients with third stage, according to KDIGO classification and staging system. One patient having severity stage II and two patients having severity stage III of AKI required initiation of RRT, using peritoneal dialysis. Two patients from the RRT group survived, one died. Median intraoperative urine output was 2.32 ml/kg/h (range from 0.42 < 5.87 ml/kg/h). Median CPB time was 163 min., median aortic cross-clamping time was 97.9 min., cooling during CPB to 29.5 °C. The diagnosis of AKI using SCr was delayed by 48 hours after CPB. In contrast, maximum increase in urine NGAL levels was 400-fold within 12 hours after CPB in patients having AKI. Mean level of urine NGAL in the sample collected 12 hours after CPB was 276.87 ± 404 ng/ml. In the group of patients with intact renal function, the corresponding level of NGAL was 64.84 ± 70.07 ng/ml ($p < 0.05$). At 12 hours after CPB AUC-ROC characteristic curve of NGAL was 0.968, sensitivity was 0.982, and specificity was 0.98 for a cutoff value of 50 ng/ml. Plasma CysC has maximum expression at 24 hours after CPB with mean level of 1.3 ± 0.44 mg/l in AKI group vs. 0.89 ± 0.25 mg/l in no-AKI group, ($p < 0.05$). AUC-ROC of CysC at 12 hours after CPB was 0.837 (95% CI 0.724–0.950); $p < 0.05$). Mean fluid balance (FB) on the first postoperative day in no-AKI patients was 3.78 ± 4.56 ml/kg vs. 54.14 ± 7.75 ml/kg in AKI patients ($p < 0.001$).

Conclusions. AKI is a frequent complication after open heart surgery in children with congenital heart lesions. Renal tubular injury marker – urinary NGAL – has maximum expression at 12 hours after CPB with high sensitivity and specificity. Renal glomerular filtration marker – plasma CysC – has maximum expression at 24 hours after CPB with high sensitivity and specificity. FB is a sensitive marker of kidney dysfunction. FB on the first postoperative day has statistically significant difference between AKI patients (54.14 ml/kg) vs. 3.78 ml/kg in patients with intact kidney function (AUC = 0.84; $p = 0.0011$).