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Evaluation of the incidence and risk factors of acute renal injury according to the pRIFLE criteria in children with ventricular septal defect (VSD) and atrioventricular septal defect (AVSD) after cardiovascular interference

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ABSTRACT

Aims: We aimed to determine the incidence and risk factors of acute kidney injury (AKI) according to pRIFLE (risk, injury, failure, loss, endstage) criteria and to evaluate its effect on prognosis in patients followed up in intensive care unit after interventions for heart disease.

Methods: The study included 84 patients who underwent surgery for VSD and AVSD between January 2016 and September 2016 in the Pediatric Cardiovascular Surgery Clinic of Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital. Patients were prospectively analyzed. Primary disease, demographic data, duration of intensive care and hospital stay, duration of follow-up on ventilator, urine output, vital signs, intraoperative data, primary and secondary problems, and renal function tests were recorded.

Results: Among the patients, 35 were male, 49 were female, 30 were diagnosed with AVSD and 54 with VSD. pRIFLE classification revealed AKI in 19 patients. When the AKI (+) and non-AKI (+) groups were compared, no significant difference was found between the duration of cardiopulmonary bypass (CPB) in the AKI (+) group, while hypothermia levels were significantly lower (p=0.003). Mortality and length of hospital stay were significantly higher in the AKI (+) group.

Conclusion: AKI is a serious complication in pediatric cardiac surgery patients. The presence and extent of damage is closely related to morbidity and mortality. The use of an inexpensive, easily applicable method such as pRIFLE criteria is recommended for the detection and grading of AKI.

Keywords: Acute kidney injury, pRIFLE criteria, congenital heart disease

INTRODUCTION

Pediatric cardiac surgery became successfully feasible with the introduction of the heart-lung machine discovered by Gibbon in 1953. The majority of these operations, which are performed as palliative and complete correction operations, require cardiopulmonary bypass support.

Acute kidney injury (AKI) describes damage to the kidneys that starts at the cellular level and can progress from transient dysfunction to permanent dysfunction. Depending on the primary cause, it may be partially or completely reversible. Acute renal failure (ARF) describes the inability of the kidneys to maintain fluid and electrolyte hemostasis.

In pediatric cardiac surgery patients, AKI may occur in the perioperative period due to many causes. In particular, approximately 30% of patients undergoing surgery with cardiopulmonary bypass (CPB) develop severe AKI. CPB initiates the inflammatory response, increases antidiuretic hormone (ADH) release and capillary membrane permeability and leads to renal damage by decreased renal perfusion

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pressure, activation of proinflammatory mediators and direct nephrotoxic effect.[1,2] In pediatric patients who have undergone cardiac surgery, volume depletion, inadequate fluid support, inadequate cardiac pump function and use of nephrotoxic drugs also contribute to AKI.

CPB duration is also important in the development of AKI.[3] As the duration of CPB increases, the risk of coagulopathy increases and more blood product transfusion support causes severe hypoperfusion and increases the frequency of AKI. Delay in the diagnosis of AKI increases morbidity and mortality, which can be reversed with early diagnosis of AKI.

RIFLE, pRIFLE and AKIN classifications have been developed to determine the severity of AKI. The common feature of these classifications is that they are cheap, simple, easily applicable and provide standardization in determining the degree of acute kidney injury.

METHODS

The study was carried out with the permission of the Haydarpaşa Numune Training and Research Hospital Clinical Researches Ethics Committee (Date: 09.05.2016, Decision No: HNEAH-KAEK 2016/KK/50). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patients hospitalized in the Pediatric Cardiovascular Intensive Care Unit of Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital between January 2016 and September 2016 were prospectively analyzed. Eighty-four patients operated for VSD and AVSD were included in the study. Patients with incomplete investigations and patients older than 15 years were excluded.

Primary disease, demographic data, duration of intensive care unit and hospital stay, duration of follow-up on ventilator, duration of operation and intraoperative body temperature, urine output, vital signs, primary and secondary problems, preop-perop and postop renal function tests were recorded.

Preoperative, intraoperative and postoperative glomerular filtration rate (GFR) values of the patients were calculated according to Schwartz formula with the collected data. To diagnose AKI, the class of the patients was determined by evaluation with pRIFLE classification.

Since our patients had congenital heart disease, were receiving preoperative or postoperative diuretic, vasopressor and inotrope support due to their existing pathologies and these treatments had effects on urine output, GFR parameter was used in all patients to determine AKI. Preop, perop and postop t-GFR values of the patients were calculated by Schwartz formula and evaluated according to the t-GFR parameter in pRIFLE classification.

Statistical Analysis

NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) programme was used for statistical analyses. Descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum) were used to evaluate the study data. Friedman Test was used for intra-group comparisons of measurements that did not show normal distribution and Wilcoxon Signed Ranks test was used for the evaluation of pairwise comparisons. Fisher's exact test and Yates' continuity correction test (Chi-square with Yates' correction) were used for comparison of qualitative data. Significance was evaluated at $p<0.01$ and $p<0.05$ levels.

RESULTS

Our study was performed with a total of 84 patients, 41.7% (n=35) male and 58.3% (n=49) female, who were followed up after VSD/AVSD operation. The mean age was 2.00±3.48 years.

AVSD was present in 35.7% (n=30), VSD in 64.3% (n=54) and 28.6% (n=24) had a family history of heart disease. Eight of the patients were in the neonatal period and 7 of them had Down syndrome. Cardiac murmurs of 3-4/6 intensity were detected in 97% (n=82) of the patients and all were diagnosed by electrocardiographic examination. Cross-clamp times of the patients operated by CPB access were 74.51±32.83 minutes (min) and total perfusion times were 102.90±44.68 min. Body temperature was 31.43±1.34 C erythrocyte suspension (ES) transfusion was required in 92.9% (n=78) of the cases. Mechanical ventilation (MV) duration was 6.33±10.48 min, intensive care unit (ICU) duration was 9.18±12.06 min, and hospital stay was 20.72±21.29 days. Postoperative cardiac arrest was observed in 6% (n=5) and AV block in 3.6% (n=3) of cases. There was no operative mortality in our patients. Postoperative inotropic support was required in 81% (n=68) of cases and MV support was required again after postoperative extubation in 17.9% (n=15). Renal replacement therapy (RRT) was administered during ICU follow-up in 6% (n=5) of cases. While 95.2% (n=80) of the patients were discharged with cure, 4.8% (n=4) of them died (**Table 1, Figure 1**).

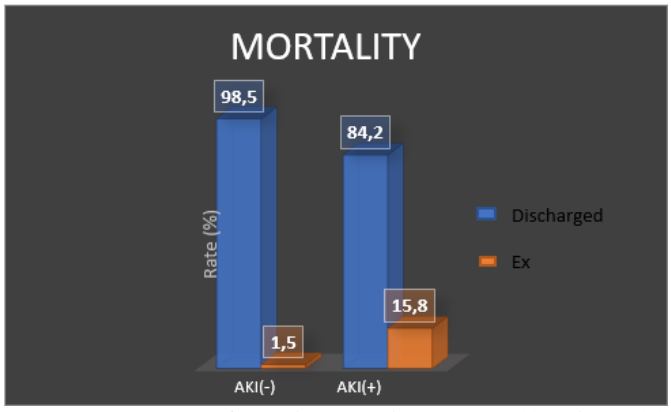

Figure 1. Comparison of mortality status between AKI (-) and AKI (+) groups

AKI: Acute kidney injury

There was no statistically significant difference between the groups when age, gender distribution, primary disease and presence of heart disease in the family were analyzed ($p>0.05$).

While Preop CrCl [creatinine clearance (ml/min)] measurements did not show significant difference between the groups ($p=0.168$; $p>0.05$), the fact that the Perop CrCl measurements of the AKI (+) group were lower than the AKI (-) group was found to be close to significance ($p=0.064$; $p>0.05$). It was found significant that the postop CrCl measurements of the AKI (+) group were lower than the AKI (-) group ($p=0.005$; $p<0.01$).

The change in preop, perop and postop CrCl measurements of the AKI (+) group was found to be significant ($p=0.001$; $p<0.01$). While the decrease of 7.96±11.44 in perop CrCl measurements was found to be significant ($p=0.001$; $p<0.01$),

Table 1. Demographic characteristics of the patients, intraoperative and postoperative results

		Min-max (median)	Mean±SD			n	(%)
Distribution of preoperative characteristics	Age (years)	0.08-15.00 (0.58)	2.00±3.48	Sex	Male	35	41.7
					Female	49	58.3
				Primary disease	AVSD	30	35.7
					VSD	54	64.3
				Family history of heart disease		24	28.6
Distribution of surgery data	Cross-clamp time (min)	25-162 (63.5)	74.51±32.83	ES replacement		78	92.9
	CPB time (min)	40-276 (90.5)	102.90±44.68				
	Body temperature (C)	28-34 (32)	31.43±1.34				
Distribution of postoperative characteristics	MV duration (days)	1-54 (2)	6.33±10.48	Cardiac arrest		5	6.0
				Re-intubation		15	17.9
	ICU time (days)	1-60 (3.5)	9.18±12.06	AV blk		3	3.6
				Inotr. support		68	81.0
				RRT		5	6.0
	Length of hospital stay (days)	5-150 (14.5)	20.72±21.29	Mortality	Discharged	80	95.2
					Ex	4	4.8

Min: Minimum, Max: Maximum, SD: Standard deviation, AVSD: Atrioventricular septal defect, VSD: Ventricular septal defect, CPB: Cardiopulmonary bypass, MV: Mechanical ventilation, ES: Erythrocyte suspension, ICU: Intensive care unit, AV: Atrio ventricular, RRT: Renal replacement therapy, Ex: Excitus

the change in postop CrCl measurements was not significant (p=0.291; p>0.05). The increase of 10.14±13.42 in postop CrCl measurements compared to Preop was found to be significant (p=0.001; p<0.01). The change in preop, perop and postop CrCl measurements of AKI (-) group was found to be significant (p=0.001; p<0.01). While the decrease of 31.04±13.55 in perop CrCl measurements compared to preop (p=0.001) and the decrease of 27.60±20.62 in postop CrCl measurements compared to preop (p=0.001) were found significant (p<0.01); the change in postop CrCl measurements compared to Perop was not found significant (p=0.546; p>0.05) (Figure 2).

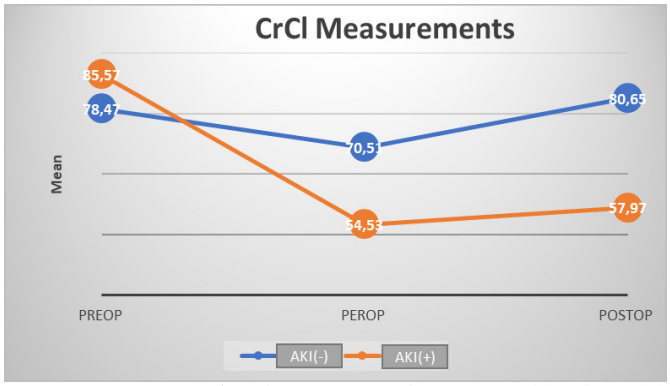

Figure 2. Comparison of CrCl measurements between AKI (-) and AKI (+) groups

CrCl: Creatinine clearance, AKI: Acute kidney injury

It was found significant that the change in perop CrCl (p=0.001) and postop CrCl (p=0.001) measurements of AKI (+) cases compared to preop was higher than the AKI (-) group (p<0.01). The change in postop CrCl measurements of the patients compared to preop did not differ significantly according to the groups (p=0.111; p>0.05) (Table 2).

Cross-clamp and CPB durations and the presence of ES transfusion were not significantly different between the groups (p>0.05), whereas the body temperatures of the AKI (+) group were significantly lower than the AKI (-) group (p=0.003; p<0.01) (Table 3).

Table 2. Comparison of CrCl measurements of AKI (-) and AKI (+) groups

		AKI (-) (n=65)	AKI (+) (n=19)	[a]p
Preop. CrCl	Min-max (median)	31-163 (70)	53-140 (81)	0.168
	Mean±SD	78.47±28.15	85.57±22.58	
Perop. CrCl	Min-max (median)	30-130 (61)	25-88 (57)	0.064
	Mean±SD	70.51±25.37	54.53±16.91	
Postop. CrCl	Min-max (median)	31.5-165 (70)	24-106 (48)	0.005**
	Mean±SD	80.65±32.86	57.97±23.26	
	[d]p	0.001**	0.001**	
Preop.-Perop. difference	Min-max (median)	-48-15 (-8)	-65-(-12) (-32)	0.001**
	Mean±SD	-7.96±11.44	-31.04±13.55	
	[c]p	0.001**	0.001**	
Preop.-Postop. difference	Min-max (median)	-34-44 (0)	-71-5 (-27)	0.001**
	Mean±SD	2.18±14.10	-27.60±20.62	
	[c]p	0.291	0.001**	
Perop.-Postop. difference	Min-max (median)	-21-52 (10)	-24-38 (1)	0.111
	Mean±SD	10.14±13.42	3.44±19.65	
	[c]p	0.001**	0.546	

CrCl: Creatinine clearance, AKI: Acute kidney injury, Preop.: Preoperative, Perop.: Peroperative, Postop.: Postoperative, Min: Minimum, Max: Maximum, SD: Standard deviation, Mann-Whitney U test, Friedman test, Wilcoxon signed ranks test, **p<0.01

Table 3. Comparison of operative data of AKI (-) and AKI (+) groups

		AKI (-) (n=65)	AKI (+) (n=19)	p
Cross-clamp time (min)	Min-max (median)	25-154 (62)	37-162 (67)	[a]0.556
	Mean±SD	73.49±32.06	78±36.01	
CPB duration (min)	Min-max (median)	40-276 (86)	56-238 (94)	[a]0.490
	Mean±SD	100.71±42.58	110.42±51.78	
Body temperature (C)	Min-max (median)	28-34 (32)	28-32 (32)	[a]0.003**
	Mean±SD	31.66±1.09	30.63±1.77	
Number of ES transfusions (%)		60 (92.3)	18 (94.7)	[c]1.000

AKI: Acute kidney injury, Min: Minimum, Max: Maximum, SD: Standard deviation, CPB: Cardiopulmonary bypass, ES: Erythrocyte suspension, Mann-Whitney U test, Fisher's exact test, **p<0.01

MV, ICU durations and the presence of cardiac arrest were not significantly different between the groups (p>0.05). The duration of hospitalization in the AKI (+) group was significantly higher than the AKI (-) group (p=0.004; p<0.01). Reintubation, AV block and inotropic support status were not significantly different between the groups (p>0.05). RRT rate (21.1%) of AKI (+) group was significantly higher than AKI (-) group (p=0.009; p<0.01). The mortality rate in the AKI (+) group was significantly higher than that in the AKI (-) group (p=0.035; p<0.05) (**Table 4**).

DISCUSSION

AKI describes a broad process that can progress from reversible loss of renal function to permanent kidney damage. There are many definitions and the RIFLE and pRIFLE classifications are used for standardization.

The pRIFLE classification provides the definition and classification of AKI in the pediatric group. In the past, the diagnosis of AKI was made by an increase in serum creatinine level, but nowadays this classification can also be used to grade the damage. Catching and treating AKI at a reversible stage significantly reduces the morbidity and mortality of the patient.

AKI is a serious complication after cardiac surgery. Decreased intraoperative renal blood flow, development of postoperative low flow syndrome and decreased autoregulation are the main reasons for AKI, and cyanosis, young age, cardiac volume changes and the presence of a single ventricle also contribute to decreased renal function.[4-6] Intraoperative CPB is also closely associated with morbidity and mortality.

In our study group, AKI was detected in 22% (n=19) patients with the pRIFLE classification, whereas this rate was 51% in the study by Scott I. Aydın et al.[7] using the same classification. The exclusion of patients with complicated surgeries other than VSD and AVSD in our study group and the fact that the proportion of patients with a mean age of <1 month was 4.7% (n=4) in our study, whereas it was 62.2% in their study constitute the main reason. The immaturity of the renal tubules in the neonatal group, inflammation caused by CPB and inadequate response to ischemic reperfusion damage increase the likelihood of renal damage in this group.

Although there was no statistical difference in the mean age of the patients between our patient groups who developed AKI and those who did not develop AKI, the most common age distribution in the AKI (+) group was around 1 year of age. In similar studies by Toth[8] and Zappitelli et al.,[9] the rate of AKI development was found to be higher in patients aged 1 year and younger.

Sami Kallel et al.[10] found a significant effect of CPB duration and degree of hypothermia on the development of AKI. In our study, no significant difference was found between CPB durations, whereas body temperature was found to be significantly lower in the AKI (+) group. The fact that VSD correction operations were performed in a shorter period of time and renal perfusion was sufficient caused the CPB duration to be insignificant in that group. Hypothermia increases the risk of AKI independent of the type of congenital heart disease.

Ricc et al.[11] found that the length of stay in MV and ICU was longer in patients with AKI (+) than in patients with AKI (-). Similar results were found in our study and no statistically significant difference was found. The duration of hospitalization in the AKI (+) group was found to be significantly higher.

In terms of postoperative complications, 17.8% (n=15) of our patients needed reintubation and 5.9% (n=5) developed cardiac arrest during postoperative follow-up. Stanimir et al.[12] observed that 28.4% of pediatric patients who underwent cardiac surgery needed postoperative reintubation and attributed this to diaphragmatic paralysis due to phrenic nerve injury during the operation. The fact that our patient group did not undergo a complex surgery caused this rate to be low. Joan Fernando et al.[13] reported a 6.5% rate of cardiac arrest after cardiac surgery, which is consistent with our study.

The incidence of heart block after pediatric cardiac surgery has been reported between 1-3% and has been associated with surgery close to the AV node.[14] In our study, AV block was observed with a rate of 4.6% (n=3), which is higher compared to other studies because surgery was performed close to the AV node.

In our study group, 6% (n=5) patients needed RRT. In the study by Zaccaria et al.[15] 8.1% RRT was performed, which supports our study.

Table 4. Comparison of postoperative characteristics of AKI (-) and AKI (+) groups

		AKI (-) (n=65)	AKI (+) (n=19)	p
MV duration (days)	Min-max (median)	1-25 (2)	1-54 (3)	[a]0.091
	Mean±SD	4.31±5.58	13.26±18.18	
ICU duration (days)	Min-max (median)	1-36 (3)	1-60 (5)	[a]0.106
	Mean±SD	7.11±8.18	16.26±19.09	
Duration of hospital stay (days)	Min-max (median)	5-81 (12)	7-150 (27)	[a]0.004**
	Mean±SD	16.18±12.52	36.26±34.70	
Cardiac arrest; n (%)		2 (3.1)	3 (15.8)	[c]0.074
Reintubation; n (%)		9 (13.8)	6 (31.6)	[c]0.094
AV block; n (%)		3 (4.6)	0 (0)	[c]1.000
Inotrope support; n (%)		51 (78.5)	17 (89.5)	[c]0.506
RRT; n (%)		1 (1.5)	4 (21.1)	[c]0.009**
Mortality; n (%)	Discharged	64 (98.5)	16 (84.2)	[c]0.035*
	Ex	1 (1.5)	3 (15.8)	

AKI: Acute kidney injury, MV: Mechanical ventilation, ICU: Intensive care unit, AV: Atrio ventricular, RRT: Renal replacement therapy, Ex: Excitus, Mann-Whitney U test, Fisher's exact test, **p<0.01, *p<0.05

Many studies have reported that patients with AKI, especially those undergoing pediatric cardiac surgery and hospitalized in the pediatric intensive care unit, have 3-4 times higher mortality.[16] In our study, total mortality was found to be 4.8% (n=4), 1.5% (n=1) of which was in the AKI (-) group and 15.8% (n=3) in the AKI (+) group, which is consistent with the literature.

Limitations

The most important limitations of our study include the lack of more congenital heart disease types and the lack of larger series. Prospective studies with larger series are needed for more definite results.

CONCLUSION

AKI is closely associated with morbidity and mortality and is more related to the degree of damage. Patients detected in early stages can be prevented from progression to AKI with appropriate treatments. Therefore, it is important to determine the degree of damage.[17] It is recommended to use an inexpensive, easily applicable method such as pRIFLE in the evaluation and grading of AKI, especially in patients undergoing pediatric cardiac surgery.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Haydarpaşa Numune Training and Research Hospital Clinical Researches Ethics Committee (Date: 09.05.2016, Decision No: HNEAH-KAEK 2016/KK/50).

Informed Consent

All parents signed an explicit and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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