Risk Factors and Outcome of Acute Kidney Injury after Congenital Heart Surgery: A Prospective Observational Study

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Abstract

Backgrounds and Aims: Acute kidney injury (AKI) is a frequent event after congenital heart surgery with increased mortality and morbidity. We investigated frequency, risk factors, and associated morbidity and mortality of AKI after pediatric cardiac surgery at a single institution. **Methods:** Children undergoing congenital heart surgery from March 2013 to February 2016 were assessed for development of AKI based on modified pediatric Risk, Injury, Failure, Loss, and End-stage renal disease criteria. They were also investigated for predictive risk factors, associated mortality, and morbidity including duration of mechanical ventilation, Intensive Care Unit (ICU), and hospital length of stay. **Results:** Five hundred and nineteen patients were recruited during the study period including 259 (49.9%) males and 260 (50.1%) females. AKI was seen in 150 (28.9%) patients including 101 (67.3%), 42 (28%), and 7 (4.7%) cases with risk, injury, and failure stages, respectively. Patients with AKI had longer ventilation time ($P = 0.002$), ICU ($P = 0.05$), and hospital ($P = 0.56$) stay. Mortality was seen in 31 (2.7%) and 44 (11.9%) patients with and without AKI, respectively ($P = 0.01$). After multivariable logistic regression, there was an association between AKI and preoperative abnormal levels of creatinine (adjusted odds ratio [aOR] = 0.47, 95% confidence interval [CI] 0.22–1.01; $P = 0.05$), presence of cyanotic heart disease (aOR = 1.97, 95% CI = 1.15–3.2; $P = 0.01$), duration of surgery (aOR = 1.05/10 min, 95% CI = 1.01–1.08; $P = 0.007$), and elevated lactate level (aOR = 1.14, 95% CI = 1.03–1.3; $P = 0.01$). **Conclusion:** The presence of cyanotic heart disease, duration of surgery, elevated postoperative lactate level, and likely preoperative creatinine level were independent risk factors for the development of AKI after congenital heart surgery.

Keywords: Acute kidney injury, congenital heart surgery, outcome, prediction

Introduction

Acute kidney injury (AKI) is a significant and common complication after pediatric cardiac surgery. The incidence has been reported from 9.6% to 64.6%[1-4] based on the definition of AKI and age group. It is associated with increased morbidity and mortality.[5-8] It also increases duration of mechanical ventilation,[1,9] Intensive Care Unit (ICU) and hospital length of stay,[7,10] and resource utilization.[5] The increased mortality depends on severity of AKI. Renal replacement therapy (RRT) is needed in 1.6%–7.7% after cardiac surgery that further increases mortality in these patients.[11-14]

A modified version of pediatric Risk, Injury, Failure and Loss, and End-Stage (p-RIFLE) has been proposed for standardization of definition of AKI that uses either a decrease in glomerular filtration rate (GFR) or urine output.

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A number of perioperative risk factors have been suggested as predictors of AKI associated with cardiac surgery. These include younger age, prolonged pump time,[1,10] pump failure, lower weight, sepsis,[3,10] need for extracorporeal membrane oxygenation (ECMO),[7] and prolonged ventilator requirement.[3]

The objective of this study was to investigate the development of AKI after congenital heart surgery at a single university-affiliated institution. The primary outcome was to determine the incidence of AKI. The secondary outcomes included investigation of risk factors and outcome including

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duration of mechanical ventilation, ICU and hospital length of stay, and inhospital mortality.

Methods

In a prospective observational study, we enrolled consecutive children undergoing congenital heart surgery for either palliation or correction with or without cardiopulmonary bypass (CPB) from March 2013 to February 2016 at a university-affiliated Hospital, Mashhad, Iran. Inclusion criteria were patients under 18 years admitted to cardiac ICU after any kind of cardiac surgery. Patients were excluded if they had preexisting end-stage renal disease, a history of renal transplant, or if no documented baseline serum creatinine was available.

Preoperative variables were age at the time of surgery, weight, preoperative hemoglobin, white blood cell (WBC), urea, creatinine, and pulmonary hypertension.

Surgical characteristics including type of surgery, use of CPB, duration of surgery, pump time, cross-clamp time, and intraoperative events including excessive bleeding, life-threatening arrhythmia, and intraoperative transfusion were recorded.

The patients were assessed postoperatively for highest lactate level and inotrope score ([dopamine + dobutamine] + [10] milrinone + [100] [epinephrine + norepinephrine + phenylephrine], μg/kg/min), WBC on postoperative day one, duration of mechanical ventilation more than 24 h, ICU and hospital length of stay, low cardiac output, need for RRT, intraoperative events, and inhospital death. RRT was used in case of refractory acid-base and electrolyte disorders, signs of hypervolemia, or uremic brain (defined as decreased level of consciousness assuming to be related to hyperuremia). RACHS-1 score was used to categorize surgeries according to their complexity.

AKI was defined according to p-RIFLE criteria that are based on postoperative fall in GFR compared to baseline as R:risk (a decrease in GFR by 25%), I:injury (a decrease in GFR by 50%), F: failure (a decrease in GFR by 75% or <35 mL/min/1.73 m^2), and L:loss (loss of renal function >4 weeks). GFR was calculated using the following equation: Estimated glomerular filtration rate (mL/min/1.73 m^2) = k × height (cm)/plasma creatinine (mg/dL) where k = 0.55; if <1 year, 0.45; if male and older than 13 years, 0.7.

Urine output was not used as a criterion for renal failure in our study. Recovery was defined as return of GFR to a level with <25% drop compared to preoperative level.

Low output syndrome was defined as hepatomegaly, oliguria, tachycardia, a fall in systolic blood pressure under the age-related normal value, a base excess lower than _4 mmol/L, or lactate level above 2 mmol/L in 2 consecutive arterial blood samples.

The patients were under standard monitoring and meticulous attention by critical care team including an intensivist, a critical care fellow, and anesthesiology residents to maintain cardiopulmonary, cerebral, and renal function. Patients were weaned from mechanical ventilation and extubated according to a standardized protocol.

Statistical analysis

Means and standard deviation were used for normal distribution variables and median and interquartile range for otherwise. Frequencies and percentages were used for categorical variables. The Student's t-test or the Mann–Whitney test was used for comparison of continuous variables between patients with and without AKI. Chi-square test or Fisher's exact test was used for categorical variables.

Binary logistic regression model was constructed for assessment of independent effect of each variable on the prediction of occurrence of AKI. Variables with $P < 0.1$ in univariable analysis consisting ventilation time, duration of ICU stay, preoperative creatinine level, history of cyanotic heart disease, intraoperative bleeding, duration of surgery, level of albumin, and lactate level were included in multivariable analysis. Model goodness of fit was evaluated by the Hosmer–Lemeshow test. Receiver operating characteristic curve was used for prediction of sensitivity and specificity of cutoff point of significant variables. Statistical significance was considered as $P < 0.05$. The statistical analysis was performed using SPSS® version 16 (IBM SPSS, Chicago, IL, USA).

Results

Five hundred and nineteen patients were included during the study period. There were 259 (49.9%) males and 260 (50.1%) females with mean age of 40.3 ± 43.7 and 40.07 ± 45.9 and median 24 and 22 months for males and females, respectively. Demographic data, types of surgery, and surgical characteristics of patients are presented in Tables 1-3, respectively.

AKI was seen in 150 (28.9%) patients. Of these, 101 (67.3%), 42 (28%), and 7 (4.7%) cases developed risk, injury, and failure, respectively. Three patients needed RRT. AKI occurred in 72 (50.3%), 44 (30.8%), and 12 (8.4%) patients on day 1, 2, and 3, respectively. Recovery was seen in 47 (63.5%), 13 (17.6%), and 7 (9.5%) patients on the 1st, 2nd, and 3rd day, respectively. The incidence of AKI based on surgical complexity using RACHS-1 score is presented in Table 4.

Thirty-one (2.7%) and forty-four (11.9%) patients with and without AKI died (P = 0.01). Mortality was seen in 13 (13%), 12 (28.6%), and 6 (85.7%) cases in those with risk, injury, and failure, respectively (P < 0.001). All three patients who needed dialysis died.

Ventilation time was 1164 ± 2402 min in the AKI group and 496 ± 1300 min in the non-AKI group (P = 0.002). Duration of ICU stay was 4.45 and 3.39 days in patients with and without AKI, respectively (P = 0.05). Hospital length of stay was 8.82 and 8.04 days in patients with and without AKI, respectively (P = 0.56). Association of RACHS-1 score and AKI is displayed in Table 5.

Table 1: Demographic data and patients' characteristics

Variables	AKI (n=150)	No AKI (n=369)	P
Age	18 (8-48)	24 (8-60)	0.3
Age categories			0.6
Neonates	10 (6.7%)	20 (5.4%)	
Infants	57 (38%)	125 (34.1%)	
Children	59 (39.3%)	149 (40.6%)	
Adolescent	24 (16%)	73 (19.9%)	
Weight (kg)	9 (6-14)	10 (5-15)	0.24
Weight <10 kg	87 (58.8%)	191 (52%)	0.16
Gender (male)	78 (52%)	181 (49.1%)	0.56
Anemia	35 (23.3%)	106 (28.8%)	0.2
Preoperative creatinine level (mg/dL)	0.47 (0.17)	0.55 (0.15)	<0.001
Pulmonary hypertension	30 (20%)	79 (21.5%)	0.6
Cyanotic heart disease	68 (45.3%)	102 (27.7%)	<0.001
RACHS categories			
1	22 (14.7%)	96 (26%)	0.04
2	81 (54%)	164 (44.5%)	
3	44 (29.3%)	104 (28.2%)	
4	3 (2%)	5 (1.4%)	
5	0	0	
6	0	0	

Table 2: Type of surgery

Surgery	Frequency
Arterial switch	2 (0.4%)
Aortic valve repair	3 (0.6%)
Atrial septal defect repair	67 (12.9%)
Atrial septostomy	4 (0.8%)
Atrioventricular canal	25 (4.8%)
Aortic valve replacement	5 (1%)
BT shunt	31 (6%)
Central shunt	12 (2.5%)
Coarctation of aorta	15 (2.9%)
Double aortic arch	2 (0.4%)
Fontan procedure	2 (0.4%)
Glenn shunt	14 (2.7%)
Hemograft	4 (0.8%)
Interrupted aorta	1 (0.2%)
Mitral valve repair	3 (0.6%)
Mitral valve replacement	1 (0.2)
Pulmonary artery banding	54 (10.4%)
Partial anomalus pulmonary vein connection	2 (0.4%)
PDA closure	62 (12%)
Pulmonary valve replacement	11 (2.1%)
Sub-aotic web resection	3 (0.6%)
Sub-pulmonary valve stenosis repair	3 (0.6%)
Total anomalus pulmonary vein connection	5 (1%)
Total correction of Ebstein anomaly	4 (0.8%)
Total correction of tetralogy of Fallot	91 (17.5%)
Correction of truncus arteriosus	1 (0.2%)
Tricuspid valve repair	1 (0.2%)
Tricuspid valve replacement	1 (0.2%)
Ventricular septal defect repair	92 (17.7%)
Total	519 (100%)

Table 3: Surgical characteristics of patients

Variables	AKI (n=150)	No AKI (n=369)	P
Duration of surgery (minutes)	192 (150-240)	180(140-215)	0.001*
Cardiopulmonary bypass	96 (64%)	227 (61.5%)	0.61
Pump duration (minutes)	31 (0-60)	21 (0-50)	0.13*
Cross clamp time (minutes)	20.5 (0-36)	10.5 (0-40)	0.16*
Intraoperative transfusion	72 (48%)	154 (41.8%)	0.2**
Intraoperative events	2 (1.3%)	3 (0.8%)	0.6**
Intraoperative Hemorrhage	1 (0.7%)	17 (4.6%)	0.03¥

*Mann-Whitney U test, **Chi square test, ¥Fisher's exact test, Data are presented as median and 25-75 percentile or numbers and percent

Table 4: Frequency of AKI according to RACHS-1 score

Score	Frequency	AKI
1	118	22 (18.6%)
2	243	81 (33.3%)
3	148	44 (29.7%)
4	8	3 (37.5%)
5	0	0 (0)
Total	519	150 (28.9%)

Data are presented as numbers (percentile)

Table 5: Univariate analysis of RACHS-1 score on predicting AKI

Score	OR (CI)	P
1	1	
2	2.15 (1.26-3.67)	0.005
3	1.84 (1.03-3.3)	0.03
4	2.61 (0.58-11.7)	0.21

Using multivariable logistic regression, we found the following variables as independent risk factor for the development of AKI.

Preoperative abnormal creatinine level (adjusted odds ratio [aOR] = 0.47, P = 0.05) and cyanotic heart disease (aOR = 1.97, P = 0.01) were independent predictors of AKI occurrence [Table 6]. There was an association between intraoperative bleeding and duration of surgery and AKI. However, after multivariable logistic regression, only duration of surgery aOR = 1.05/10 min (P = 0.007) was found to be an independent predictor for AKI [Table 6]. Of postoperative variables, only a high lactate level (aOR = 1.13, P = 0.01) was an independent predictor for development of AKI [Table 6].

Operation time longer than 137 min had a sensitivity of 82% and specificity of 76% for prediction of AKI (area under curve [AUC] = 59%, P = 0.02). Lactate level of higher than 1.35 had a sensitivity of 81% and specificity of 74% for prediction of AKI (AUC = 59%, P = 0.02) [Figure 1]. Young age, weight <10 kg, preoperative albumin level, preoperative anemia, pulmonary hypertension, use of high dose inotropes, and reoperation were not significantly associated with AKI.

Table 6: Perioperative risk factors associated with AKI after congenital heart surgery

Variables	OR (CI)	*P**
Age	1.005 (0.99-1.01)	0.3
Sex (male)	1.13 (0.74-1.71)	0.55
Weight	1.003 (0.96-1.04)	0.87
preoperative creatinine level	0.47 (0.22-1.01)	0.05
Preoperative Hb level	1.07 (0.98-1.18)	0.09
Cyanotic heart disease	1.97 (1.15-3.2)	0.01
Pulmonary hypertension	0.95 (0.57-1.6)	0.86
Pump duration (per 10 minute)	1.02 (0.98-1.2)	0.73
Cross clamp time (per 10 minute)	1. 02 (0.97-1. 1)	0.78
Duration of surgery (per 10 minute)	1.05 (1.01-1.08)	0.007
Intraoperative bleeding	0.13 (0.1-1.008)	0.051
Intraoperative transfusion	1.17 (0.77-1.7)	0.45
On pump surgery	1.47 (0.85-2.52)	0.16
ICU stay	1.02 (0.95-1.1)	0.48
Lactate after operation	1.14 (1.03-1.3)	0.01
Base deficit	0.97 (0.93-1.02)	0.33
Fluid balance	1.001 (0.98-1.008)	0.86
Weaning time	1.001 (0.99-1.003)	0.08
Mechanical ventilation >24 hours	2.74 (0.45-16.2)	0.27

*Binary logistic multivariable model

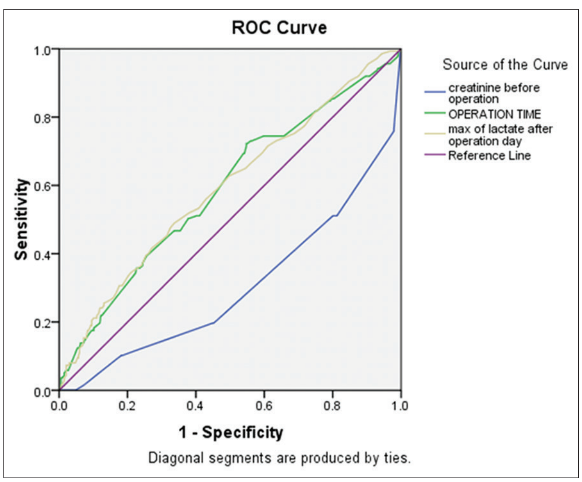

Figure 1: Receiver operating characteristic curve for prediction of sensitivity and specificity of cutoff point for creatinine

Discussion

Our study revealed that AKI was seen in 28.9% of patients following congenital heart surgery and was associated with increased morbidity and mortality. We also found that preoperative creatinine level, presence of cyanotic heart disease, duration of surgery, and postoperative lactate level were independent risk factors for AKI.

A number of mechanisms have been proposed as the etiology for development of AKI after congenital heart surgery including altered renal blood flow, hypoperfusion, inflammation and loss of pulsatile flow, ischemia, decreased autoregulation, and nephrotoxic drugs including antibiotics.

Similar to Cardoso *et al*.,[9] we found that higher postoperative lactate level, a sign of hypoperfusion, is an independent risk factor for AKI confirming hypoperfusion as a proposed mechanism of AKI.

In line with findings of other reports,[1,9] patients who developed AKI in our study had a higher baseline preoperative creatinine level. However, the association was not very strong and is not clinically significant (aOR = 0.47, $P = 0.05$). This discrepancy can be explained by different age group population and use of CPB in these studies.

Unlike other studies,[1,10] we did not find an association between younger age than 12 months and weight <10 kg and development of AKI. Aydin *et al*.[1] suggested intrinsic immaturity of neonatal renal tubules and its inability to adapt to inflammatory and ischemic changes induced by CPB as the possible mechanism. In contrast, our patients' population was not limited to infancy and use of CPB.

Similar to other studies, we found that AKI is associated with increased mortality and morbidity.[1,15,16] Even those with mild drop in GFR (risk score) had higher mortality than those without AKI. The mortality increased to 18.8%, 50%, and 85.7% in those with risk, injury, and failure scores, respectively, indicating an increase in mortality as the severity of AKI worsens.

Our finding is in keeping with other studies showing that AKI increases duration of mechanical ventilation, ICU, and hospital length of stay.[9,17,18] Nevertheless, the difference for ICU and hospital length of stay was not statistically significant. It seems that factors other than AKI might affect these morbidities.

Unlike Sethi *et al*.[10] and Aydin *et al*.,[1] we did not find a strong association between duration of CPB and development of AKI. This can be explained by shorter pump time in our series compared to these reports.

Our study had a few limitations. First, we did not know the baseline preoperative blood pressure of our patients and did not investigate the changes in comparison to intraoperative ones. This might affect the incidence of AKI as is reported in adults.[19,20] However, to our best of knowledge, there is no such report in pediatric population. Second, this was a single center study with limited resources that can affect patients' management and hence the findings cannot be generalized. Third, there was a vast range of different cardiac surgeries in our survey that makes it difficult to correlate type of surgery to development of AKI because of small sample size. Fifth, we did not use urine output as a definition for AKI since many patients received diuretics and this might affect accuracy of urine output as a variable for the definition of AKI.

Conclusion

We found a significant association between development of AKI and presence of cyanotic heart disease, duration of surgery, elevated postoperative lactate level, and likely preoperative creatinine level after congenital heart surgery.

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Conflicts of interest

There are no conflicts of interest.

References

1. Aydin SI, Seiden HS, Blaufox AD, Parnell VA, Choudhury T, Punnoose A, *et al.* Acute kidney injury after surgery for congenital heart disease. Ann Thorac Surg 2012;94:1589-95.
2. Sugimoto K, Toda Y, Iwasaki T, Shimizu K, Kanazawa T, Muto N, *et al.* Urinary albumin levels predict development of acute kidney injury after pediatric cardiac surgery: A prospective observational study. J Cardiothorac Vasc Anesth 2016;30:64-8.
3. Krastins J, Straume Z, Auzins J, Petersons A, Petersons A. Open heart surgery associated acute kidney injury in children. Acta Chir Latviensis 2013;13:37-42.
4. Sethi SK, Kumar M, Sharma R, Bazaz S, Kher V. Acute kidney injury in children after cardiopulmonary bypass: Risk factors and outcome. Indian Pediatr 2015;52:223-6.
5. Tóth R, Breuer T, Cserép Z, Lex D, Fazekas L, Sápi E, *et al.* Acute kidney injury is associated with higher morbidity and resource utilization in pediatric patients undergoing heart surgery. Ann Thorac Surg 2012;93:1984-90.
6. Lopez-Delgado JC, Esteve F, Torrado H, Rodríguez-Castro D, Carrio ML, Farrero E, *et al.* Influence of acute kidney injury on short- and long-term outcomes in patients undergoing cardiac surgery: Risk factors and prognostic value of a modified RIFLE classification. Crit Care 2013;17:R293.
7. Alabbas A, Campbell A, Skippen P, Human D, Matsell D, Mammen C, *et al.* Epidemiology of cardiac surgery-associated acute kidney injury in neonates: A retrospective study. Pediatr Nephrol 2013;28:1127-34.
8. dos Santos El Halal MG, Carvalho PR. Acute kidney injury according to pediatric RIFLE criteria is associated with negative outcomes after heart surgery in children. Pediatr Nephrol 2013;28:1307-14.
9. Cardoso B, Laranjo S, Gomes I, Freitas I, Trigo C, Fragata I, *et al.* Acute kidney injury after pediatric cardiac surgery: Risk factors and outcomes. Proposal for a predictive model. Rev Port Cardiol 2016;35:99-104.
10. Sethi SK, Goyal D, Yadav DK, Shukla U, Kajala PL, Gupta VK, *et al.* Predictors of acute kidney injury post-cardiopulmonary bypass in children. Clin Exp Nephrol 2011;15:529-34.
11. Alkan T, Akçevin A, Türkoglu H, Paker T, Sasmazel A, Bayer V, *et al.* Postoperative prophylactic peritoneal dialysis in neonates and infants after complex congenital cardiac surgery. ASAIO J 2006;52:693-7.
12. Boigner H, Brannath W, Hermon M, Stoll E, Burda G, Trittenwein G, *et al.* Predictors of mortality at initiation of peritoneal dialysis in children after cardiac surgery. Ann Thorac Surg 2004;77:61-5.
13. Conlon PJ, Stafford-Smith M, White WD, Newman MF, King S, Winn MP, *et al.* Acute renal failure following cardiac surgery. Nephrol Dial Transplant 1999;14:1158-62.
14. Fleming F, Bohn D, Edwards H, Cox P, Geary D, McCrindle BW, *et al.* Renal replacement therapy after repair of congenital heart disease in children. A comparison of hemofiltration and peritoneal dialysis. J Thorac Cardiovasc Surg 1995;109:322-31.
15. Ricci Z, Di Nardo M, Iacoella C, Netto R, Picca S, Cogo P, *et al.* Pediatric RIFLE for acute kidney injury diagnosis and prognosis for children undergoing cardiac surgery: A single-center prospective observational study. Pediatr Cardiol 2013;34:1404-8.
16. Watkins SC, Williamson K, Davidson M, Donahue BS. Long-term mortality associated with acute kidney injury in children following congenital cardiac surgery. Paediatr Anaesth 2014;24:919-26.
17. Alkandari O, Eddington KA, Hyder A, Gauvin F, Ducruet T, Gottesman R, *et al.* Acute kidney injury is an independent risk factor for pediatric Intensive Care Unit mortality, longer length of stay and prolonged mechanical ventilation in critically ill children: A two-center retrospective cohort study. Crit Care 2011;15:R146.
18. Gil-Ruiz Gil-Esparza MA, Alcaraz Romero AJ, Romero Otero A, Gil Villanueva N, Sanavia Morán E, Rodríguez Sánchez de la Blanca A, *et al.* Prognostic relevance of early AKI according to pRIFLE criteria in children undergoing cardiac surgery. Pediatr Nephrol 2014;29:1265-72.
19. Ono M, Arnaoutakis GJ, Fine DM, Brady K, Easley RB, Zheng Y, *et al.* Blood pressure excursions below the cerebral autoregulation threshold during cardiac surgery are associated with acute kidney injury. Crit Care Med 2013;41:464-71.
20. Kanji HD, Schulze CJ, Hervas-Malo M, Wang P, Ross DB, Zibdawi M, *et al.* Difference between pre-operative and cardiopulmonary bypass mean arterial pressure is independently associated with early cardiac surgery-associated acute kidney injury. J Cardiothorac Surg 2010;5:71.