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Incidence, risk factors, and outcomes of acute kidney injury after pediatric cardiac surgery – a prospective multicenter study

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Abstract

Objective—To determine the incidence, severity and risk-factors of AKI in children undergoing cardiac surgery for congenital heart defects.

Design—Prospective observational multicenter cohort study

Setting—Three pediatric intensive care units at academic centers.

Patients—311 children between the ages of 1 month and 18 years undergoing pediatric cardiac surgery.

Interventions—None.

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Measurements and Main Results—AKI was defined as a ≥ 50% increase in serum creatinine from the pre-operative value. Secondary outcomes were length of mechanical ventilation, length of ICU and hospital stays, acute dialysis, and in-hospital mortality. The cohort had an average age of 3.8 years with 45% females and was mostly white (82%). One third had prior cardiothoracic surgery, 91% of the surgeries were elective, and almost all patients required cardiopulmonary bypass (CPB). AKI occurred in 42% (130 patients) within 3 days after surgery. Children ≥ 2 years old and less than 13 years old had 72% lower likelihood of AKI (adjusted OR: 0.28, 95% CI: 0.16, 0.48), and patients 13 years and older had 70% lower likelihood of AKI (adjusted OR: 0.30, 95% CI: 0.10, 0.88) compared to patients less than 2 years old. Longer CPB time was linearly and independently associated with AKI. Development of AKI was independently associated with prolonged ventilation and with increased length of hospital stay.

Conclusions—AKI is common after pediatric cardiac surgery and is associated with prolonged mechanical ventilation and increased hospital stay. CPB time and age were independently associated with AKI risk. CPB time may be a marker for case complexity.

Keywords

Renal Insufficiency, Acute; Heart Defects, Congenital; Cardiac Surgical Procedures; Intensive Care Units, Pediatric; Cardiopulmonary Bypass; Risk Factors

Introduction

Acute kidney injury (AKI) is common after pediatric cardiac surgery, occurring in 5 – 33%, with an associated mortality of 20 – 79% depending on the AKI definition used in the study (1). Retrospective studies suggest that the presence of pediatric cardiac surgery-associated AKI (CS-AKI) is correlated with longer length of hospital stay (2) and may be associated with the development of chronic kidney disease (3–5).

Evidence from the literature implies that the risk factors for AKI in pediatric cardiac surgery include elevated preoperative serum creatinine (SCr), age less than 1 year old, cyanotic lesions, prolonged cardiopulmonary bypass (CPB) time and postoperative low cardiac output syndrome (6–13). Although some of these studies were large, they were limited by their retrospective design or single center enrollment over many years. These and more recent studies were also limited by AKI definitions which varied across the studies (2, 12–19). Fortunately, consensus-based, standardized AKI definitions are now available for use in children (20–22).

The National Institute of Health (NIH) and American Society of Nephrology (ASN) recently called for the development of more efficient diagnostic tools for AKI. This has led to a flurry of activity in the development of novel biomarkers for more sensitive and earlier diagnosis of AKI (23). With the advent of these biomarkers there is a need to clearly define AKI disease patterns in the pediatric heart surgery population in order to understand how to apply these early diagnostic tests in the clinical and research setting. Additionally, understanding of the epidemiology of AKI, the modifiable and non-modifiable risk factors and to what extent AKI is associated with short-term outcomes in our population will help to guide future interventional studies.

Thus, we performed a prospective, observational, multicenter cohort study to determine the rate, severity, risk-factors and characteristics of cardiac surgery associated AKI (CS-AKI) in children undergoing cardiac surgery using the new consensus definitions.

Methods

Study cohort

The cohort of children was prospectively enrolled from 3 pediatric sites: Cincinnati Children's Hospital Medical Center, Montreal Children's Hospital, and Yale New-Haven Children's Hospital as part of the consortium investigating new biomarkers in AKI known as the Translational Research Investigating Biomarker Endpoints in Acute Kidney Injury (TRIBE-AKI). Enrollment started in July 2007, November 2007, and November 2008, respectively, and completed in December 2009. Cincinnati has a dedicated pediatric cardiac care unit (CCU) with approximately 225 cardiopulmonary bypass cases annually and both Montreal and Yale have mixed medical surgical units including cardiac patients with approximately 60 cardiopulmonary bypass cases annually. This study was approved by the Institutional Review Board or Research Ethics Board of each institution. Written informed consent from legal guardians and assent from patients were obtained before enrollment.

All patients less than 18 years of age undergoing cardiac surgery with cardiopulmonary bypass were eligible for the study. Exclusion criteria included history of prior renal transplantation, dialysis requirement, or participation in a conflicting research study. We utilized the Risk Adjustment for Congenital Heart Surgery 1 (RACHS-1) consensus-based scoring system to categorize the complexity of surgery (24). This method of risk stratification is a widely accepted tool for the evaluation of differences in outcomes of surgery for congenital heart disease. We only retained children older than 1 month for this study, since defining AKI in neonates is unclear and likely different than the AKI definition in older children (25).

AKI and Other Outcomes

AKI was defined as rise in SCr of 50% or more from preoperative baseline within the first 7 days after surgery. This definition and severity of AKI was based on the AKIN Staging system, which has been described for use in previous pediatric studies (26). Baseline SCr was obtained preoperatively, either in the preoperative clinic (usually within 1 week of surgery) or on the day of surgery. Postoperative serum creatinine values were routinely available on arrival to the ICU (day 1) and daily for the first five days after surgery as part of routine clinical care. We also recorded peak serum creatinine during hospital stay and serum creatinine before discharge on all patients. Each patient's pre- and postoperative serum creatinine measurements were performed at the same clinical laboratory. AKI resolution was defined as serum creatinine returning to less than 1.5 times the baseline serum creatinine.

Outcomes evaluated were mechanical ventilation longer than 2 or 7 days, length of intensive care unit (ICU) stay, length of hospital stay, and in hospital mortality.

Clinical Variables

Since 2002, the Society of Thoracic Surgeons' (STS) has collected international outcomes data for congenital heart surgery in the Congenital Heart Surgery Database. There are 95 participating cites. They have created definitions for important variables surrounding congenital heart surgery. Definitions for our variables are from their data specifications version 3.0 (http://www.sts.org/sections/stsnationaldatabase/new/). If the STS did not provide a definition for variable we were interesting in, the TRIBE-AKI collaborators created a consensus definition.

Preoperative variables included age at operation, sex, weight, previous cardiac surgery, history of preoperative shock, mechanical ventilator support, mechanical circulatory support, RACHS-1 category, cardiac catheterization < 72 hours prior to the operation, estimated glomerular filtration rate (eGFR) by updated Schwartz equation (27), and categorization of the surgery as emergent, urgent, or elective. Pre-operative urine was analyzed by dipstick (Siemens Multistix®) to assess for any undetected kidney disease manifested by frank proteinuria and hemturia.

Intraoperative variables included CPB time, need for and duration of aortic cross clamp, need for and duration of circulatory arrest, and length of intraoperative hypotension, defined as mean arterial blood pressure (MAP) less 50mmHg (or if < 1 years old MAP < 40 mmHg or MAP < 50 mmHg with inotropic support: epinephrine > 0.1 mcg/kg.min, dopamine > 10mcg/kg/min, any vasopressin or norepinephrine use). This intraoperative hypotension cutoff was based on a consensus discussion amongst our multidisciplinary team recognizing that these blood pressure cut-offs may be adequate in the setting of pediatric cardiac surgery and may not necessarily correlate with inadequate kidney perfusion or oxygen delivery.

Postoperative variables included unplanned reoperation, cardiopulmonary arrest, mechanical ventilation for greater than 2 or 7 days after surgery, need for mechanical circulatory support (e.g. extracorporeal membrane oxygenation or intraaortic balloon pump), and any inotropic or chronotropic medications (e.g. epinephrine, dopamine, milrinone, etc). Patients who developed AKI underwent additional chart review to determine factors which may lead to AKI such as daily fluid balance, use of radiocontrast, gentamicin or nonsteroidal anti-inflammatory drugs (NSAID). We utilized a postoperative hypotension score based on the cardiovascular portion of the sepsis-related organ failure assessment (SOFA) score (28). This is a 0 to 4 point scoring system where each point must be sustained for more than 2 hours. If mean arterial pressure is less than 70mmHg = 1 point; use of dopamine at ≤ 5 mcg/kg/min, dobutamine, or milrinone at any dose = 2 points; use of dopamine > 5 mcg/kg/min, epinephrine ≤ 0.1 mcg/kg/min, norepinephrine ≤ 0.1 mcg/kg/min, or vasopressin at any dose = 3 ponts; use of dopamine > 15 mcg/kg/min, epinephrine > 0.1 mcg/kg/min, or norepinephrine > 0.1 mcg/kg/min = 4 points.

Statistical Analyses

Univariate analyses were performed using t-test or Wilcoxon rank sum for continuous variables and χ^2 or Fisher's exact test for categorical variables. Colinearity was assessed and those with high correlation (r > 0.45) were eliminated from the multivariate models. Simple and multiple logistic regression models were used to evaluate independent risk factors of AKI. For the multivariate analysis, all significant variables (p < 0.1) from the univariate analyses were utilized in a stepwise approach to create the most parsimonious model (29). Preoperative creatinine value was not added in the analysis due to its strong correlation with age (r = 0.77, p < 0.001). The association of AKI with categorical outcomes was evaluated using multiple logistic regression models controlling for potential confounders. The association of AKI with continuous variables was evaluated using ANOVA models. SAS version 9.1 (SAS Institute, Inc, Cary, NC) was used for the analysis.

Results

Study population and AKI incidence

After application of the inclusion and exclusion criteria, 311 patients were part of the pediatric study cohort (Figure 1). The distribution of cases by study site is shown in Table 1, representing approximately 50% of the eligible cases performed in each center per year. Rate of consent was approximately 75% and the remainder of eligible patients were not approached mostly due to logistical reasons (e.g. unable to approach in time prior to surgery; research team unaware of the scheduled pre-operative clinic). The characteristics of the study population by AKI status are given in Table 1. Mean age of the study cohort was 3.76

years with a range of 33 days to 17 years old. The mean RACHS-1 category was 2.43 with no patients in the RACHS-1 category 5 or 6. Baseline SCr was obtained within 1 day prior to surgery in 70% of patients and within 3 days prior to surgery in 93% of the patients. One child older than 2 years old had eGFR of < 60 ml/min/1.73m^2. AKI occurred in 130 patients (42%) within 3 days of surgery (Table 4). There were no differences in age, gender, CPB time, and incidence of AKI among sites ($p = 0.84$, 0.5, 0.31, and 0.09 respectively).

Characteristics of AKI after Pediatric cardiac Surgery

Of the 130 patients that developed AKI, 37% doubled their SCr and 2% required dialysis within the 7 day period after the operation (Figure 2). More than half of these patients (53%) developed AKI within the first 24 hours after the operation and 97.7% had developed by 48 hours (Figure 2). Serum creatinine peaked after 48 hours of surgery in 78% of the cohort. AKI lasted only one day in 47% of the patients and 11% had not recovered completely and still met the AKI definition by the fourth post-operative day.

In regards to possible etiologies, 87% of the patients who had AKI also had intraoperative hypotension, and many were also exposed to gentamicin (15%) and NSAIDs (56%) postoperatively (Table 4). Few patients in the AKI group had low cardiac output syndrome (6%), sepsis (2%), or urinary tract obstruction (4%).

Using daily fluid balances we calculated 24 hour oliguria as defined by less than 0.5 ml/kg/hr. Based on urine output on the day of surgery, 12 patients (8 in the group that developed AKI and 4 in the group that did not develop AKI) had oliguria. On the first postoperative day 15 patients (7 in the group that developed AKI and 8 in the group that did not develop AKI) had oliguria.

Risks factors associated with AKI

Lower mean age, weight, body surface area and preoperative serum creatinine were all associated with a higher incidence of AKI ($p \leq 0.005$, Table 1) and were also highly correlated with each other. There were no differences in preoperative eGFR, race/ethnicity, sex, history of prior cardiothoracic surgery and urgency of surgery in those with and without AKI.

After adjustment for other variables, younger children were more likely to develop AKI (Table 2). Patients in the 2 to 13 years old age group were 72% less likely to have AKI ($p < 0.0001$) and those in the older age strata of 13 to 18 years were 70% less likely to have AKI ($p = 0.0173$), compared to patients less than 2 years old.

Average RACHS-1 category was also significantly higher in those who developed AKI ($p = 0.02$), however after adjusting for age, site and CPB time this relationship was no longer significant. None of the patients who had RACHS-1 category 1 surgeries developed AKI. 43% and 44% of those with category 2 and 3, respectively, developed AKI, and 75% of patients with RACHS-1 category 4 developed AKI.

Among intraoperative risk factors, average cardiopulmonary bypass time was significantly higher in those who developed AKI ($p < 0.0001$). When we separated CPB time into increasing intervals starting at 60 minutes we found a linear trend of increasing CPB time and percent of patients who develop AKI (Figure 3). After adjustment, patients with CPB time of 91 to 120 minutes had a 2.5 fold greater odds of having AKI (95% CI: 1.08, 5.65). 68% of the patients developed AKI in those that had bypass time > 180 minutes, with a 7.57 fold greater odds of AKI (95% CI: 2.62, 21.92) compared to those with bypass time < 60 minutes. Mean cross clamp time and utilization of circulatory arrest, although higher in AKI, did not reach statistical difference between those who developed AKI and those who did not. However, in our study only 6 patients went through circulatory arrest thus limiting our ability to interpret this variable.

AKI association with outcomes

Thirty percent of patients who developed AKI were mechanically ventilated at 2 days after surgery compared to only 8% without AKI ($p < 0.0001$). Median PICU and hospital stay were 2 and 3 days longer, respectively, in AKI patients (Table 1). After adjustment for covariates, those who developed AKI had 3.2 fold greater odds of requiring mechanical ventilation for longer than 2 days (95% CI: 1.55, 6.52, Table 3). AKI was independently associated with longer length of hospital stay (median 7 vs. 4 days, $p = 0.0097$) and trended towards longer PICU stay (median 4 vs. 2 days, $p=0.08$). Five patients in the AKI group died compared to only 1 death in the non AKI group. In the multivariate analysis, there was a non-statistically significant association of AKI and mortality (adjusted OR: 7.34 95% CI: 0.71, 75.92, $p=0.095$), related to low events in these groups.

Discussion

This is the first multicenter prospective study using the current accepted standard definition of AKI with the intent of examining the risks, characteristics and outcomes of AKI in pediatric cardiac surgery. We found an AKI incidence of 42% in children undergoing heart surgery. Prior to 2005 there were no studies of cardiac surgery associated AKI using the currently accepted definition. These studies used definitions ranging from doubling of serum creatinine to requirement of dialysis. Pederson et al (1) performed one of the larger single center prospective studies enrolling children from 1993 to 2002 and used dialysis as their AKI definition. They found that 11.5% of their patients developed AKI. However, the use of dialysis as the definition of AKI is concerning since most clinicians agree that AKI develops before the need for dialysis. Besides the problems with the definition of AKI, the authors also found that there was a length time bias resulting in the rate of AKI changing significantly during the long study period. All of the prospective studies of CS-AKI after 2005 were from a single center, Cincinnati Children's Hospital (15–19), that was designed with the intent to discover and validate new biomarkers and thus limited their generalizability. Nevertheless these studies found that the incidence of AKI, defined by a ≥ 50% SCr rise, ranged from 28 to 52%. In a recent large study of CS-AKI by Zappitelli et al (2) 35.9% of all children having cardiac surgery developed AKI. This was slightly lower than the AKI incidence from our study. However, our study was limited to children undergoing cardiopulmonary bypass, and their study was retrospective and based on a single center cohort thus limiting ascertainment of clinical factors. The present study was devised in a comprehensive manner to reliably determine a generalizable AKI event rate so future studies can utilize this.

Analysis of preoperative risk factors demonstrated that even after adjustment for surgical complexity (RACHS-1 category) and CPB time, children who were in the youngest age group were at higher risk for developing AKI compared to the older age groups. The reason for this is not completely clear. Though full term infants are usually born with their full complement of nephrons, maximal GFR is not achieved until about 2 years of age (30). Thus, children less than 2 years old may be more susceptible to the ischemic and inflammatory insults that may be occurring in patients undergoing heart surgery.

No patients from the RACHS-1 category 1 surgeries developed AKI. Examples of these surgeries include simple ASD closures and repair of partially anomalous pulmonary veins. This is not surprising since these surgeries are less complex and relatively quick with low CPB times (24, 31). Additionally, we did not find an association of increased risk of AKI with increased surgical complexity by RACHS-1 category. However, in our study exclusion of patients less than 30 days old also led to omitting RACHS-1 category 5 or 6 patients, a group with high likelihood of developing AKI. Given the complexity associated with defining AKI in newborns this will be an important population to study further.

Consistent with numerous past studies, we found that longer CPB times were associated with an increased risk of AKI. Moreover, we found an interesting linear relation between increasing bypass time and increasing AKI. The mechanism for this is probably due to a combination of ischemia, loss of pulsatile flow and progressive inflammation which adds to kidney injury (32). Further research into issues such as temperature, pressure and the amount and type of bypass circuit flows will be needed to explore this relationship. Strategies to limit bypass time may help decrease the rate of cardiac surgery-associated AKI. Although we controlled for RACHS-1 category in the multivariate analysis of CPB, it is possible that in children who have surgery requiring bypass the duration may also be a marker for case complexity and severity of the congenital anomaly.

Our study highlights the importance of studying AKI as a risk and as an outcome separately in children from adults; especially since the epidemiology is completely different. Adults undergoing cardiac surgery typically have several pre-operative cardiovascular risk factors such as diabetes, peripheral vascular disease, and chronic kidney injury. These same risk factors often emerge as pre-operative cardiovascular risk factors for developing AKI in adults (33). In children with congenital heart disease these factors are not usually present. In fact most children do not have any other co-morbidities. Risk factors for AKI in children are usually limited to the age of the child and the severity of insult (e.g. CPB time).

Pre-operative serum creatinine was lower in the group of patients who developed AKI. However, this was most likely due to expected age-associated lower SCr values, which is evidenced by the fact that pre-operative baseline estimated GFR was not statistically different between the AKI and non-AKI groups.

We also found that a large proportion of patients who developed AKI were exposed to nephrotoxic drugs. In our cohort 15% were exposed to gentamicin and 56% to non-steroidal anti-inflammatories (NSAIDs). NSAIDs in the pediatric CS-AKI population are mostly used to provide postoperative analgesia without the side effects of sedation and respiratory depression. This combination is thought to allow earlier wean from mechanical ventilation. Gentamicin is a commonly used drug in younger children to empirically treat gram negative infections. The extent to which use of these drugs is independently associated with AKI development or AKI severity should be the focus of future studies in order to determine whether there is a need to change our current practice.

In our exploration of the phenotype of AKI, we found that in more than half the patients, AKI was diagnosed by SCr criteria by day 1 and by day 2 in 97%. The day of diagnosis is earlier than seen in recent studies using the current definition of AKI, where only 40–67% of patients met the AKI definition within two days of the operation (15, 17–18). This discrepancy may be due to intraoperative factors related to surgical or perfusionist technique and perioperative factors such as volume administration and timing of diuresis. We found that in about half of AKI patients, AKI only lasted for 1 day and that 76% of these patients had AKI resolution by the end of 2 days, similar to the findings from the retrospective study by Zappitelli et al (2).

In terms of outcomes associated with AKI, we found that those who developed AKI were more likely to remain on mechanical ventilation for a longer period of time. The reason for this is likely to be multifactorial including increased fluid retention in the lungs, restrictive lung disease due to interstitial edema, and prolongation of sedation secondary to decreased drug elimination because of AKI (34). The heterogenous cohort of congenital heart patients makes assessment of variables that reflect risk for pulmonary edema, such as central venous pressure, B-type natriuretic peptide, and fluid balance difficult. They may be confounded by variables such as postoperative right ventricular dysfunction, right ventricular hypertrophy, residual lesions, and low cardiac output states. The present study was not designed to examine the mechanisms of lung injury that might explain the association between AKI and prolonged mechanical ventilation. Future studies should attempt to elucidate the reasons behind this relation.

The duration of PICU stay and hospital stay was longer in those with AKI compared to those without AKI, suggesting that CS-AKI is associated with an increased use of hospital resources and increased overall health cost. This is consistent with recent studies of AKI (16–18). Although the association between AKI and in hospital mortality did not reach significance, there was a strong trend that is consistent with the association that has been demonstrated in the adult literature (35, 36).

There are some limitations to our study. First, our study consisted predominantly of white patients, thus limiting generalizability to other racial groups. Second, our AKI definition did not include urine output as we did not record hourly urine output. However, in one pediatric study, addition of urine output did not substantially add to the classification by serum creatinine (21). In addition the use of intraoperative ultrafiltration and early postoperative diuretics would confound the urine output variable as a marker of AKI. Finally, we recognize that our definition of intraoperative hypotension is not necessarily synonymous with inadequate kidney perfusion or oxygen delivery. It may be that utilization of certain cardiopulmonary bypass flows along with reducing metabolic demand provides the support needed even in the setting of low blood pressures. However, a recent prospective study indicating an association between AKI and the difference between preoperative and intraoperative blood pressure in adults indicates a need for further investigation into this issue (37). Additionally, we feel that given our exclusion of neonates, the lack of coronary artery surgeries, and that we only had 4 patients with circulatory arrest, there is little chance of confounding by this problem.

Conclusions

We found that the rate of AKI in the current approach of pediatric cardiac surgery in North America is high and is associated with important patient outcomes. It is important to further our understanding of the potentially reversible risk factors for AKI and study them in randomized clinical trials to comprehend their role in the causation of AKI.

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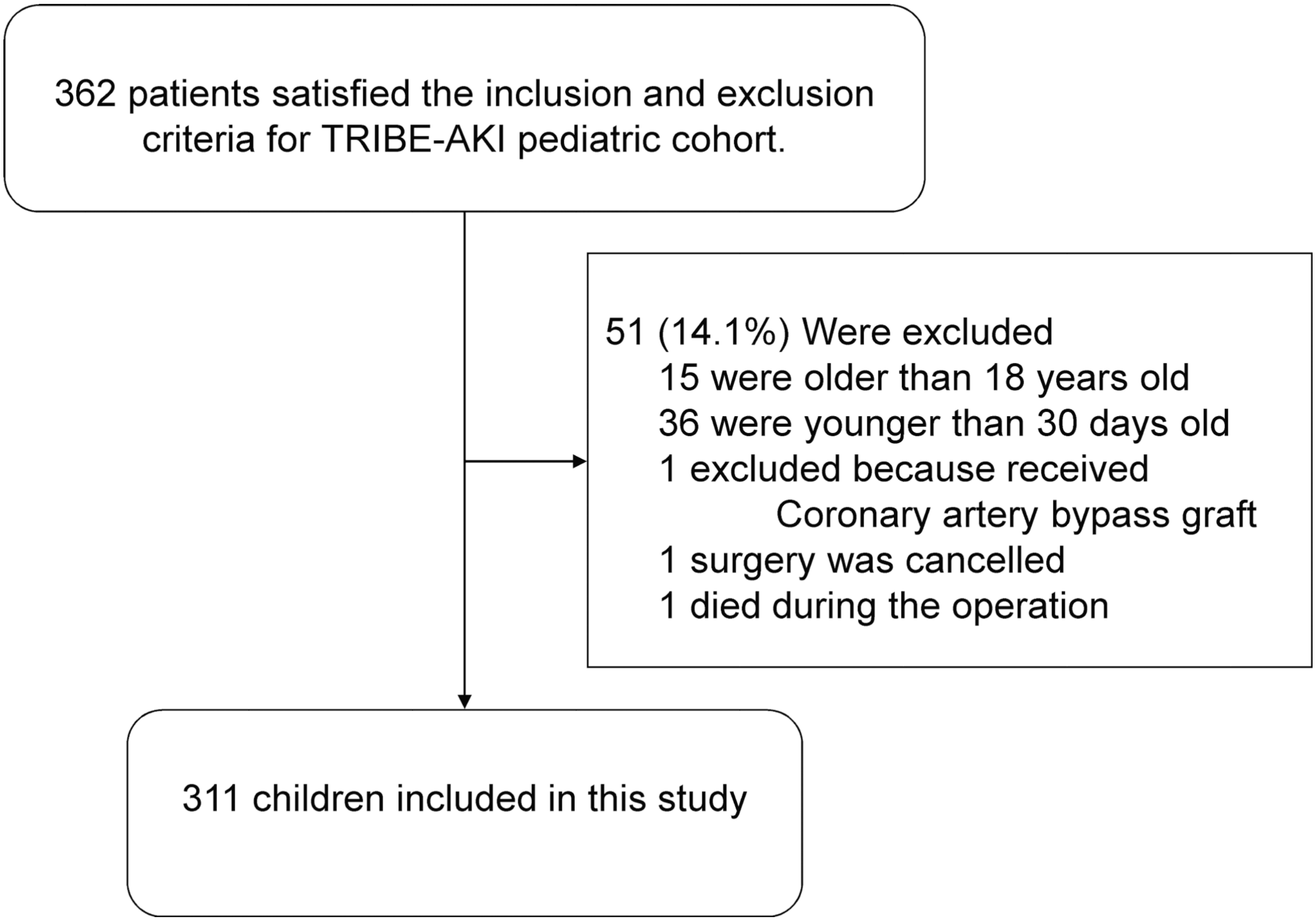

Figure 1.
Study population. *TRIBE-AKI,* Translational Research Investigating Biomarker Endpoints in Acute Kidney Injury

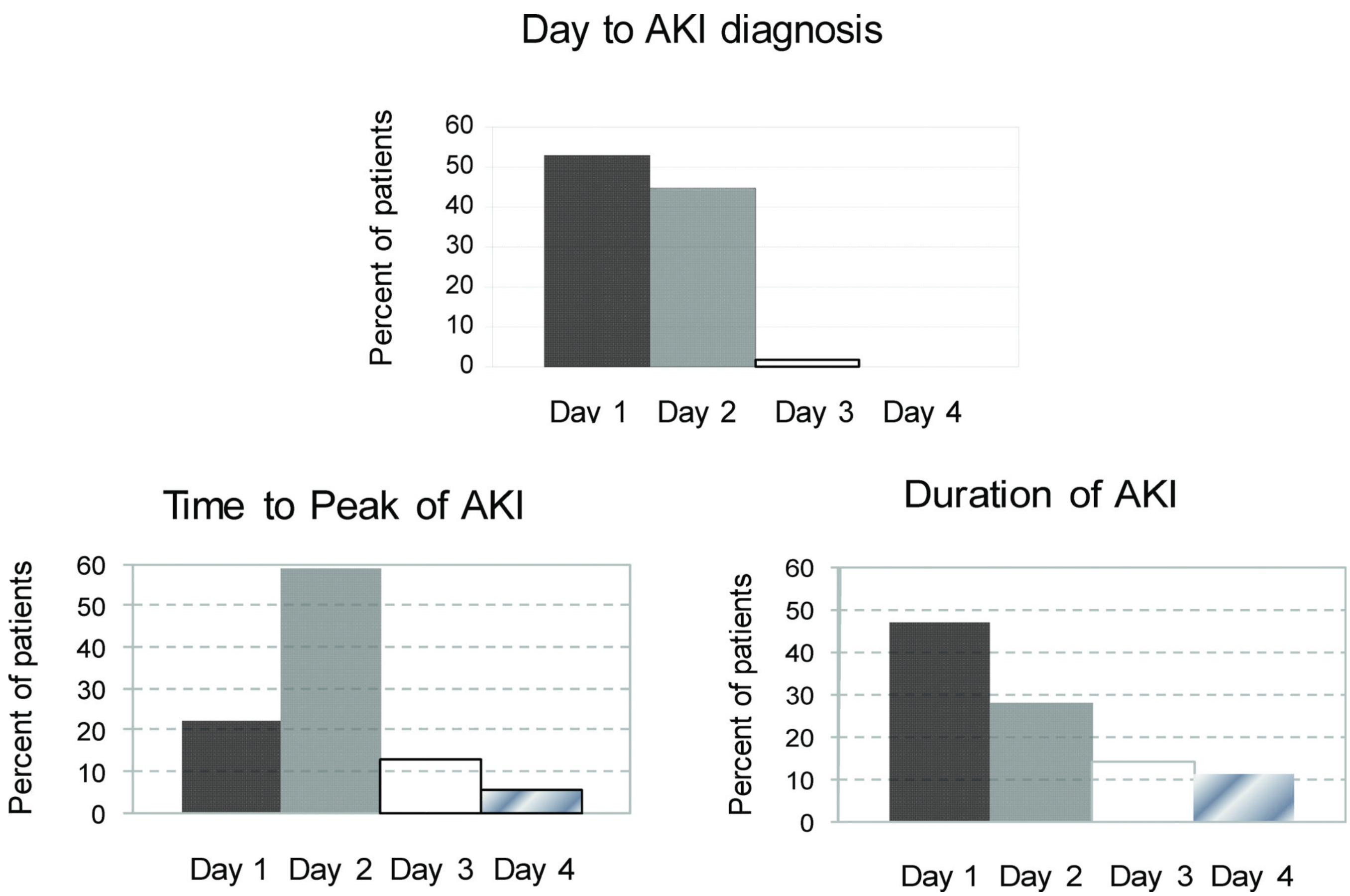

Figure 2.
Characteristics of acute kidney injury in pediatric heart surgery. *AKI*, acute kidney injury

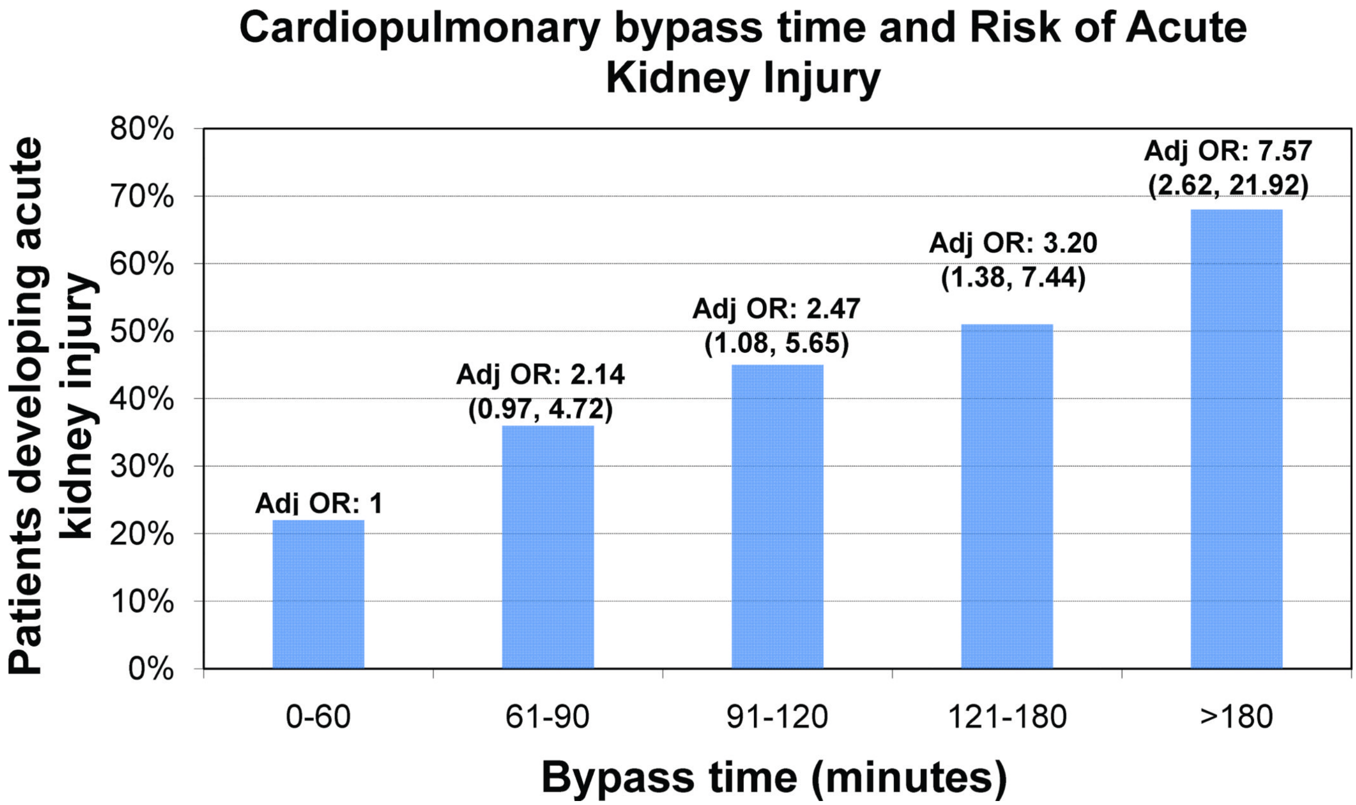

Figure 3.
Multivariable adjusted odds ratios for acute kidney injury are shown according to bypass time in increasing intervals from 60 minutes. The analysis included age, RACHS-1 score and site. *Adj*, adjusted; *RACHS-1*, Risk Adjustment for Congenital Heart Surgery 1.

Table 1

Characteristics of study cohort by AKI Status

Characteristics	AKI[a]	No AKI	P value[b]
	N (%) or mean ± SD		
Pre-operative Clinical Status			
Patients, N	130	181	
Age (years), mean ± SD	2.6 ± 4.1	4.6 ± 4.5	< 0.0001
Age by groups			< 0.0001
> 30 days old and ≤ 2 years old	87 (67%)	71 (39%)	
> 2 and < 13 years old	36 (28%)	98 (54%)	
≥ 13 and < 18 years old	7 (5%)	12 (7%)	
Sex			0.73
Female	57 (44%)	83 (46%)	
Male	73 (56%)	98 (54%)	
Race			0.55
White	106 (82%)	148 (82%)	
Black	13 (10%)	24 (13%)	
Hispanic ethnicity	5 (4%)	7 (4%)	1
Weight (kg), mean ± SD	12.4 ± 16.1	19.0 ± 18.2	0.001
Body surface area (m^2), mean ± SD	0.39 ± 0.79	0.66 ± 0.9	0.005
Prior cardiothoracic surgery	54 (42%)	68 (38%)	0.54
Preoperative kidney function assessment			
Preop creatinine (mg/dl), mean ± SD	0.37 ± 0.15	0.47 ± 0.16	< 0.0001
Preop eGFR (ml/min/1.73 m^2), mean ± SD	93 ± 30	88 (21)	0.13
Preop proteinuria by dipstick[c]	13 (12%)	16 (10%)	0.69
Preop hematuria by dipstick[c]	5 (5%)	6 (4%)	0.76
Urgency of surgery			0.35
Elective	116 (89%)	167 (92%)	
Urgent	14 (11%)	14 (8%)	
Emergent	0 (0%)	0 (0%)	
RACHS-1 category[d], mean ± SD	2.6 ± 0.6	2.3 ± 0.7	0.02
RACHS-1 by category groups			0.0003
1	0 (0%)	18 (10%)	
2	65 (50%)	88 (49%)	
3	55 (42%)	71 (39%)	
4	9 (7%)	3 (2%)	
Site			
Cincinnati Children’s Hospital Medical Center	82 (63%)	134 (74%)	0.09
Montreal Children’s Hospital	29 (22%)	32 (18%)	
Yale New-Haven Children's Hospital	19 (15%)	15 (8%)	
Intraoperative Factors			
Use of Cardiopulmonary bypass intraop	129 (99%)	178 (98%)	1

	AKI[a]	**No AKI**	**P value[b]**
Characteristics	**N (%) or mean ± SD**		
Cardiopulmonary bypass time (min), mean ± SD	126 ± 68	94 ± 68	< 0.0001
Bypass time > 60 minutes	117 (90%)	134 (74%)	0.0011
Bypass time > 90 minutes	86 (66%)	79 (44%)	0.0001
Bypass time > 120 minutes	56 (43%)	43 (24%)	< 0.0001
Cross clamp time (min), mean ± SD	53 ± 60	44 ± 42	0.15
Circulatory Arrest	4 (3%)	2 (1%)	0.24
Outcomes of cohort			
AKI severity			
≥ 50 and < 100% rise in serum creatinine	79 (61%)	…	N/A
≥ 100% rise in serum creatinine	48 (37%)	…	N/A
Dialysis in first 7 days after surgery	3 (2%)	…	N/A
Length of ICU stay (days), median (IQR)	4 (2,6)	2 (1,3)	< 0.0001
Length of hospital stay (days), median (IQR)	7 (5,14)	4 (3,6)	< 0.0001
Mechanical ventilation > 2 days post operatively	39 (30%)	14 (8%)	< 0.0001
Mechanical ventilation > 7 days post operatively	9 (8%)	5 (3%)	0.08
In hospital death	5 (4%)	1 (1%)	0.09
Complications			
Unplanned reoperation	6 (5%)	4 (2%)	0.33
Postoperative cardiopulmonary arrest	2 (2%)	2 (1%)	0.62
Mechanical circulatory support (ECMO or IABP)	2 (2%)	2 (1%)	0.61

AKI, acute kidney injury; SD, standard deviation; eGFR, estimated glomerular filtration rate; RACHS-1, Risk Adjustment for Congenital Heart Surgery 1; min, minutes; IQR, interquartile range; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump.

[a] ≥ 50% rise in serum creatinine.

[b] Comparing AKI with no AKI.

[c] Percentages and numbers are excluding missing data.

[d] Uncategorizable RACHS-1 scores were not included in the continuous summary of RACHS-1 scores.

Table 2

Multivariate adjusted risk for AKI

Variables	% AKI cases	Adjusted OR	95% CI	P Value
Age				
> 30 days old and ≤ 2 years old	55%	1	…	…
> 2 and < 13 years old	27%	0.28	(0.16, 0.48)	< 0.0001
≥ 13 and < 18 years old	37%	0.3	(0.10, 0.88)	0.03
RACHS-1 category				
1 or 2	38%	1	…	…
3	44%	1.47	(0.83, 2.59)	0.2
4	71%	1.93	(0.50, 7.41)	0.3
Site				
Cincinnati Children’s Hospital	38%	1	…	…
Montreal Children’s Hospital	48%	2.08	(1.08, 4.02)	0.03
Yale New-Haven Children's Hospital	56%	2.1	(0.95 4.67)	0.07
Cardiopulmonary Bypass Time (minutes)				
0–60	22%	1	…	…
61–90	36%	2.14	(0.97, 4.72)	0.06
91–120	45%	2.47	(1.08, 5.65)	0.03
121–180	51%	3.2	(1.38, 7.44)	<0.01
> 180	68%	7.57	(2.6, 21.9)	<0.01

AKI, acute kidney injury; RACHS-1, Risk Adjustment for Congenital Heart Surgery 1.

[a]Adjusted factors were age, RACHS-1 category, cardiopulmonary bypass time, and site.

Table 3

Association of outcomes with development of AKI[a]

Outcome	AKI	No AKI	P Value
Adjusted length of ICU stay (days), median (IQR)	4 (2, 6)	2 (1, 3)	0.08
Adjusted length of hospital stay (days), median (IQR)	7 (5, 14)	4 (3, 6)	0.01
	Adjusted OR	**95% CI**	**P Value**
Mechanical ventilation > 2 days postoperative	3.18	(1.55, 6.52)	0.001
Mechanical ventilation > 7 days postoperative	1.16	(0.33, 4.09)	0.8
In hospital death	7.34	(0.7, 75.9)	0.1

AKI, acute kidney injury; IQR, interquartile range; RACHS-1, Risk Adjustment for Congenital Heart Surgery 1.

[a]Adjusted factors were age, RACHS-1 score, cardiopulmonary bypass time > 90 min, and site.

Table 4

Clinical characteristics in patients with AKI

Characteristics	N (%) or mean ± SD
Fluid Balance in AKI cases	
Day 1 (ml), mean ± SD	167 ± 513
Day 2 (ml), mean ± SD	165 ± 580
Day 3 (ml), mean ± SD	−76 ± 561
Low blood pressure in Surgery[a] (yes)	96 (88%)
Minutes of Low blood Pressure, mean ± SD	75 ± 82
Hypotension score[b] on day 1, mean ± SD	2.7 ± 1.3
Hypotension score on day 2, mean ± SD	2.3 ± 1.4
Gentamicin Use	17 (15%)
NSAID Use	64 (56%)
Aprotinin Use	6 (5%)
Radiocontrast exposure	1 (1%)
Low cardiac output syndrome[c]	3 (6%)
Postoperative septicemia[c]	1 (2%)
Pneumonia[c]	5 (4%)
Arrythmia[c]	10 (8%)
Mechanical circulatory support[c]	2 (2%)

AKI, acute kidney injury; SD, standard deviation; NSAID, nonsteroidal anti-inflammatory drug.

[a]Defined as mean arterial blood pressure (MAP) less 50mmHg (or if < 1 years old MAP < 40 mmHg or MAP < 50 mmHg with inotropic support: epinephrine > 0.1 mcg/kg.min, dopamine > 10mcg/kg/min, any vasopressin or norepinephrine use)

[b]Hypotension score is 0 to 4 point scoring system where each point must be sustained for more than 2 hours. If mean arterial pressure is less than 70mmHg = 1 point; use of dopamine at ≤ 5 mcg/kg/min, dobutamine, or milrinone at any dose = 2 points; use of dopamine > 5 mcg/kg/min, epinephrine ≤ 0.1 mcg/kg/min, norepinephrine ≤ 0.1 mcg/kg/min, or vasopressin at any dose = 3 ponts; use of dopamine > 15 mcg/kg/min, epinephrine > 0.1 mcg/kg/min, or norepinephrine > 0.1 mcg/kg/min = 4 points.

[c]Definitions from the Society of Thoracic Surgeons' data specifications version 3.0 for the Congenital Heart Surgery Database.