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# Analysis of risk factors and outcomes of acute kidney injury in young children after cardiac surgery

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**ABSTRACT: The aim of this study was to analysis of risk factors and outcomes of acute kidney injury (AKI) in young children with congenital heart disease (CHD) after cardiac surgery. The study included 137 young children with CHD after various types of cardiac surgery. The stages of AKI and indications for peritoneal dialysis (PD) were determined based of Kidney Disease: Improving Global Outcomes (KDIGO) guidelines. The incidence of AKI in young children in the general group was 40.9% (n=56). Stage 1 AKI was diagnosed in 21.9% (n=29) of patients, stage 2 AKI in 12.4% (n=17), and stage 3 AKI in 7.3% (n=10) of patients. Peritoneal dialysis was performed in 11.7% (n=16) of children. The incidence of AKI development after radical correct transposition of the great vessels (TGV) was 55.5% (n=5), truncus arteriosus (TA) was 100%, pulmonary atresia (PA)=25%, tetralogy of Fallot (TF)=38.1%, total anomalous pulmonary vein drainage (TAPVD)=60%, partial anomalous pulmonary vein drainage (PAPVD)=37.5%, atrioventricular canal (AVC)=44.4%, double outlet of main vessels from the right ventricle (DOMV from the RV)=60% , interventricular septal defect with high pulmonary hypertension (VSD)=21.6%, and combined operations was 46.6%. The need for PD after TGV correction was 22.2% (n=2), after TA=100%, after TF=33.3%, after TAPVD=20%, after AVC=11.1%, after VSD=1.9%, and after combined operations was 13.3%. Risk factors for AKI in young children were: younger age, initial heart failure, type of operation, prolonged cardiopulmonary bypass (CPB) and aortic clamping (AC), low cardiac output syndrome, inotropic and vasopressor therapy, hyperlactatemia. The development of AKI led to increased length of stay in the intensive care unit, overall hospitalization and infant mortality.**

**KEYWORDS:** **Acute kidney injury, Children, Risk factors, AKI outcomes, Peritoneal dialysis.**

## INTRODUCTION

AKI is a common and very serious complication in pediatric cardiac surgery, which allows confident prediction of treatment results [1]. This is a clinical syndrome characterized by a sharp decrease in kidney function over several hours or days. According to the KDIGO (Kidney Disease: Improving Global Outcomes) criteria, the diagnosis of AKI and the severity of these lesions are based on changes in serum creatinine levels and urine output. Progression in the severity of AKI increases the risk of postoperative complications, death, or the need for renal replacement therapy (RRT) [2, 4, 5]. According to the literature, after cardiac surgery in children, the incidence of AKI reaches 42%, with the need for dialysis in 1–17% of patients and mortality from 20 to 100% [3, 7–9]. At the same time, young children, especially newborns, are more predisposed to the development of AKI due to the immaturity of the nephrons, the difficulties of cardiac surgical correction and often prolonged CPB [16, 17-19]. Particular importance is the early initiation of RRT in children after correction of CHD [20, 21]. One of the methods of this therapy is peritoneal dialysis (PD). Peritoneal dialysis is a safe and relatively inexpensive type of RRT, widely used in the immediate postoperative period and is used, if necessary, in 8% - 25% of cases with AKI [10, 13]. Despite improvements in the quality of treatment of this disease in intensive care units, the mortality rate has not changed significantly over the past three decades and remains still high [22-25]. Therefore, the problem of assessing the risk of development and outcomes of AKI remains relevant.

The purpose of the study was to analysis of risk factors and outcomes of AKI in young children after cardiac surgery using one of the type of RRT - PD.

## MATERIALS AND METHODS

The prospective study included 137 young children (91 boys and 46 girls) aged 0.1-3.2 years (median=1.6) who underwent surgical correction of transposition of the great vessels (TGV), truncus arteriosus (TA), pulmonary atresia (PA), tetralogy of Fallot (TF), total anomalous pulmonary venous drainage (TAPVD), partial anomalous pulmonary venous drainage (PAPVD), atrioventricular canal (AVC), double origin of the great vessels from the right ventricle (DOGV from the RV), ventricular septal defect (VSD) with high pulmonary hypertension, combined operations from January 2018 to June 2022. The operations were performed at the Republican Specialized Scientific and Practical Medical Center for Surgery (RSSPMCS) named after Academician V. Vakhidov (Tashkent, Uzbekistan) using CPB. Patients who underwent surgery for emergency reasons, with symptoms of decompensated multiple organ failure, congenital kidney diseases, urological pathology, children undergoing program hemodialysis before surgery, as well as patients with incomplete information from the medical history were excluded from the study.

The patients are divided into two groups. The group without AKI (AKI-) included all those who underwent open-heart surgery and did not have renal dysfunction in the early postoperative period. The group AKI+ consisted of patients who developed AKI to varying degrees in the postoperative period. AKI was diagnosed based on KDIGO guidelines [16]. According to the KDIGO Clinical Practice Guidelines on AKI published in 2012, the following stratification of stages of AKI was given in Table 1, where several criteria were taken into account [6].

**Table 1.** Stages of AKI (KDIGO, 2012)

| Stages | Plasma creatinine | Urine output |
|---|---|---|
| 1 | 1.5-1.9 times the baseline or increase in | <0.5 ml/kg/hour over 6-12 hours |
| 2 | 2.0-2.9 times higher than baseline | <0.5 ml/kg/hour for >12 hours |
| 3 | 3.0 times baseline or increase to <0.3 ml/kg/hour in >24 hours >4.0 mg/dl (≤353.6 mcmol/L) or initiation of RRT or in patients <18 years of age, decrease in estimated GFR to <35 ml/min/1.73m$^2$ | <0.3 ml/kg/hour for >24 hours or anuria for >12 hours hours |

The decision to initiate PD was made not only on the basis of plasma urea and creatinine values, but, to a greater extent, on the basis of predicted low cardiac output, high doses of catecholamines, as well as assessment of the dynamics of laboratory results and comprehensive analysis of the clinical situation as a whole [17].

All children received standard anesthesia according to the department's protocol. CPB was performed after administering a calculated dose of heparin, on roller pumps with a perfusion coefficient of 0.25-1.40 l/m2/min, in hypothermic mode (venous blood temperature within 24-33°C). Blood pressure was maintained at 30-40 mm Hg. Heparin-coated oxygenators and lines were used.

After completion of cardiac surgery, all patients were transported to the cardiac intensive care unit, where appropriate standard intensive care protocols were applied. Monitoring in the cardiac intensive care unit included: invasive blood pressure, central venous pressure, gas and electrolyte compositions of arterial and venous blood, monitoring of general and biochemical blood tests, taking into account creatinine levels at least 1 time/day. Hourly monitoring of diuresis was carried out. On average, after 168 hours - 240 hours, children were transferred to the surgical department, where creatinine levels and GFR were monitored on average once a day with the relative possibility of progression of AKI. Diuresis was taken into account for 24 hours. If the postoperative period was smooth, blood was taken for biochemical analysis on days 3-5 and/or before the patient is discharged from the hospital.

### Statistical analysis

All clinical and laboratory data about patients are taken from the standard and electronic medical history (“1 C”). Statistical processing of the obtained results was carried out using the IBM® SPSS® StatisticsVersion 21 (21.0) program. All quantitative variables were checked for the type of distribution using the Kolmogorov–Smirnov test, graphically using quantile diagrams, as well as asymmetry and kurtosis indicators. The results are presented as median and quartiles of median (Q1; Q3). The obtained data with skewed distribution were compared using the intergroup nonparametric Mann-Whitney test. The results are presented with the level of significance (p).

Qualitative results were compared using Pearson's $\chi^2$ between-group test. Risks were assessed using stepwise multivariate logistic regression analysis. The latter was used to select a set of independent predictors included in the statistical model that influence the dependent variable (the likelihood of AKI in the postoperative period). The critical significance level was taken to be ≤0.05. Depending on the statistical significance and clinical importance, the identified risk factors are given a score. The results are presented as group size (n), proportion of the group (%), absolute value of Pearson's $\chi^2$ test, achieved level of significance (p), odds ratio (OR), 95% confidence interval (95% CI).

## RESULTS

The incidence of AKI in young children in the general group (n=137) was 40.9% (n=56). Stage 1 AKI was diagnosed in 21.9% (n=29) of children, stage 2 AKI in 12.4% (n=17), stage 3 AKI in 7.3% (n=10) of patients. PD was performed in 11.7% (n=16) of children (Table 2).

The incidence of AKI after radical corrections of TGV was 55.5% (n=5), TA as 100% (n=1), PA as 25% (n=2), TF as 38,1% (n=8), TAPVD as 60% (n=9), PAPVD as 37.5% (n=3), AVC as 44.4% (n=4), DOGV from the RV as 60% (n=6), VSD as 21.6 % (n=11), combined operations 46.6% (n=7). The need for PD after correction of TGV as 22.2% (n=2), after TA as 100% (n=1), after TF as 33.3% (n=5), after TAPVD as 20% (n=3), after AVC as 11.1% (n=1), after VSD as 1.9% (n=1), after combined operations was 13.3% (n=2). The results of the single-factor logistic regression analysis of the putative predictors of AKI are presented in Table 3. Table 4 presents data on the initial functional state of the kidneys and clinical course of the perioperative period in patients without signs of AKI and in the development of this complication.

The results of multivariate logistic regression analysis of predictors of the development of acute kidney injury in young children after cardiac surgery are presented in Table 5. The data presented above indicate that the risk factors for the development of AKI in infants are: young age, initial significant heart failure, cardiotonic support before surgery, complex type of surgery, prolonged BP and AC, low cardiac output syndrome, inotropic and vasopressor therapy in the early postoperative period, hyperlactatemia.

Younger age (less than 1 year) increases the odds of AKI by 36% (OR 1.36; 95% CI 1.12-1.47; p<0.01). The presence of heart failure (HF) events increases the likelihood of AKI by 12% (OR 1.12; 95% CI 1.08-1.22; p<0.01). The addition of catecholamines in tonic doses leads to an increase in the occurrence of AKI by 27% (OR 1.27; 95% CI 1.15-1.36; p<0.01). Depending on the type of performed cardiac surgery, the risk of developing AKI increases by 25% (OR 1.25; 95% CI 1.13-1.41; p<0.01). Long-term bypass increases the risk of developing AKI by 2.33 times (OR 2.33; 95% CI 1.13-4.36; p<0.01). With long-term AC, the risk of developing AKI increases by 2.52 times (OR 2.52; 95% CI 1.81-3.05; p<0.01). Low cardiac output syndrome leads to a 1.58-fold increase in the risk of developing AKI (OR 1.58; 95% CI 1.05-2.38; p<0.01). The need for high inotropic and vasopressor therapy in the postoperative period leads to an increase in the incidence of AKI by 67% (OR 1.67; 95% CI 1.13-2.72; p<0.01). Hyperlactatemia increases the risk of AKI by 24% (OR 1.24; 95% CI 1.19-3.05; p=0.019).

The long-term in the ICU (12 vs. 7 days) and the long-term in the hospital (23 vs 14.5 days) were significantly longer in the AKI+ group (p<0.01). Hospital mortality in the AKI+ group was higher - 16.5% vs 4.3% (p <0.01).

**Table 2.** Frequency of acute kidney injury after different types of cardiac surgery performed in young children, n=137

| Type of surgery | n, (%) | AKI I | AKI II | AKI III | PD |
|---|---|---|---|---|---|
| TGV | 9 (6.6%) | 2 (22.2%) | 2 (22.2%) | 1 (11.1%) | 2 (22.2%) |
| TA | 1 (0.7%) | - | - | 1 (100%) | 1 (100%) |
| PA | 8 (5.8%) | 1 (25%) | 1 (40%) | - | - |
| TF | 21 (15.3%) | 3 (14.2%) | 3 (14.2%) | 2 (9.5%) | 5 (23.8%) |
| TAPVD | 15 (10.9%) | 5 (33.3%) | 3 (20%) | 1 (6.6%) | 3 (20%) |
| PAPVD | 8 (5.8%) | 1 (16.6%) | 4 (66.6%) | - | - |
| AVC, p.f | 9 (6.6%) | 2 (22.2%) | 1 (11.1%) | 1 (11.1%) | 1 (11.1%) |
| DOGV fr RV | 10 (7.3%) | 3 (30%) | 2 (20%) | 1 (10%) | 1 (10%) |
| VSD | 51 (37.2%) | 8 (15.7%) | 2 (3.9%) | 1 (1.9%) | 1 (1.9%) |
| Combined | 15 (10.9%) | 3 (20%) | 2 (13.3%) | 2 (13.3%) | 2 (13.3%) |
| Total | 137 (100%) | 29 (21.9%) | 17 (12.4%) | 10 (7.3%) | 16 (11.7%) |

TGV: transposition of the great vessels, TA: truncus arteriosus, PA: pulmonary arteria atresia, TOF: tetralogy of Fallot, TAPVD: total anomalous pulmonary vein drainage, AVC-artioventricular canal; DOGV-double outlet of the great vessels; VSD-ventricular septal defect.

**Table 3.** General characteristics of patients and data of the perioperative course

| Index | | AKI - (n=81) | | AKI + (n=56) | | χ2 | P | RR | 95% CI |
|---|---|---|---|---|---|---|---|---|---|
| | | n | % | n | % | | | | |
| Preoperative | | | | | | | | | |
| Girls | | 37 | 45.7 | 26 | 46.4 | 0.007 | =0.932 | 1.03 | 0.52-2.04 |
| Boys | | 44 | 54.3 | 30 | 53.6 | 0.007 | =0.932 | 1.03 | 0.52-2.04 |
| Age | Up to 1 year | 25 | 30.9 | 39 | 69.6 | 20.00 | <0.001 | 5.14 | 2.45-10.76 |
| | From 1 to 3 years | 56 | 69.1 | 17 | 30.3 | 20.00 | <0.001 | 0.19 | 0.09-0.41 |
| HF and FC II, modified of Ross | | 38 | 46.9 | 27 | 48.2 | 0.022 | =0.88 | 1.05 | 0.53-2.08 |
| HF and FC III, modified of Ross | | 43 | 53.1 | 29 | 51.8 | 0.022 | =0.88 | 0.95 | 0.48-1.88 |
| Cardiotonic support before surgery | | 21 | 25.9 | 41 | 73.2 | 29.88 | <0.001 | 7.81 | 3.60-16.91 |
| Intraoperative | | | | | | | | | |
| Types of operation | Intracardiac left- to-right shunts | 40 | 49.4 | 11 | 19.6 | 12.53 | <0.001 | 0.25 | 0.11-0.55 |
| | Cyanotic heart defects | 29 | 35.8 | 33 | 58.9 | 7.15 | =0.008 | 2.57 | 1.28-5.18 |
| | Translocation of the main vessels | 4 | 4.9 | 5 | 8.9 | 0.86 | =0.35 | 1.89 | 0.48-7.36 |
| | Combined operations | 8 | 9.9 | 7 | 12.5 | 0.23 | =0.63 | 1.3 | 0.44-3.83 |
| Prolonged CPB | | 23 | 28.4 | 41 | 73.2 | 26.72 | <0.001 | 6.89 | 3.21-14.79 |
| Prolonged AC | | 19 | 23.4 | 36 | 64.3 | 22.97 | <0.001 | 5.87 | 2.77-12.44 |
| Hypothermia below 33°C | | 42 | 51.8 | 48 | 85.7 | 16.85 | <0.001 | 5.57 | 2.34-13.25 |
| Anemia (Hb <100 g/l) | | 27 | 33.3 | 33 | 58.9 | 8.81 | =0.003 | 2.87 | 1.42-5.81 |
| Post-operative | | | | | | | | | |
| Hyperlactatemia | | 35 | 43.2 | 51 | 91.1 | 32.46 | <0.001 | 13.40 | 4.84-37.11 |
| Decrease in hourly diuresis, ml/hour on day 1 | | 44 | 54.3 | 47 | 83.9 | 13.01 | <0.001 | 4.39 | 1.90-10.14 |
| Prolonged MV | | 29 | 35.8 | 34 | 60.7 | 8.27 | =0.004 | 2.77 | 1.37-5.59 |
| Low ejection syndrome | | 21 | 25.9 | 28 | 50 | 22.18 | <0.001 | 2.86 | 1.39-5.88 |
| Inotropic/vasopressor support | | 43 | 53.1 | 51 | 91.1 | 6.54 | =0.011 | 9.01 | 3.26-24.92 |
| Haemotransfusion | | 38 | 46.9 | 44 | 78.6 | 13.81 | <0.001 | 4.15 | 1.91-8.99 |
| Hospital mortality | | 5 | 6.2 | 11 | 19.6 | 5.82 | =0.016 | 3.72 | 1.21-11.38 |

AKI: acute kidney injury, HF: heart failure, FC: functional class, MV: mechanical ventilation, CPB: cardiopulmonary bypass, AC: aortic clamping

**Table 4.** Indicators of renal functional status and clinical course of the perioperative period in the studied groups, IQR (Q1; Q3), n=137

| Index | | AKI- (n=81) | AKI+ (n=56) | P |
|---|---|---|---|---|
| Preoperative | Initial serum creatinine, mg/dl | 22 (14; 39.3) | 29 (18.6; 45) | <0.01 |
| | GFR>140 ml/ml per 1.73 m2 | n = 43<br>195.6 (152; 226.5) | n = 16<br>163 (143; 186.5) | <0.05 |
| | GFR 90-140 ml/ml per 1.73 m2 | n=27<br>106.5 (101.4;133.5) | n= 21<br>106.9 (95.6;118.2) | <0.05 |
| | GFR <90 ml per 1.73 m2 | n = 11<br>69.5 (47.9;78.5) | n=19<br>58.5 (57;63.5) | <0.05 |
| | Initial albumin, g/L | 55 (44;68) | 51(42;64) | >0.05 |
| Post-operative | Time of MV, hours. | 36.5 (25.5;96.5) | 82 (60.5;116.5) | <0.05 |
| | Peritoneal Dialysis, days | - | n = 16  10 (7; 12) | <0.05 |
| | Long-term in ICU, days. | 7 (5.5;9) | 12 (9; 15) | <0.05 |
| | Long-term of hospitalisation, days. | 14.5 (12;19) | 23 (18;25) | <0.05 |

GFR: glomerular filtration rate, MV: mechanical ventilation.

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**Table 5.** Perioperative predictors of AKI in infants undergoing cardiac surgery according to multivariate logistic regression analysis, n=137

| Index | | p | OR | 95% CI |
|---|---|---|---|---|
| Age, years | | <0.01 | 1.36 | 1.12-1.47 |
| HF | | <0.01 | 1.12 | 1.08-1.22 |
| Tonic support preoperatively | | <0.01 | 1.27 | 1.15-1.36 |
| Type of operation | Intracardiac left-to- right shunts<br>Cyanotic heart defects<br>Translocation of the main vessels<br>Combined operations | <0.01 | 1.85 | 1.13-3.42 |
| long-term CPB | | <0.01 | 2.33 | 1.55-4.36 |
| long-term AC | | <0.01 | 2.52 | 1.81-3.05 |
| Low cardiac output syndrome in the early postoperative period | | <0.01 | 1.98 | 1,46-2.78 |
| Inotropic and vasopressor therapy | | <0.01 | 1.67 | 1.13-2.92 |
| Hyperlactatemia in the early postoperative period | | =0.019 | 1.84 | 1.19-3.15 |

HF: heart failure, GFR: glomerular filtration rate, CPB: cardiopulmonary bypass, AC: aortic clamping.

## DISCUSSION

The incidence of AKI was 40.9% among young children with various types of cardiac surgery, which correlates with studies by other authors. It is known that the incidence of AKI depends on the performed type of surgery. Correction of septal heart defects is characterized by the lowest incidence of AKI: 4-7%. During operations on the great vessels of the heart or multicomponent interventions, including operations on the outflow tract of both ventricles, it reaches 40% [10-12]. PD was performed in 11.7% of children, thus, the overall level of procedures performed generally coincides with the results of foreign studies. Comparing the number of PD installations, depending on the type of cardiac surgery, it was found that in the RSSPMCS the frequency of PD after TGV correction was 22.2%, this slightly more than in the studies of a number of authors. In study of Bailey [21], the total number of PD was 18%. After correction of intracardiac shunts and cyanotic defects, PD was performed in 0.8% and 16.7% of children, respectively. After translocations of large arteries and combined operations it reached 13% and 10.5%, respectively. In the study done by Boneva [12], PD was performed in 26.4% of cases, after correction of intracardiac shunts and cyanotic defects was 1.1% and 18.3%, after translocations of large arteries was 9% and it was 7.4% after combined operations.

As in other studies, risk factors for the development of AKI were younger age [7, 14], initial heart failure [8, 10, 18], complex or combined cardiac surgery [15], long-term bypass and aortic clamping [13], low cardiac output syndrome, prescription of inotropic and vasopressor therapy [15, 21], hyperlactatemia [22]. Low GFR has also become a risk factor for the development of AKI. A review of domestic and foreign literature sources did not reveal such a pattern. This low rate appears to reflect the degree of profound changes in renal function, thus implying the presence of underlying damage to the renal parenchyma before complex operations are performed. Hypercreatininemia and hypoalbuminemia are also predictors of postoperative complications such as AKI.

The development of AKI in the presented study was associated with an increase in the length of stay in the ICU and in the hospital. AKI increases mortality in the immediate postoperative period. In AKI- patients it was 4.3%, and in AKI+ patients it was 16.5%. In the studies done by McAlister et al. [11] and Polito et al. [14], mortality after correction of cyanotic defects in the AKI+ group was reported as 41.7%. In comparison, the mortality rate in the non-AKI group was 12.9%. Mortality in the group in which PD was performed reached 53%. When analyzing mortality, depending on the duration of AKI (recovery of renal function was taken to be normalization of GFR and creatinine levels to acceptable values). The minimum mortality rate was 2.9%, where kidney function was restored within 1-2 days. In the group where AKI lasted >7 days, mortality reached 24.8% [13].

## CONCLUSIONS

The incidence of acute kidney injury (AKI) after cardiac surgery was 40.9%. The need for PD was in 11.7% of cases. Risk factors for AKI were such as younger age, initial heart failure, type of operation, long-term bypass and aortic clamping, low cardiac output syndrome, inotropic and vasopressor therapy, hyperlactatemia. The development of AKI significantly increased the length of hospital stay and hospital mortality.

## DECLARATIONS


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### Authors contributions

All authors contributed equally to this work.


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### Competing interests

All authors declare that they have no conflict of interest.

### Ethical approval

The review board and ethics committee of RSCS named after acad. V.Vakhidov approved the study protocol and informed consents were taken from all the participants.

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