Renal replacement therapy in the pediatric cardiac intensive care unit

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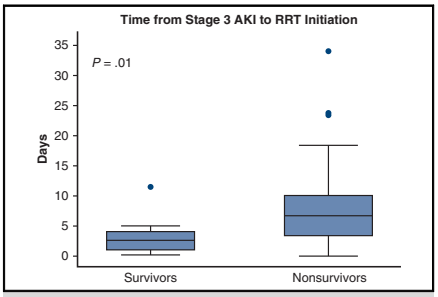
ABSTRACT

Objective: There is an increased risk of mortality in patients in whom acute kidney injury and fluid accumulation develop after cardiothoracic surgery, and the risk is especially high when renal replacement therapy is needed. However, renal replacement therapy remains an essential intervention in managing these patients. The objective of this study was to identify risk factors for mortality in surgical patients requiring renal replacement therapy in a pediatric cardiac intensive care unit.

Methods: We performed a retrospective review of patients requiring renal replacement therapy for acute kidney injury or fluid accumulation after cardiothoracic surgery between January 2009 and December 2017. Survivors and nonsurvivors were compared with respect to multiple variables, and a multivariable logistic regression analysis was performed to identify independent risk factors associated with mortality.

Results: The mortality rate for the cohort was 75%. Nonsurvivors were younger (nonsurvivors: 0.8 years; interquartile range, 0.1-8.2; survivors: 14.6 years; interquartile range, 4.2-19.7; $P = .002$) and had a lower weight-for-age z-score (nonsurvivors: −1.5; interquartile range, −3.1 to −0.4; survivors: −0.5; interquartile range, −0.9 to 0.3; $P = .02$) compared with survivors. There was no difference with respect to fluid accumulation. In multivariable analysis, a longer duration of stage 3 acute kidney injury before initiation of renal replacement therapy was independently associated with mortality (adjusted odds ratio, 1.39; 95% confidence interval, 1.05-1.83; $P = .021$).

Conclusions: Mortality in patients requiring renal replacement therapy after congenital heart disease surgery is high. A longer duration of acute kidney injury before renal replacement therapy initiation is associated with increased mortality. (J Thorac Cardiovasc Surg 2019;■:1-10)



Nonsurvivors had a longer duration of AKI before RRT initiation compared with survivors.

Central Message

A longer duration of AKI before initiation of RRT in surgical patients in the pediatric CICU is associated with mortality.

Perspective

AKI requiring RRT after surgery for CHD is a risk factor for mortality. In these patients, there is a need to identify modifiable risk factors that may improve outcomes. Starting RRT earlier in relation to when AKI develops may improve mortality.

See Commentary on page XXX.

CONG

Acute kidney injury (AKI) is common after surgery for congenital heart disease (CHD), with a reported incidence of 15% to 52%,[1-4] and is associated with increased intensive care unit (ICU) length of stay and duration of mechanical ventilation.[1,5] AKI requiring renal replacement therapy (RRT) is less common, with a reported incidence of approximately 5%,[6] but is associated with significant mortality after cardiac surgery.[7,8] Nevertheless, RRT remains an essential intervention in managing AKI. The use of early RRT may augment solute clearance and prevent detrimental fluid accumulation while simultaneously allowing for provision of necessary medications, nutrition, and blood products. However, it also exposes patients to an invasive therapy

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Abbreviations and Acronyms

AKI = acute kidney injury
CHD = congenital heart disease
CICU = cardiac intensive care unit
ECMO = extracorporeal membrane oxygenation
eGFR = estimated glomerular filtration rate
ICU = intensive care unit
PD = peritoneal dialysis
RRT = renal replacement therapy

that may not be necessary should renal function ultimately recover without intervention. As such, the ideal use and timing of RRT in postoperative pediatric cardiothoracic surgical patients remain unknown.

Several studies have evaluated early administration of peritoneal dialysis (PD) after cardiac surgery,[9,10] but these studies have been limited in their ability to determine clinically important outcomes. There is a need to further explore modifiable risk factors associated with mortality in surgical patients requiring RRT in the pediatric cardiac intensive care unit (CICU). Identifying these factors will be useful in identifying patients who could benefit from early RRT. The objective of this study was to explore a single-center cohort of pediatric cardiothoracic surgical patients receiving RRT and to assess risk factors for mortality. We hypothesized that earlier initiation of RRT and a lower degree of fluid accumulation at the time of RRT initiation would be associated with more favorable outcomes.

MATERIALS AND METHODS

This was a retrospective cohort study conducted at a single tertiary-level pediatric CICU. Patients receiving any mode of RRT during an inpatient hospital encounter between January 1, 2009, and December 31, 2017, were identified using Current Procedural Terminology codes. Patients initiated on RRT for the indications of fluid accumulation or AKI after cardiothoracic surgery in the CICU were included in the analysis. Patients were excluded if they had chronic kidney disease (defined as an estimated glomerular filtration rate [eGFR] <60 mL/min/1.73 m^2), if they received RRT for an indication other than AKI or fluid accumulation (eg, hyperkalemia), and if they initiated RRT in a location other than the CICU. Patients with incomplete documentation and those who did not undergo cardiothoracic surgery (eg, patients with medical cardiac disease) were also excluded. Given the increasing prevalence of adult patients with CHD, the study group elected to include all age ranges.[11] There were also no exclusion criteria based on the nature of the surgical procedure performed. This study was approved by the institutional review board at Boston Children's Hospital with waiver of consent.

Data were manually extracted from the medical record on standardized data-collection forms. Data collected included patient age at RRT initiation, gender, weight on admission to the CICU, weight-for-age z-score, native cardiac anatomy, surgical procedure, the need for extracorporeal membrane oxygenation (ECMO) at any point during hospitalization, and ICU length of stay. ECMO details recorded include mode of ECMO, indication for ECMO cannulation, and the amount of ultrafiltration performed on ECMO. The Pediatric Risk Index of Mortality 3 score[12] was calculated retrospectively using values in the first 24 hours of admission to the CICU. The Society of Thoracic Surgery-European Association for Cardiothoracic Surgery (STAT) mortality categories were used to categorize surgical procedures.[13]

Baseline creatinine was defined as the lowest serum creatinine in the 3 months before admission. If there was no baseline creatinine available, it was estimated[14] assuming a normal creatinine clearance of 120 mL/min/1.73 m^2. The highest serum creatinine value between the hospital admission and the initiation of RRT was also obtained. eGFR was calculated using the modified Schwartz formula[15] with both the baseline creatinine and the creatinine just before initiation of RRT, and the percent change was calculated. Urine output over the 24 hours before initiation of RRT was also recorded. The degree of AKI at the time of RRT initiation was established using the Kidney Disease: Improving Global Outcomes Criteria.[16] Both serum creatinine and urine output were used to classify the stage of AKI. If there was a discrepancy between the 2, the marker that placed the subject in the higher category of AKI was used. Fluid balance was recorded from the moment of return from the operating room until RRT initiation and calculated as a percentage using the equation[17]: [Fluid in (L)-Fluid out (L)]/[ICU admission weight (kg)] * 100%. Patients with a negative fluid balance were given a value of 0.0%. This calculation was limited to the 7 days before RRT initiation in the event that the duration between surgery and RRT initiation was longer than 7 days. Fluid balance in the 72 hours after initiating RRT was also calculated using the same equation.

Timing of RRT initiation was measured from several intervals, including return from the operating room and from when the peak creatinine was recorded. Additionally, we measured the duration to RRT from the moment an individual first met criteria for stage 3 AKI. Subjects who did not meet criteria for stage 3 AKI were assigned a time of 0.0 days. The indication for commencing RRT was identified from the documentation of the attending cardiac intensive care physician and the attending nephrologist in charge of the patient's care. Mode of RRT and complications related to RRT were also recorded. Patients with PD catheters for drainage only were not included. The primary outcome was in-hospital mortality.

Descriptive statistics were used to explore the cohort. Data are presented as medians with interquartile ranges or frequencies with percentages where appropriate. Survivors and nonsurvivors were compared using Fisher exact test and Mann–Whitney *U* test for categoric and continuous variables, respectively. A stepwise multivariable logistic regression model was constructed to identify risk factors associated with mortality. Several variables were included in the model a priori because of known effect on mortality (eg, ECMO, single ventricle status), and the rest were included from variables identified on univariate analysis. A *P* value of less than .1 was required for entry into the model. Results are presented as odds ratio with 95% confidence interval. All statistical analyses were performed using STATA version 15.1 (StataCorp LP, College Station, Tex).

RESULTS

A total of 463 patients received RRT while inpatients at our institution over the study period. Of these, there were 48 cardiac surgical patients who met eligibility criteria and were included in the final analysis (Figure 1). For reference, there were approximately 6500 cardiac surgeries requiring cardiopulmonary bypass performed during the study period. Patients were predominantly male (67%). Surgical procedures and associated diagnoses are listed in Table 1. Some 68.8% of patients were in Society of Thoracic Surgeons-European Association for Cardiothoracic Surgery 4 or 5 categories. A total of 26 patients (54.2%) required a repeat surgery or a catheter-based

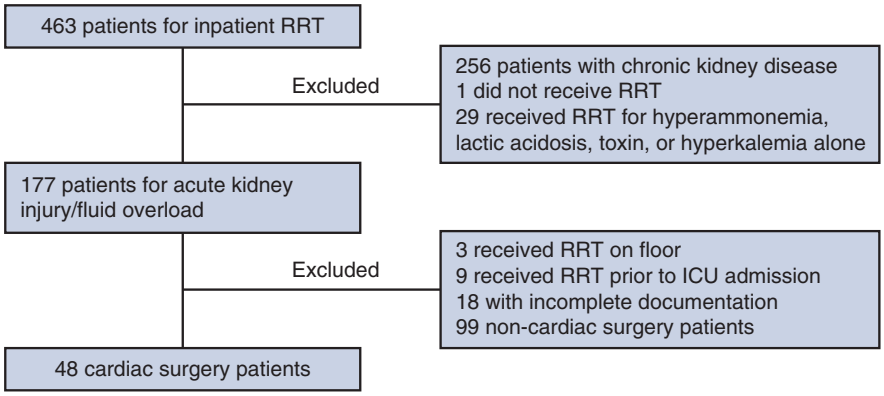


FIGURE 1. Flow chart of patient selection. Patients requiring RRT while inpatients over a 9-year period were identified. Patients were excluded if they had preexisting chronic kidney disease, if they received RRT for an indication other than AKI or fluid accumulation, or if they received RRT before admission to the ICU. *RRT*, Renal replacement therapy; *ICU*, intensive care unit.

intervention to manage a residual lesion after this initial surgery. AKI developed in 14 patients (56%) after the second intervention, and 24 patients (92.3%) were initiated on RRT after the second intervention. The median age of the cohort was 1.5 years (IQR, 0.3-13.5), and the median weight on admission to the ICU was 10.8 kg (IQR, 3.4-43.1) with a weight-for-age z-score of −1.0 (IQR, −2.3 to −0.2) (Table 2).

The most common primary mode of RRT used was PD (37.5%, n = 18) followed by continuous RRT (31.3%, n = 15) and intermittent hemodialysis (31.3%, n = 15). Mode of RRT was not associated with mortality. The primary indication for initiating RRT was evenly split throughout the cohort, with fluid accumulation alone being the most common indication in 35.4% (n = 17), followed by both fluid accumulation and uremia (33.3%, n = 16) and uremia alone (31.3%, n = 15). All but 1 patient (97.9%, n = 47) met criteria for stage 3 AKI. A total of 28 patients met criteria for AKI based on creatinine alone, 16 patients met criteria based on both creatinine and urine output, and only 3 patients met criteria based on urine output alone. AKI developed in 4 patients, and they were initiated on RRT after a period of time on the inpatient ward postoperatively.

The mortality rate for the cohort was 75% (n = 36). The median ICU length of stay from admission to death/discharge was 45.2 days (IQR, 29.3-72.0). A total of 20 of the 21 patients less than 1 year old requiring RRT died (95.2%). None of the neonates (n = 10, 100%) survived. Of the 12 survivors, 7 had complete recovery of renal function before discharge. Two patients had stage 2 AKI, and 3 patients had stage 3 AKI at discharge. One survivor continued to require RRT at the time of discharge.

In the univariate analysis, nonsurvivors were younger (0.8 vs 14.6 years, $P = .002$) and had lower weight-for-age z-scores (−1.5 vs −0.5, $P = .001$) compared with survivors (Table 2). There was no significant difference between survivors and nonsurvivors in terms of the percentage fluid accumulation from the operating room until RRT initiation (survivors: 10.7% [IQR, 4.1-14.6]; nonsurvivors: 7.5% [IQR, 0.0-12.5]; $P = .214$), and more than half of the patients (n = 29, 60.4%) had less than 10% fluid accumulation. Nonsurvivors had a slightly higher eGFR at RRT initiation (20.3 vs 15.8 mL/min/1.73 m^2, $P = .069$) and a higher urine output in the 24 hours before RRT initiation than survivors (0.9 vs 0.3 mL/kg/h, $P = .122$), although neither was statistically significant. Figure 2 summarizes the time intervals that were evaluated with respect to RRT initiation. Nonsurvivors were started on RRT later than survivors with respect to all time points analyzed. Patients aged less than 1 year were started on RRT later than patients aged more than 1 year (7.4 vs 3.4 days, $P = .008$). The difference in timing of RRT initiation between survivors and nonsurvivors from when the diagnosis of stage 3 AKI was made is highlighted in Figure 3.

A total of 29 patients (60%) required ECMO at some point during their hospitalization. A higher percentage of nonsurvivors required ECMO, but the difference was not significant. Details of the patients requiring ECMO are presented in Table 3. The majority of these patients were cannulated to venoarterial ECMO (n = 28, 96.6%). Six patients (20.7%) had 2 ECMO cannulations during their hospitalization. Indications for initial ECMO cannulation were low cardiac output (n = 10, 34.5%), cardiac arrest (n = 8, 27.6%), and failure to wean from cardiopulmonary bypass (n = 6, 20.7%). In addition to the 8 patients with cardiac arrest as their initial indication for ECMO cannulation, 3 patients had cardiac arrest as an indication for their second ECMO cannulation. Extracorporeal cardiopulmonary resuscitation was not found to be significantly associated with mortality ($P = 1.000$). A total of 12 patients (41.4%) received RRT on ECMO. All of these were primarily for clearance purposes, with a median blood urea nitrogen of 144.5 (IQR, 128.5-172.5) at the time of RRT

TABLE 1. Surgical procedures performed with associated diagnoses

Surgical procedure	n (%)	Diagnoses
Norwood procedure*	6 (12.5)	- HLHS (MS/AS) (2 patients) - HLHS (MS/AA) (2 patients) - Unbalanced right dominant CAVC - DORV/MA
Heart transplant	6 (12.5)	- Heart transplant rejection - Dilated cardiomyopathy - HLHS after failed stage 1 palliation - HLHS palliated to Fontan in failure - L-TGA with heart failure - Critical AS status post-Ross procedure with heart failure
Lung transplant	4 (8.3)	- Lung transplant rejection (2 patients) - Pulmonary vein stenosis after TAPVC repair - Cystic fibrosis
Ventricular assist device	4 (8.3)	- HLHS palliated to Fontan with ventricular fibrillation - Heart transplant rejection - HLHS after BDG in heart failure (2 patients)
Aortic valve/root replacement†	4 (8.3)	- Aortic root aneurysm - IAA after repair with mixed aortic valve disease - Congenital AS after failed Ross procedure - D-TGA status post-Rastelli procedure with aortic insufficiency
Biventricular repair	4 (8.3)	- Unbalanced CAVC palliated to bilateral BDG and right BT shunt - Left ventricular fibroma palliated to Fontan - CAVC, DORV, PS status postaortopulmonary shunt - Left dominant CAVC, VSD, PS status post-BDG
ASO and VSD repair	3 (6.3)	- D-TGA with VSD (3)
CAVC repair	3 (6.3)	- CAVC status postpulmonary artery bands - Right dominant CAVC - TOF with right dominant CAVC
Pulmonary artery banding‡	2 (4.2)	- Critical AS - HLHS with intact atrial septum
Systemic to pulmonary shunt§	2 (4.2)	- Unbalanced CAVC, DORV, IAA type B status post-BDG - DORV/MA, pulmonary vein stenosis
Congenitally corrected TGA repair	2 (4.2)	- L-TGA, CAVC, PS - L-TGA, VSD, PS status post-BT shunt
Other‖	8 (16.7)	- VSD repair (multiple VSDs status postpulmonary artery bands) - Mitral valve replacement (CAVC status postrepair with mitral stenosis, tricuspid regurgitation) - Pulmonary venous stenosis repair (TAPVC status postrepair with pulmonary vein stenosis) - Pulmonary artery sling repair (left pulmonary artery sling, tracheal stenosis) - MAPCA occlusion (TOF/PS/MAPCAs) - Ebstein's repair (Ebstein's anomaly) - Aortic arch repair plus VSD repair (newborn with IAA type B and VSD) - RV-PA conduit replacement (truncus arteriosus with RV-PA conduit obstruction)

HLHS, Hypoplastic left heart syndrome; *MS*, mitral stenosis; *AS*, aortic stenosis; *AA*, aortic atresia; *CAVC*, complete atrioventricular canal; *DORV*, double outlet right ventricle; *MA*, mitral atresia; *L-TGA*, levo-transposition of the great arteries; *TAPVC*, total anomalous pulmonary venous connection; *BDG*, bidirectional Glenn; *IAA*, interrupted aortic arch; *D-TGA*, dextro-transposition of the great arteries; *BT*, Blalock–Taussig; *PS*, pulmonary stenosis; *VSD*, ventricular septal defect; *ASO*, arterial switch operation; *TOF*, tetralogy of Fallot; *TGA*, transposition of the great arteries; *MAPCA*, major aortopulmonary collateral arteries; *RV-PA*, right ventricle to pulmonary artery. *Four patients had a Sano shunt placed, and 2 patients had a Blalock–Taussig shunt placed. †There were 2 aortic valve replacements and 2 aortic root replacements. ‡One patient had pulmonary artery bands placed as part of a hybrid stage 1 procedure. §One patient received an aortopulmonary shunt, and 1 patient received a modified BT shunt. ‖Other procedures listed with diagnoses in parentheses.

TABLE 2. Univariate analysis of survivors versus nonsurvivors

Variable	All patients (n = 48)	Survivors (n = 12, 25%)	Nonsurvivors (n = 36, 75%)	*P* value
Age, y	1.5 (0.3 to 13.5)	14.6 (4.2 to 19.7)	0.8 (0.1 to 8.2)	.002
Male, n	32 (66.7)	8 (66.7)	24 (66.7)	1.000
ICU admission weight, kg	10.8 (3.4 to 43.1)	50.4 (14.0 to 63.8)	7.1 (2.8 to 24.1)	.001
Weight-for-age z-score	−1.0 (−2.3 to −0.2)	−0.5 (−0.9 to 0.3)	−1.5 (−3.1 to −0.4)	.02
Pediatric risk index of mortality 3 score	13 (6 to 19.5)	13 (8 to 20.5)	13.5 (6 to 18)	.512
STAT score, n				.109
1	1 (2.1)	1 (8.3)	0 (0)	
2	1 (2.1)	0 (0)	1 (2.8)	
3	9 (18.8)	2 (16.7)	7 (19.4)	
4	25 (52.1)	9 (75.0)	16 (44.4)	
5	8 (16.7)	0 (0)	8 (22.2)	
Unable to assign	4 (8.3)	0 (0)	4 (11.1)	
Need for surgical or catheter-based reintervention	26 (54.2)	4 (33.3)	22 (61.1)	.101
Single ventricle, n	19 (39.6)	4 (33.3)	15 (41.7)	.739
Need for ECMO, n*	29 (60.4)	5 (41.7)	24 (66.7)	.176
Mechanical ventilation at RRT initiation, n	46 (95.8)	10 (83.3)	36 (100)	.059
HFOV, n	9 (18.8)	2 (16.7)	7 (19.4)	1.00
Vasoactive support at RRT initiation, n	44 (91.7)	11 (91.7)	33 (91.7)	1.00
Operative variables				
Cardiopulmonary bypass time, min	219 (145 to 285.5)	230 (141 to 329.5)	219 (157 to 248)	.694
Crossclamp time, min	101 (62 to 181)	119 (30 to 160)	92 (65 to 205)	.512
Modified ultrafiltration used, n	16 (33.3)	2 (16.7)	14 (38.9)	.289
Percent fluid accumulation from surgery to RRT, n†				.084
Negative	14 (29.2)	1 (8.3)	13 (36.1)	
0%-10%	15 (31.3)	4 (33.3)	11 (30.6)	
10%-20%	12 (25.0)	6 (50.0)	6 (16.7)	
>20%	7 (14.6)	1 (8.3)	6 (16.7)	
Percent fluid accumulation from surgery to RRT, %†	8.3 (0.0 to 13.5)	10.7 (4.1 to 14.6)	7.5 (0.0 to 12.5)	.214
Change in creatinine from baseline to peak‡	7.4 (5.5 to 10.4)	7.5 (4.5 to 9.8)	6.8 (5.7 to 10.4)	.905
eGFR pre-RRT, mL/min/1.73 m^2§	18.4 (14.4 to 26.0)	15.8 (13.8 to 16.5)	20.3 (15.2 to 29.1)	.069
Percentage decrease of eGFR rate, %‖	84.8 (76.7 to 89.8)	86.7 (77.7 to 89.6)	84.2 (76.7 to 89.8)	.49
Urine output, mL/kg/h¶	0.5 (0.2 to 1.9)	0.3 (0.1 to 0.5)	0.9 (0.2 to 2.0)	.122
Indication for RRT, n (%)				.415
Fluid removal alone	17 (35.4)	6 (50.0)	11 (30.6)	.300
Fluid removal and clearance	16 (33.3)	4 (33.3)	12 (33.3)	1.000
Clearance alone	15 (31.3)	2 (16.7)	13 (36.1)	.292
Time from surgery to RRT, d	12.9 (7.4 to 29.3)	8.4 (6.2 to 12.9)	17.7 (9.7 to 38.3)	.016
Time from stage 3 AKI stage to RRT, d	4.9 (2.5 to 9.2)	2.6 (1.0 to 4.2)	6.7 (3.3 to 10.2)	.01
Time from peak creatinine to RRT, d	0.7 (0.2 to 6.2)	0.1 (0.0 to 0.4)	0.9 (0.5 to 9.3)	.002
Fluid balance after RRT initiation, %#	−0.75 (−6.5 to 6.3)	−3.1 (−4.7 to 1.2)	0.1 (−6.6 to 6.6)	.475

All values are median (IQR) or n (%). *ICU*, Intensive care unit; *STAT*, Society of Thoracic Surgeons-European Association for Cardiothoracic Surgery; *ECMO*, extracorporeal membrane oxygenation; *RRT*, renal replacement therapy; *HFOV*, high-frequency oscillatory ventilation; *eGFR*, estimated glomerular filtration rate; *AKI*, acute kidney injury. *Need for ECMO at any point during hospitalization. †Limited to the 7 days before RRT initiation if the duration from operating room to RRT was longer than 7 days. ‡Change from baseline creatinine to highest recorded creatinine between surgery and initiation of RRT. §Estimated using modified Schwartz formula using height and creatinine just before RRT. ‖Percentage decrease from baseline eGFR to eGFR at initiation of RRT. ¶Calculated over 24-hour period before RRT initiation. #Calculated as a percentage over the 72 hours after initiating RRT.

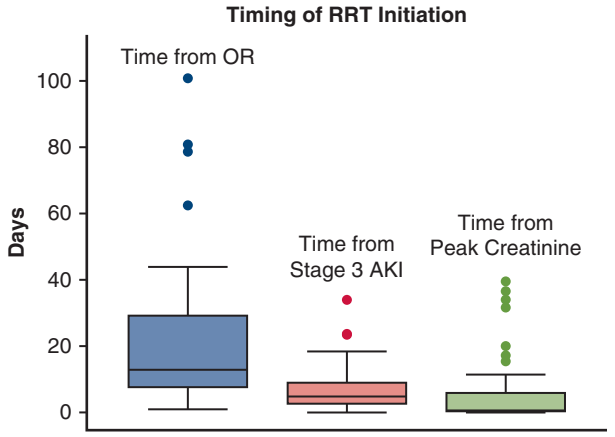


FIGURE 2. Timing of RRT initiation. The timing of RRT initiation was measured with respect to 3 separate time intervals. The *first bar* represents the duration between when patients returned from the operating room and the initiation of RRT. The *second bar* represents the duration between when stage 3 AKI developed in patients and RRT was initiated. The *third bar* represents the duration between when the peak creatinine was drawn and RRT was initiated. In general, stage 3 AKI developed in patients after returning from the operating room, and some continued to have an increase in creatinine after developing stage 3 AKI before RRT initiation. The median duration from surgery to RRT initiation was 12.9 days (IQR, 7.4-29.3). The median duration from patients meeting criteria for stage 3 AKI to RRT initiation was 4.9 days (IQR, 2.5-9.2). The median duration from when peak creatinine was drawn to RRT initiation was 0.7 days (IQR, 0.2-6.2). *RRT*, Renal replacement therapy; *OR*, operating room; *AKI*, acute kidney injury.

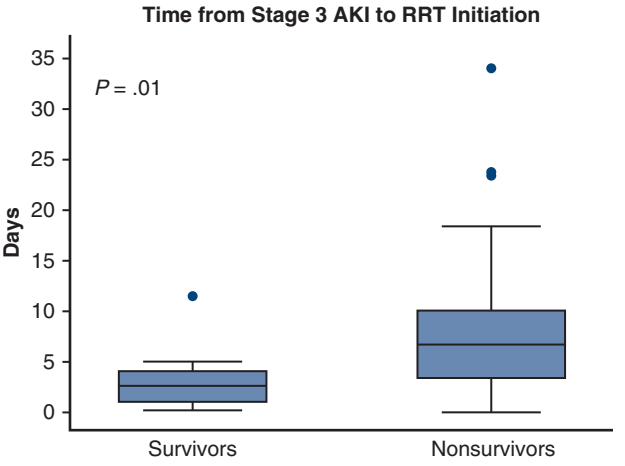


FIGURE 3. *Box* and *whiskers* plot comparing timing of RRT initiation in relationship to being diagnosed with stage 3 AKI. The *middle horizontal line* represents the median of each group, and the *lower* and *upper borders* of the boxes represent the 25th and 75th percentiles, respectively. The *lower* and *upper whiskers* represent the minimum and maximum values of nonoutliers, respectively. The *extra dots* represent outliers. Nonsurvivors had a longer duration of AKI before RRT initiation compared with survivors (6.7 vs 2.6 days, $P = .01$). *AKI*, Acute kidney injury; *RRT*, renal replacement therapy.

CONG

initiation. Six of these patients (50%) were able to survive to decannulation. A total of 14 patients (48.3%) were decannulated from ECMO before initiating RRT, and 3 patients (10.3%) were receiving RRT before their ECMO cannulation. Eight patients (27.6% of ECMO patients) died on ECMO.

In the group of patients who did not receive ECMO, nonsurvivors were younger (0.8 vs 14.7 years, $P = .042$) and had a lower weight-for-age z-score (-2.6 vs -0.6, $P = .043$). The duration of stage 3 AKI before RRT initiation was longer in nonsurvivors compared with survivors (7.4 vs 2.5 days, $P = .014$).

In the multivariable logistic regression model for mortality (Table 4), a longer duration of stage 3 AKI before RRT initiation was independently associated with an increased odds of mortality (adjusted odds ratio, 1.39; 95% confidence interval, 1.05-1.83 per day of delay in RRT initiation). For this model, the Hosmer–Lemeshow goodness of fit statistics indicated adequate model fit ($P = .413$), and the area under the receiver operating curve was 0.84, demonstrating good classification accuracy. A brief description of the main findings from the study is presented in Video 1.

DISCUSSION

In this retrospective cohort study, we sought to identify risk factors for mortality in cardiac surgical patients requiring RRT for AKI or fluid accumulation. The mortality rate was high at 75%, and the ICU length of stay was long (45.2 days; IQR, 29.3-72.0). Notably, there were no survivors among neonates needing RRT and only 1 survivor among patients aged less than 1 year. The cohort had a high acuity of illness, with more than half of the patients needing ECMO at some point during their hospitalization. The majority were high STAT categories, and a significant amount of patients needed another intervention after their initial surgery. There was a long delay between returning from the operating room and initiating RRT (median, 12.9 days; IQR, 7.4-29.3). There was also a long duration of AKI before initiating RRT, with the median time from when a patient met criteria for stage 3 AKI to initiation of RRT of 4.9 days (IQR, 2.5-9.2). A longer duration of stage 3 AKI before RRT initiation was associated with increased odds of mortality in our multivariable logistic regression analysis.

AKI after cardiac surgery requiring RRT has been associated with mortality.[7,8] Previous studies have reported mortality rates ranging from 20% to 52.9%.[18-21] The higher mortality rate in our cohort may be related to the complexity of the patient population as indicated by the high incidence of mechanical circulatory support with ECMO. Santiago and colleagues[19] reported a mortality

TABLE 3. Univariate analysis of survivors versus nonsurvivors of patients requiring extracorporeal membrane oxygenation

Variable	All patients (n = 29)	Survivors (n = 5, 17.2%)	Nonsurvivors (n = 24, 82.8%)	*P* value
Age, y	1.3 (0.1-8.9)	5.3 (5.1-19.6)	0.1 (0.7-7.8)	.058
ICU admission weight, kg	8.4 (3.1-23.1)	20.5 (15.1-56.3)	7.5 (2.8-20.9)	.057
Weight-for-age z-score	−1.1 (−1.9 to −0.2)	−0.4 (−1.5 to −0.2)	−1.2 (−2.1 to −0.4)	.356
Pediatric risk index of mortality 3 score	14 (7-20)	20 (19-23)	13.5 (5-18.5)	.06
STAT score, n				.738
2	1 (3.5)	0 (0)	1 (4.2)	
3	6 (20.7)	2 (40.0)	4 (16.7)	
4	16 (55.2)	3 (60.0)	13 (54.2)	
5	3 (10.3)	0 (0)	3 (12.5)	
Unable to assign	3 (10.3)	0 (0)	3 (12.5)	
Single ventricle, n	12 (41.4)	2 (40.0)	10 (41.7)	1.000
VA ECMO	28 (96.6)	4 (80.0)	24 (100)	.172
Multiple ECMO runs*	6 (20.7)	0 (0)	6 (25.0)	.553
Indication for ECMO				.224
Low cardiac output state	10 (34.5)	0 (0)	10 (41.7)	
Cardiac arrest	8 (27.6)	2 (40.0)	6 (25.0)	
Failure to wean from cardiopulmonary bypass	6 (20.7)	2 (40.0)	4 (16.7)	
Other†	5 (17.2)	1 (20.0)	4 (16.7)	
E-CPR‡	11 (37.9)	2 (40.0)	9 (37.5)	1.000
Percent fluid accumulation from surgery to RRT, n§				.27
Negative	8 (27.6)	0 (0)	8 (33.3)	
0%-10%	9 (31.0)	2 (40.0)	7 (29.2)	
10%-20%	8 (27.6)	3 (60.0)	5 (20.8)	
>20%	4 (13.8)	0 (0)	4 (16.7)	
Percent fluid accumulation from surgery to RRT, %§	8.9 (0.0-12.5)	11.2 (5.3-11.6)	8.8 (0.0-14.1)	.484
Fluid accumulation on ECMO, %‖	10.3 (0-24.7)	14.4 (6.2-21.6)	9.8 (0-24.7)	.669
Urine output, mL/kg/h	0.4 (0.1-1.9)	0.2 (0.1-0.4)	0.8 (0.2-2.0)	.126
Ultrafiltration amount on ECMO, mL/kg/h	2.3 (0.6-4.9)	0.6 (0.3-4.9)	2.4 (1.1-3.6)	.54
ECMO and RRT				1.000
RRT on ECMO	12 (41.4)	2 (40.0)	10 (41.7)	
RRT after ECMO	14 (48.3)	3 (60.0)	11 (45.8)	
RRT before ECMO	3 (10.3)	0 (0)	3 (12.5)	
Indication for RRT, n				.695
Fluid removal alone	7 (24.1)	2 (40.0)	5 (20.8)	
Fluid removal and clearance	10 (34.5)	1 (20.0)	9 (37.5)	
Clearance alone	12 (41.4)	2 (40.0)	10 (41.7)	
Time from surgery to RRT, d	12 (7.6-24.5)	7.6 (6.4-9.2)	13 (9.3-24.9)	.106
Time from stage 3 AKI stage to RRT, d	4.2 (2.3-8.8)	3.4 (0.8-3.5)	6.5 (2.4-11)	.119
Time from peak creatinine to RRT, d	0.5 (0.1-5.3)	0.1 (0.1-0.2)	1.2 (0.3-6.2)	.03

All values are median (IQR) or n (%). Data presented are that of the first ECMO cannulation for patients who had multiple cannulations. *ICU*, Intensive care unit; *STAT*, Society of Thoracic Surgeons-European Association for Cardiothoracic Surgery; *VA*, venoarterial; *ECMO*, extracorporeal membrane oxygenation; *E-CPR*, extracorporeal cardiopulmonary resuscitation; *RRT*, renal replacement therapy; *AKI*, acute kidney injury. *All 6 patients had 2 ECMO runs. †Other indications include pulmonary hemorrhage (n = 2), hypercarbic respiratory failure (n = 1), pulmonary hypertension (n = 1), and multisystem organ failure (n = 1). ‡Eight patients had CPR as their initial indication for ECMO cannulation; an additional 3 patients underwent extracorporeal cardiopulmonary resuscitation for their second cannulation. §Limited to the 7 days before RRT initiation if the duration from operating room to RRT was more than 7 days. ‖Fluid accumulation from ECMO cannulation to the initiation of RRT.

rate of 43% in patients requiring continuous RRT after cardiac surgery, with 16% of the overall cohort requiring ECMO. In contrast, 60% of our cohort required ECMO at some point during their hospitalization. Another potential contributor to our high mortality rate was the young age of the population. Pederson and colleagues[18] reported a

TABLE 4. Multivariable logistic regression model for mortality

Variable	OR (95% CI)	Adjusted OR (95% CI)	*P* value
Age	0.94 (0.88-1.00)		
Weight for age z-score	0.69 (0.46-1.02)	0.67 (0.43-1.04)	.077
Single ventricle	1.43 (0.36-5.63)		
Need for ECMO	2.8 (0.73-10.7)	4.72 (0.87-25.73)	.073
eGFR pre-RRT	1.04 (0.98-1.10)		
Fluid accumulation from surgery to RRT	0.98 (0.93-1.03)		
Time from surgery to RRT	1.09 (1.00-1.19)		
Time from first meeting criteria for stage 3 AKI to RRT	1.28 (1.02-1.59)	1.39 (1.05-1.83)	.021
Time from peak creatinine to RRT	1.17 (0.93-1.47)		

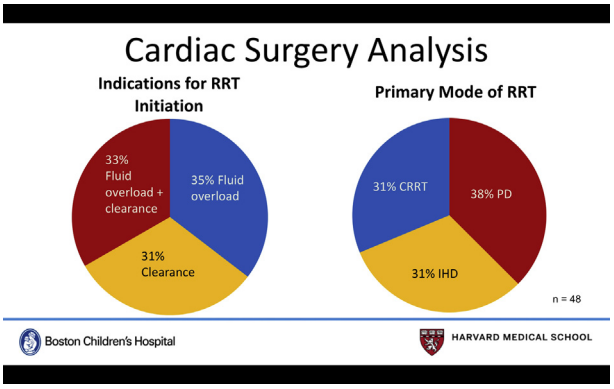
Presented as OR and adjusted OR with 95% CIs. *OR*, Odds ratio; *CI*, confidence interval; *ECMO*, extracorporeal membrane oxygenation; *eGFR*, estimated glomerular filtration rate; *RRT*, renal replacement therapy; *AKI*, acute kidney injury.

mortality rate of 20% in patients with AKI requiring PD after cardiac surgery, and age less than 1 year was independently associated with mortality. Hornik and colleagues[8] identified AKI requiring RRT after the Norwood procedure as a significant risk factor for mortality, with a mortality rate of 66.7% among infants requiring temporary RRT and 91.7% among infants requiring permanent RRT. The high mortality in our neonatal and infant population is consistent with these results.

Hornik and colleagues[8] also identified weight less than 2.5 kg as a risk factor for postoperative complications after the Norwood procedure. In our cohort, nonsurvivors had a significantly lower admission weight and weight-for-age z-score compared with survivors. Patients aged less than 1 year underwent some of the most high-risk operations, and they had a median weight-for-age z-score of −1.9 (IQR, −4.0 to −0.5). Pederson and colleagues[18] identified weight less than 5 kg as a risk factor for mortality in patients requiring PD after CHD surgery. In a study evaluating patients receiving continuous RRT from the Prospective Pediatric Continuous Renal Replacement Therapy Registry, the mortality rate was higher in children weighing 10 kg or less compared with children weighing more than 10 kg.[22] Technical aspects make providing RRT in low-weight populations difficult, and this may have contributed to challenges in providing effective RRT to manage AKI in these patients.

There have been a number of studies discussing the degree of fluid accumulation in postcardiac surgery patients and adverse outcomes.[23-25] This has led some to advocate for earlier initiation of RRT to prevent significant degrees of fluid accumulation. Kwiatkowski and colleagues[9] randomized patients with oliguria after cardiac surgery to receive furosemide or PD, and found that patients in the PD group were less likely to develop fluid accumulation greater than 10%. We found no difference between survivors and nonsurvivors in terms of fluid balance from surgery to initiation of RRT. One potential explanation is that we looked at the cumulative fluid balance over this time period up to 7 days, whereas these studies focused on the degree of fluid accumulation limited to the first 1 to 2 days postoperatively.

In the multivariable analysis, a longer duration of stage 3 AKI before RRT initiation was associated with mortality. Nonsurvivors were started on RRT over 2 times later than survivors with respect to all time points analyzed. Chan and colleagues[21] reported a median time interval between surgery and institution of PD of 12 hours in a group of patients aged less than 3 years undergoing cardiac surgery. Santos and colleagues[26] reported a mean time between diagnosis of AKI and PD initiation of 12 hours and a median time between surgery and PD of 2 days. Bojan and colleagues[27] reported improved mortality rates in neonates and infants with AKI initiated on PD before postoperative day 2 compared with those started on or after postoperative day 2. Sanchez-de-Toledo and colleagues[28] reported



VIDEO 1. Brief description of the main findings from the study. Video available at: https://www.jtcvs.org/article/S0022-5223(19)31360-1/fulltext.

improved mortality in patients with AKI receiving RRT within 24 hours of cardiac surgery compared with those patients receiving it later.

The timing of RRT initiation in our cohort was later than in these studies. Traditionally, patients at our institution do not come out of surgery with a PD catheter in place, which may lead to some delay in initiation of RRT for certain patients. Additionally, RRT is used relatively infrequently as demonstrated by the small number of patients in this cohort over a 9-year period. However, the extended duration of AKI after surgery may have contributed to the overall mortality of our cohort and suggests that it would be reasonable to consider earlier RRT in postoperative patients who develop AKI that does not improve despite several days of medical management. This was especially evident in patients aged less than 1 year. It is important to be mindful of patients who have preserved urine output in the setting of AKI because this group may be at higher risk for delaying RRT beyond a point where it may provide some benefit. In our cohort, nonsurvivors tended to have higher urine output and a higher eGFR leading up to RRT (although neither was statistically significant). Lower urine output may have prompted some clinicians to initiate RRT sooner than they otherwise would for a similar patient with nonoliguric stage 3 AKI, which could have contributed to improved outcomes for this group. Further studies are needed to better elucidate the optimal timing of RRT initiation in relation to when AKI develops, especially in patients with preserved urine output and in children aged less than 1 year.

Study Limitations

There are several important limitations to this study. First, this is a retrospective study and reliant on accurate documentation in the medical record. Additionally, there were long hospital lengths of stay and durations before initiating RRT, which could have led to inaccurate fluid balance calculations. Insensible losses were also not accounted for in the fluid balance calculation. Some have recommended using weight-based definitions of fluid accumulation,[29] but weights were not always available at the start of RRT, limiting the use of weight-based definition of fluid accumulation. A second limitation is the small sample size, which may limit the power to detect meaningful differences in mortality due to some of the risk factors evaluated. There also may have been other risk factors for mortality not accounted for in the retrospective design. Third, this is a single-center study and subject to institutional bias and may not be generalizable. In our hospital, the decision to initiate RRT is a collaborative one among the surgical, ICU, and nephrology physicians caring for the patient. Fourth, patients on ECMO were included in the analysis. In our ICU, patients on ECMO receive ultrafiltration at the discretion of the attending intensivist and cardiac surgeon. Therefore, patients who received RRT on ECMO were only identified if they received RRT for clearance purposes, because this is the only time patients would have a Current Procedural Terminology code for RRT. This may have led to a selection bias. Additionally, ultrafiltration via the ECMO circuit in our cohort likely mitigated the amount of fluid accumulation before initiation of RRT. Fifth, all modes of RRT were included for completeness. Although there was no difference in mortality between the different modes, it may be difficult to compare patients receiving different modes of RRT because there are multiple factors that play a role in the type of RRT a patient receives. Finally, the long ICU length of stay and long duration from admission to RRT initiation may highlight other complexities and complications in the cohort that may have contributed to the high mortality rate.

CONCLUSIONS

We highlight a high mortality rate for patients needing RRT in the pediatric CICU after cardiothoracic surgery. The mortality rate is especially high in young and smaller children, but it is unclear whether this is related to technical factors associated with administration of RRT or additional comorbidities. Fluid balance at the time of RRT initiation did not play a significant role in outcome. However, we identified a longer duration of stage 3 AKI before RRT initiation as an independent risk factor for mortality. Future studies should explore whether initiating RRT closer to the time of stage 3 AKI diagnosis improves outcomes.

Conflict of Interest Statement

Dr Thiagarajan has financial relationships with Bristol-Myers Squibb and Pfizer. All other authors have nothing to disclose with regard to commercial support.

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Key Words: renal replacement therapy, acute kidney injury, congenital heart disease

CONG

000 Renal replacement therapy in the pediatric cardiac intensive care unit

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A longer duration of AKI before initiation of RRT in surgical patients in the pediatric CICU is associated with mortality.