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RESEARCH ARTICLE

Acute Kidney Injury Following Congenital Heart Surgery and Its Associated Risk Factors

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ABSTRACT

Objectives: This study aimed to determine the incidence of acute kidney injury (AKI) and identify risk factors associated with its development in pediatric patients undergoing congenital heart surgery with cardiopulmonary bypass (CPB).

Methods: A prospective study was conducted between May 1, 2022, and May 1, 2023, in a pediatric cardiac intensive care unit. Children under 16 years of age who underwent congenital heart surgery with CPB were included. Postoperative AKI was classified using the pRIFLE criteria. Various clinical and perioperative factors were analyzed for their association with AKI.

Results: A total of 640 patients were included, with a median age of 12 months (IQR 6–24); 52% were male. AKI occurred in 24% of patients: 10% were classified as "Risk," 10% as "Injury," and 4% as "Failure." Patients with AKI had significantly longer durations of mechanical ventilation, ICU and hospital stays, and higher mortality rates. Independent risk factors for AKI included prolonged CPB time (>120 minutes), age<6 months, preoperative pulmonary hypertension, low preoperative serum albumin (<3.5 g/dL), STAT score≥3, red blood cell transfusion>50 mL/kg, and inotrope score≥8.

Conclusion: AKI is a frequent and serious complication after congenital heart surgery. Several modifiable and non-modifiable risk factors contribute to its development, emphasizing the need for early risk stratification and preventive strategies in high-risk pediatric patients.

Keywords: Acute kidney injury, children, congenital heart surgery

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Introduction

Acute kidney injury (AKI) is a common complication observed in the intensive care unit following congenital heart surgery in pediatric patients. Various studies have reported an incidence ranging between 20% and 50%, with higher rates noted in neonates during the postoperative period.[1,2]

The presence of AKI is associated with poor surgical outcomes. It contributes to increased morbidity by potentially progressing to chronic kidney disease, prolonging mechanical ventilation and ICU stays, and increasing healthcare costs.[3,4]

Several risk factors have been identified in the development of AKI in these patients, including prematurity, younger age, high-dose inotropic support, prolonged CPB time, degree of hypothermia, greater surgical complexity, and the presence of postoperative low cardiac output syndrome.[5]

Different scoring systems such as pediatric RIFLE (pRIFLE) criteria—Risk, Injury, Failure, Loss, and End-stage renal disease, KDIGO (Kidney Disease: Improving Global Outcomes), and AKIN (Acute Kidney Injury Network) are used to evaluate AKI. The pediatric RIFLE (pRIFLE) criteria are commonly utilized for assessing AKI in critically ill

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pediatric populations and have been shown to reliably indicate AKI incidence in various studies.[1–3]

This study aimed to investigate the incidence of AKI and the risk factors affecting its development in pediatric patients undergoing congenital heart surgery with cardiopulmonary bypass.

Methods

Study Design and Patient Selection

Our study was a single-center, retrospective study. The study was designed in accordance with the tenets of the Declaration of Helsinki and obtained the necessary approval from the local ethics committee (Ethics Committee of Istanbul Basaksehir Çam and Sakura City Hospital, University of Health Sciences of Türkiye, Protocol Code: 2022/166, date: 25.05.2022). This prospective study was conducted between May 1, 2022, and May 1, 2023, and included pediatric patients under the age of 16 who were followed in the pediatric cardiac intensive care unit and underwent congenital heart surgery with cardiopulmonary bypass. Data were obtained from the hospital's electronic medical records system. Patients with a history of kidney disease or those who had received peritoneal dialysis or hemodialysis prior to surgery were excluded from the study.

Clinical and Laboratory Parameters

- Preoperative data included patient weight, sex, diagnosis of heart disease (cyanotic & acyanotic, single ventricle & biventricular), and laboratory values such as serum creatinine (Cr) and blood urea nitrogen (BUN).
- Intraoperative data comprised CPB time, aortic cross-clamp time, and surgical complexity scores based on the Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery (STAT) classification.
- Postoperative data included intensive care unit monitoring outcomes such as serum creatinine, BUN, lactate levels, duration of mechanical ventilation, mortality, morbidity, vasoactive-inotropic score (VIS), and data from classification systems used to evaluate AKI (RIFLE criteria).

All operations were performed by one of four surgeons experienced in pediatric cardiac surgery for over ten years with more than 150 surgeries per year. Midazolam (0.1–0.3 mg/kg) and fentanyl (1–2 μg/kg) were used for induction of anesthesia. Anesthesia was maintained by inhalation anesthetics or total intravenous anesthesia. For CPB, arterial cannulation was performed in the ascending aorta, and venous cannulations were bicaval or in the right appendage according to the type of surgery. For CPB, high-performance, low prime volume oxygenators were used to reduce the pump priming volume. Modified ultrafiltration was conducted in the operating room during the CPB weaning process.

For the STAT, the scale ranged from 0.1 to 5.0, and a corresponding mortality category level between 1 and 5 was assigned (level 1: 0.1–0.3; level 2: 0.4–0.7; level 3: 0.8–1.2; level 4: 1.3–2.6; level 5: 2.9–5.0).[6] The types and doses of inotropic agents used were recorded, and the daily VIS was calculated for each patient. VIS was calculated using the following formula:

VIS=Dopamine dose (μg/kg/min)+Dobutamine dose (μg/kg/min)+100×Epinephrine dose (μg/kg/min)+10×Milrinone dose (μg/kg/min)+10,000×Vasopressin dose (μg/kg/min)+100×Norepinephrine dose (μg/kg/min).

A VIS score of<8 was considered low inotropic support, while a VIS score of≥8 was defined as high inotropic support.[7]

Acute Kidney Injury and Definitions

The pediatric RIFLE (pRIFLE) classification system was used to define AKI. The pRIFLE criteria are based on the postoperative reduction in glomerular filtration rate (GFR) compared to the baseline GFR. The modified Schwartz formula was used to estimate GFR:

eGFR (mL/min/1.73 m^2)=k×Height (cm)/SCr, where k=0.413, Height=patient height in cm, and SCr=serum creatinine in mg/dL.[8,9]

Baseline BUN and serum creatinine values were taken from laboratory results obtained within 24 hours prior to surgery. Each patient was categorized into a pRIFLE class—R (Risk), I (Injury), or F (Failure)—based on the postoperative decline in creatinine clearance. Class R, I, and F correspond to decreases in GFR of 25%, 50%, and 75%, respectively, relative to baseline values. Patients with a postoperative GFR of<35 mL/min/1.73 m^2 were also classified as class F.[9,10]

Urine output was not used as a criterion for kidney injury due to its susceptibility to intraoperative factors and postoperative diuretic use.

Statistical Analysis

Data were analyzed using SPSS for Windows version 23.0 software. Descriptive statistics were performed in relation to the distribution of variables and characteristics of the study population. Categorical variables were represented as frequencies, and numeric variables as mean or median with the respective measures of dispersion. The Student's t test or the Mann-Whitney test was used in univariate analysis of continuous variables, and the chi-square test or Fisher's exact test was used to analyze categorical variables. A logistic regression model was constructed for multivariate analysis.

Table 1. Characteristics of the study population

Variables	Total n =640		AKI (-) n =486		AKI (+) n=154		p
	n	%	n	%	n	%	
Male	333	52	256	53	77	50	NS
Age (months old)	12 (6–24)		15 (12–18)		6 (4–8)		**0.030**
Weight (kg)	7.2 (6–8.4)		8.5 (7.5–10)		5.5 (4–7.5)		**0.020**
Newborn	256	40	166	34	90	58	**<0.001**
Genetic disorders	39	6	24	5	15	9.7	NS
Cyanotic heart disese	256	40	191	39	65	42	NS
Single ventricle	192	30	152	31	40	26	NS
Preoperative pulmonary hypertension	220	34	145	29	75	48	**<0.001**
Preoperative use of nephrotoxic drugs	133	20	95	19	38	24	NS
Creatinine (mg/dL)	0.40 (0.36–0.44)		0.42 (0.38–0.45)		0.38 (0.36–0.40)		NS
Preoperative Albumin (g/dL)	3.9 (3.7–4.2)		4.1 (3.8–4.5)		3.6 (3.4–3.8)		**<0.001**
POD1 albumin (g/dL)	4.1 (3.9–4.3)		4.1 (3.9–4.3)		4 (3.8–4.2)		NS
Preoperative hematocrit (%)	35.5 (33–37)		36 (32–40)		34 (30–38)		**0.003**
POD1 Hematocrit (%)	34 (32–36)		34 (30–36)		35 (33–38)		NS
Platelet count ($\times10^3/\mu L$)	310 (300–320)		310 (280–340)		320 (300–340)		NS
Lactic acid (mmol/L)	1.8 (1.6–2)		1.8 (1.5–2.1)		1.9 (1.7–2.2)		NS
STAT score ≥3	320 (50)		224 (46)		96 (62)		**<0.001**
CPB time (min)	105 (110–115)		100 (90–110)		130 (110–150)		**<0.001**
Aorta cross clamp time (min)	55 (50–65)		50 (40–60)		65 (55–75)		**0.025**
Packed red blood cells (ml/kg)	40 (30–50)		30 (20–40)		55 (45–65)		**<0.001**
Total circulatory arrest	5	0.8	3	0.6	2	1.3	NS
Fresh frozen plasma (ml/kg)	15 (10–20)		10 (5–20)		25 (20–35)		**<0.001**
Platelet concentrate (ml/kg)	0 (0–5)		0 (0–5)		0 (0–10)		NS
Intraoperative urine output (ml/kg)	15 (12–18)		14 (12–16)		15 (11–18)		NS
Total fluid intake during postoperative three days (ml/kg/day)	258 (245–270)		260 (220–280)		250 (230–290)		NS
High (≥8) Vazoactive Inotropic score	189	29	97	20	92	60	<0.001
Baseline cerebral NIRS (%)	52 (42–56)		51 (40–58)		50 (41–57)		NS

n (%); Median (IQR). AKI: Acute kidney injury; POD: Postoperative day; STAT: The society of thoracic surgeons-european association for cardio-thoracic surgery; CPB: Cardiopulmonary bypass; NS: Not significant; NIRS: Near-infrared spectroscopy.

Postoperative AKI was defined as the dependent variable. A p value of<0.05 was considered statistically significant.

Results

During the study period, a total of 640 cases were included. The median age was 12 months (IQR: 6–24 months). Of the cases, 52% were male and 48% were female. Forty percent were neonates, and 40% were diagnosed with cyanotic congenital heart disease. According to the pRIFLE classification, AKI was diagnosed in 24% of the cases. In terms of subgroups, 10% were classified as "Risk," 10% as "Injury," and 4% as "Failure." There was no statistically significant variation observed across different types of heart disease. Table 1 shows the characteristics of the population under study. The distribution of specific cardiac diagnoses and their association with AKI incidence is presented in Table 2.

The parameters of the postoperative course are presented in Table 3. In patients with acute kidney injury, neurological complications (18% vs. 2%), days of mechanical ventilation after surgery (3 vs. 1 days), postoperative ICU stay (7 vs. 3 days), length of hospital stay after surgery (13 vs. 9 days), and mortality (13.6% vs. 4%) were significantly higher (p<0.05).

The results of the multivariate analysis identifying predictors of AKI following pediatric cardiac surgery are presented in Table 4. Prolonged CPB time (>120 minutes), age<6 months, neonatal status, preoperative pulmonary hypertension, low preoperative albumin levels (<3.5 g/dL), high STAT scores (≥3), transfusion of packed red blood cells (>50 mL/kg), and a high vasoactive-inotropic score (≥8) were independently associated with postoperative AKI in children undergoing cardiac surgery.

Table 2. Distribution of cardiac diagnoses and AKI Incidence

Cardiac diagnoses	Total		AKI (-)		AKI (+)		p
	n	%	n	%	n	%	
Cyanotic congenital heart disease	256	40.0	191	39.3	65	42.2	NS
Tetralogy of fallot	70	10.9	51	10.5	19	12.3	NS
Transposition of great arteries	45	7.0	32	6.6	13	8.4	NS
Hypoplastic left heart syndrome	25	3.9	16	3.3	9	5.8	NS
Truncus arteriosus	40	6.3	26	5.3	14	9.1	NS
Total anomalous pulmonary venous return	41	6.4	29	6.0	12	7.8	NS
Others*	35	5.5	27	5.6	8	5.2	NS
Acyanotic congenital heart disease	384	60.0	295	60.7	89	57.8	NS
Ventricular septal defect	110	17.2	88	18.1	22	14.3	NS
Arcus hypoplasia / coarctation of aorta	76	11.9	55	11.3	21	13.6	NS
Atrioventricular septal defect	70	10.9	53	10.9	17	11.0	NS
Atrial septal defect	50	7.8	40	8.2	10	6.5	NS
Patent ductus arteriosus	36	5.6	25	5.1	11	7.1	NS
Others**	42	6.6	31	6.4	11	7.1	NS

*: Others in cyanotic group include: Double outlet right ventricle, pulmonary atresia with intact ventricular septum, Ebstein's anomaly, single ventricle variants; **: Others in acyanotic group include: Partial anomalous pulmonary venous return, aortic stenosis, pulmonary stenosis, mitral valve disease, anomalous coronary arterie. AKI: Acute kidney injury; NS: Not significant.

Table 3. Parameters of postoperative course

Variables	AKI (-)		AKI (+)		p
	n	%	n	%	
ECMO	6	1.2	10	6.4	NS
Infection	29	6	11	7.1	NS
Bleeding	15	3	6	3.8	NS
Cardiorespiratory arrest	20	4.1	9	6	NS
Neurological complications	10	2	27	18	**0.005**
Liver complications	5	1	3	1.9	NS
Postoperative pulmonary hypertension	29	6	10	6.4	NS
Arrhythmia	39	8	25	16.2	NS
Delayed chest closure	15	3	27	18	**0.002**
Death	19	4	21	13.6	**0.030**
Days of MV after surgery	1 (0–2)		3 (2–4)		**<0.001**
Postoperative ICU stay (days)	3 (1–5)		7 (5–10)		**<0.001**
Length of hospital stay after surgery (days)	9 (7–11)		13 (10–16)		**<0.001**

n (%); Median (IQR). AKI: Acute kidney injury; ECMO: Extracorporeal membrane oxygenation; ICU: Intensive care unit; MV: Mechanical ventilation.

Discussion

In this prospective study, we investigated the incidence of AKI and the risk factors influencing its development in pediatric patients under 16 years of age who underwent congenital heart surgery with cardiopulmonary bypass at our center. Using the pRIFLE criteria, we identified an AKI incidence of 24%. We found that prolonged cardiopulmonary bypass time (>120 minutes), younger age at surgery (<6 months), presence of preoperative pulmonary hypertension, low preoperative serum albumin levels (<3.5 g/dL), high STAT score (≥3), excessive red blood cell transfusion (>50 mL/kg), and high inotropic score (≥8) were independent risk factors for the development of AKI. Furthermore, AKI was associated with increased morbidity and mortality. Given these findings, our study stands as a significant contribution to the existing literature, particularly due to its prospective design and comprehensive evaluation of perioperative risk factors in a large pediatric cohort.

Table 4. Multivariate analysis: Predictors of acute kidney injury after pediatric cardiac surgery

Variables	Odds ratio	(95% CI)	p
Prolonged CPB time (>120 minutes)	1.6	1.2–2.8	**<0.001**
Age (<6 months)	1.2	1–2.1	**0.02**
Newborn	3.6	2.4–8	**<0.001**
Preoperative pulmonary hypertension	0.9	0.5–1.6	**0.045**
Preoperative albumin (<3.5 g/dL)	0.8	0.6–1.2	**0.030**
STAT scores (≥3)	6	3.2–12	**<0.001**
Packed red blood cells (>50 ml/kg)	0.7	0.4–1.5	**0.040**
High (≥8) vazoactive inotropic score	2	1.2–6	**<0.001**

CPB: Cardiopulmonary bypass; STAT: The society of thoracic surgeons-european association for cardio-thoracic surgery

AKI is one of the most common complications following cardiac surgery in pediatric patients undergoing CPB and is closely associated with postoperative outcomes.[11,12] Depending on the scoring system and biochemical parameters used, the reported incidence of AKI varies between 20% and 50%. In a cohort of 570 patients with a median age of 12 months, Xiao et al.[11] reported an AKI incidence of 36.1%. Graziani et al.,[13] using the KDIGO criteria, found an incidence of 35%. Park et al.[14] reported an AKI incidence of 41.8% in a cohort of 220 patients aged 10 days to 19 years, also based on KDIGO criteria. A large meta-analysis that included 61 studies and a total of 19,680 participants (7,257 with AKI and 12,423 without) reported an overall AKI incidence of 34.3%.[12] In contrast, Cardoso et al.,[9] using the pRIFLE criteria, reported a lower incidence of 12.3% in their cohort.

In our study, the incidence of AKI was found to be 24%. This variability in AKI incidence across studies may be attributed to the heterogeneity of congenital heart defects, differences in patient age distributions, and the use of different scoring systems for AKI evaluation.

AKI adversely affects both short- and long-term outcomes following pediatric cardiac surgery and contributes to increased morbidity and mortality. In the study by Park et al.,[14] patients with AKI had significantly longer durations of mechanical ventilation (median 4.8 vs. 2.4 days), ICU stay (median 7 vs. 4 days), and hospital stay (median 14 vs. 13 days) compared to those without AKI. However, no significant difference in mortality was observed between the groups (1.1% vs. 0%). Similarly, in the study by Graziani et al.,[13] although there was no statistically significant difference in mortality between AKI and non-AKI groups (11.4% vs. 3.7%), the incidence of complications such as bleeding (22.7% vs. 4.9%), neurological complications (18.2% vs. 2.5%), and liver complications (6.8% vs. 0%) was significantly higher in patients with AKI.

In our study, both mortality (13.4% vs. 4%) and the incidence of neurological complications (18% vs. 2%) were significantly higher in patients with AKI. Similar to studies in the literature, we also observed longer durations of mechanical ventilation, intensive care unit stay, and hospital stay in the AKI group.

Risk factors for AKI after cardiac surgery can be classified into two types: renal and extrarenal. The latter includes constitutional, hemodynamic, or inflammatory causes. In pediatric patients, younger age, prolonged CPB time, prolonged ventilation time, pump failure, sepsis, and hematological complications predispose to AKI after cardiac surgery.[3,4,8,15] In the study by Aydin et al.,[2] younger age, higher RACHS-1 (Risk-Adjusted Classification for Congenital Heart Surgery) category, and longer cardiopulmonary bypass time were found to be associated with the development of AKI. In the study by Cardoso et al.,[9] younger age and higher postoperative serum creatinine, blood urea nitrogen, and lactate levels were strong predictors of renal injury in this population. Similarly, in the study by Lee et al.,[4] preoperative serum albumin level, age<12 months, preoperative pulmonary hypertension, and cardiopulmonary bypass duration were identified as risk factors for postoperative AKI in children who underwent congenital heart surgery. In another study involving 840 patients who underwent congenital heart disease (CHD) surgery, prolonged CPB time>120 minutes (adjusted OR [AOR]: 1.87; 95% CI: 1.22–2.88; p=0.004) and hemoglobin>16 g/dL (AOR: 1.80; 95% CI: 1.16–2.78; p=0.008) were found to be associated with the development of AKI in multivariate analysis.[16]

In our study, prolonged CPB time (>120 minutes), younger age at surgery (<6 months), presence of preoperative pulmonary hypertension, low preoperative albumin levels (<3.5 g/dL), high STAT scores (≥3), transfusion of packed red blood cells (>50 mL/kg), and a high vasoactive-inotropic score (≥8) were identified as independent risk factors for the development of AKI.

Limitation

This study has several limitations. First, it was a single-center study with limited follow-up data; therefore, the management practices of our center may not be generalizable to the entire population. Second, there was a wide variety of cardiac surgeries, categorized as cyanotic, acyanotic, and single-ventricle heart diseases, which made it difficult to establish a clear association between the type of surgery and the development of AKI. Third, we used the pRIFLE criteria to determine the incidence of AKI; the use of alternative scoring systems might have resulted in different incidence rates. Lastly, since many patients received diuretics, which could affect the accuracy of urine output as a diagnostic criterion, we did not include urine output in the definition of AKI.

Conclusion

AKI is a common complication following congenital heart surgery and has a negative impact on prognosis. Prolonged CPB time (>120 minutes), younger age at surgery (<6 months), presence of preoperative pulmonary hypertension, low preoperative albumin levels (<3.5 g/dL), high STAT scores (≥3), transfusion of packed red blood cells (>50 mL/kg), and a high vasoactive-inotropic score (≥8) can increase the risk of AKI development.

Disclosures

Ethics Committee Approval: The study was approved by the Istanbul Basaksehir Çam and Sakura City Hospital, University of Health Sciences of Türkiye Ethics Committee (no: 2022/166, date: 25/05/2022).

Informed Consent: Informed consent was obtained from all participants.

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