The association of acute kidney injury with hospital readmission and death after pediatric cardiac surgery

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ABSTRACT

Background: Acute kidney injury (AKI) in children undergoing cardiac surgery (CS) is strongly associated with increased hospital mortality and length of stay. The association of AKI with postdischarge outcomes is unclear. We evaluated the association of AKI with all-cause readmissions and death within 30 days and 1 year of CS discharge.

Methods: This was a prospective, 3-center cohort study of children after CS with cardiopulmonary bypass. The primary exposures were postoperative ≥ stage 1 AKI and ≥ stage 2 AKI defined by Kidney Disease: Improving Global Outcomes AKI definition. Two separate outcomes were hospital readmission and death within 30 days and 1 year of discharge. Association of AKI with time to outcomes was determined using multivariable Cox-proportional hazards analysis. Age, The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery risk adjustment tool score ≥3, cardiopulmonary bypass >120 minutes, and cyanotic heart disease were evaluated as effect modifiers.

Results: Of 402 participants included (median age 1.8 years [interquartile range 0.4, 5.2]), 32 (8.0%) and 109 (27.1%) were readmitted; 7 (1.7%) and 9 (2.2%) died within 30 days and 1 year of CS, respectively. AKI was not associated with readmission at 30 days or 1 year postdischarge. ≥ Stage 2 AKI (adjusted hazard ratio, 11.68 [1.88, 72.61]) was associated with mortality 30 days post-CS.

Conclusions: Postoperative AKI was not associated with readmission at 30 days and 1-year postdischarge. However, more severe AKI (≥ stage 2) appears to be associated with increased mortality risk at 30 days post-CS. (JTCVS Open 2020;4:70-85)

CENTRAL MESSAGE

Children with severe AKI (≥ stage 2) after cardiac surgery are at a higher risk for mortality, but not readmission, within 30 days of discharge, compared with children without AKI.

PERSPECTIVE

Reducing postoperative readmission and death is a priority. This is the first prospective cohort study to evaluate the relationship between AKI and post-cardiac surgery discharge readmission in children. Identifying risk factors for readmission and death may enable targeted follow up of at-risk groups and potentially decrease long-term morbidity and mortality.

See Commentaries on pages 86 and 88.
Acute kidney injury (AKI) occurs in 25% to 60% of children undergoing cardiac surgery and is strongly associated with increased hospital morbidity.\(^1,2\) In adults undergoing cardiac surgery, postoperative AKI has been shown to be associated with postdischarge mortality, cardiovascular events, development of chronic kidney disease (CKD), and end-stage renal disease.\(^3-7\) In noncardiac surgery children admitted to the intensive care unit, AKI has also been shown to be associated with increased health care use at 1 year postdischarge.\(^8\) In a retrospective study of children undergoing cardiac surgery, a strong association of AKI with CKD development 1 to 3 years postdischarge was shown.\(^9\) However, there is a lack of published data on the extent to which AKI after pediatric cardiac surgery is associated with non-kidney outcomes, including morbidity or health care use. Given data published in other patient populations, this association is important to elucidate as AKI after cardiac surgery may negatively impact long-term health, independent of a potential relationship with CKD and hypertension development. Previous clinical and epidemiologic research has demonstrated mechanisms between AKI and subsequent pulmonary, cardiac, and neurologic dysfunction that may contribute to morbidity and mortality after hospital discharge.\(^10,11\) Exploring health care use after cardiac surgery–associated AKI may also provide insight into long-term health burden for these patients, resource allocation, and health care use patterns. Finally, it is possible that the association of AKI with health care use and mortality is modified by factors known to affect long-term outcomes in children undergoing cardiac surgery, including age, cardiac surgery complexity, cardiopulmonary bypass (CPB) time, and cyanotic heart disease.\(^1,12,13\)

The goal of this study was to determine whether postoperative cardiac surgery–associated AKI is associated with increased risk for readmission to hospital and with death, within 30 days and 1 year after pediatric cardiac surgery discharge. A second goal was to determine whether the association of AKI with these outcomes is modified by age, surgical risk score, CPB time, and cyanotic heart disease.

### METHODS

#### Design, Setting, and Patient Selection

This study was a secondary analysis of a prospective multicenter cohort study of children undergoing cardiac surgery with cardiopulmonary bypass at Cincinnati Children’s Hospital, Montreal Children’s Hospital, and Yale New Haven Children’s Hospital. Children aged 1 month to 18 years undergoing cardiac surgery were enrolled between July 2007 and December 2010 in the Translational Research Investigating Biomarker Endpoints in AKI (TRIBE-AKI) study. Children with renal transplantation, dialysis, or the presence of AKI before cardiac surgery were excluded. Detailed patient recruitment methods for this study have been published elsewhere.\(^1,14\) Previously published TRIBE-AKI studies included children enrolled over 3 years (to 2009); this cohort includes an additional year of enrollment (to 2010). Parents or legal guardians of participants provided informed consent to participate and children provided assent when appropriate (age >7 years old). Research ethics board (Canada) and internal review board (United States) approvals were obtained from each institution before initiating study activities (ethics approval REB #1000061924; expiration date: 2020-09-28).

#### Data Collected From the Index Cardiac Surgery

**Admission From the Prospective TRIBE-AKI Study**

After preoperative recruitment, baseline variables collected included age at surgery, sex, previous cardiac surgeries, presence of cyanotic heart disease, congenital heart defect type, and noncardiac abnormalities. Participants were classified with cyanotic heart disease through review of surgical and defect type. Surgery-related variables collected included urgent versus elective surgery, risk adjustment using The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery (STAT) score (categorizes mortality risk associated with congenital heart surgery procedures on a scale of 1 to 5 with 1 being associated with the lowest mortality risk),\(^15\) CPB time, and duration of aortic crossclamp use. Postoperative variables collected prospectively while in hospital included (but were not limited to): daily serum creatinine (SCr), length of intensive care unit stay, length of hospital stay, and hospital mortality.

#### Primary Exposure Definition: Postoperative AKI

The presence of postoperative AKI during index cardiac surgery admission was defined based on the SCr criteria of the Kidney Disease: Improving Global Outcomes guidelines definition.\(^16\) Stage 1 AKI was a SCr rise of 1.5 to <2 times baseline SCr within 7 days or a >0.3 mg/dL (26.5 µmol/L) rise from baseline SCr within 48 hours; stage 2 AKI was SCr rise to 2.0 to <3 times baseline SCr; stage 3 AKI was SCr rise to ≥3 times baseline SCr or receiving acute dialysis for AKI or a decrease of estimated glomerular filtration rate to less than 35 mL/min/1.73 m\(^2\) for children over 3 months. The primary exposures were the presence of any AKI (≥stage 1) and the presence of severe AKI (≥stage 2).

#### Outcome Definitions: 30-Day and 1-Year

**Rehospitalization and Death**

Outcome data were collected retrospectively by medical chart and hospital electronic health records review, in addition to consultation with the cardiology services who cared for the patients. The 2 separate outcomes were rehospitalization for any reason and all-cause mortality at 30 days.
and 1-year postdischarge. One-year outcomes include all events up to and within the first 30 days as well as events from 30 to 365 days. Index admission and postdischarge deaths were included in mortality analyses. Descriptive data on primary diagnoses for rehospitalizations were collected and categorized for descriptive purposes.

### Statistical Analysis

Characteristics of patients with versus without each of the outcomes at 30 days and 1 year and of patients with versus without postoperative AKI were compared. Continuous variables were compared using \( t \) tests or Wilcoxon rank sum tests and categorical variables were compared using \( \chi^2 \) tests or Fisher exact tests, as appropriate. The associations of postoperative \( \geq \)stage 1 AKI, \( \geq \)stage 2 AKI, and the increasing AKI stage (no AKI to stage 3) with time to readmission were evaluated using multivariable Cox proportional hazards analysis using Fine and Gray’s subdistribution method (with death as a competing event). In a sensitivity analysis, the association of AKI with 1-year readmission, only in patients still alive at 30 days, was also analyzed. Regular cause-specific Cox proportional hazards models were used to analyze associations of AKI with mortality. Covariates to include in the multivariable models were selected a priori based on known risk factors for AKI in this population and also by examining univariable associations of patient characteristics with readmission and mortality. Age (continuous), STAT score \( \geq 3 \), CPB time \( > 120 \) minutes, and cyanotic heart disease were included with AKI in multivariable models. Effect modification of the associations between AKI and the outcomes were evaluated for age \( > 1 \), STAT surgical severity score \( \geq 3 \), presence of CPB time \( > 120 \) minutes and cyanotic heart disease by including interaction terms of AKI with each of these variables. SAS, version 9.4 (SAS Institute, Inc, Cary, NC) was used to conduct analyses.

### RESULTS

#### Cohort Characteristics

A total of 429 patients undergoing cardiac surgery between 2007 and 2010 were included in the TRIBE-AKI study (Figure 1). Of these, 402 participants had available rehospitalization and mortality data at 1 year and were included in the analysis. 179 (45%) participants developed AKI during index admission. Nineteen (11%) and 54 (30%) participants with postoperative AKI were readmitted within 30 days and 1 year of cardiac surgery discharge, respectively. Seven (4%) and 8 (5%), 7 from index admission and 1 from 30 to 365 days, participants with postoperative AKI died within 30 days and 1 year, respectively. Thirteen (6%) and 55 (25%) participants without postoperative AKI were readmitted within 30 days and 1 year of discharge, respectively. Zero and 1 (0.5%) participants without postoperative AKI died within 30 days and 1 year, respectively. AKI, Acute kidney injury.
the analyses (19 participants from Cincinnati and 8 from Yale’s Children’s Hospitals were excluded due to lack of follow-up data). The median age of participants was 1.8 years (interquartile range 0.4, 5.2), with 179 (45%) participants younger than the age of 1 year. One-hundred ninety-two children (48\% of participants) had a STAT score >3, had a CPB time of 105.78 (60.01) minutes, and 109 (29\%) had a CPB time >120 minutes. The median age of participants was 1.8 (0.4, 5.2) years, with 179 (45\%) of participants younger than the age of 1 year. One-hundred ninety-two children (48\% of participants) had a STAT score >3, and 109 (29\%) had a CPB time >120 minutes (Table 1). One hundred seventy-nine (45\%) of participants required renal replacement therapy during index admission. Appendix Table 3 shows that the most common reasons for readmission in patients with postoperative AKI were cardiac issues or procedures (31\%), followed by other (26\%)

### Table 1. Patient characteristics by readmission at 30 days postcardiac surgery

| Patient characteristics | Overall (n = 402) | No readmission at 30 d (n = 370) | Readmission at 30 d (n = 32) | P value |
|-------------------------|------------------|----------------------------------|-----------------------------|---------|
| **Preoperative/baseline variables** | | | | |
| Age, y – continuous | 1.8 (0.4, 5.2) | 1.99 (0.44, 5.29) | 0.76 (0.47, 4.21) | .580 |
| Age – categorized | | | | |
| 31 d to <1 y | 179 (45\%) | 162 (44\%) | 17 (53\%) | .308 |
| >1 to <18 y | 223 (55\%) | 208 (56\%) | 15 (47\%) | |
| Female sex | 192 (48\%) | 179 (48\%) | 13 (41\%) | .400 |
| Previous cardiothoracic operations | 165 (42\%) | 151 (41\%) | 14 (45\%) | .690 |
| Cyanotic heart disease | 134 (35\%) | 119 (34\%) | 15 (52\%) | .057 |
| Noncardiac abnormalities | 101 (26\%) | 91 (25\%) | 10 (32\%) | .374 |
| **Surgery-related variables** | | | | |
| STAT category (dichotomized) | | | | |
| <3 | 359 (90\%) | 332 (90\%) | 27 (87\%) | .612 |
| ≥3 | 41 (10\%) | 37 (10\%) | 4 (13\%) | |
| Surgery type | | | | |
| Septal defect repair | 134 (35\%) | 124 (35\%) | 10 (33\%) | .850 |
| Inflow/outflow tract or valve procedure | 62 (16\%) | 56 (16\%) | 6 (20\%) | |
| Combined procedure | 184 (48\%) | 170 (49\%) | 14 (47\%) | |
| **Urgency of surgery** | | | | |
| Elective | 368 (92\%) | 340 (92\%) | 28 (88\%) | .392 |
| Urgent | 34 (8\%) | 30 (8\%) | 4 (13\%) | |
| CPB time, min | 105.78 (60.01) | 104.51 (59.39) | 104.51 (59.39) | .106 |
| CPB time >120, min | 126 (31\%) | 112 (30\%) | 14 (44\%) | .115 |
| Crossclamp time, min | 45.85 (44.08) | 46.15 (44.06) | 42.41 (44.93) | .551 |
| **Postoperative variables** | | | | |
| Length of ICU stay, d | 2 (1.4) | 2 (1.4) | 3 (2.5) | .079 |
| Length of hospital stay, d | 5 (4, 9) | 5 (3, 9) | 7 (5.5, 10.5) | .010 |
| KDIGO AKI stages | | | | |
| No AKI | 223 (55\%) | 210 (57\%) | 13 (41\%) | .334 |
| Stage 1 AKI | 121 (30\%) | 109 (29\%) | 12 (38\%) | |
| Stage 2 AKI | 23 (6\%) | 20 (5\%) | 3 (9\%) | |
| Stage 3 AKI | 35 (9\%) | 31 (8\%) | 4 (13\%) | |

Categorical variables are reported as n (%) and continuous variables are reported as mean (SD) or median (IQR). SD, Standard deviation; IQR, interquartile range; STAT, The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery risk adjustment tool; CPB, cardiopulmonary bypass; ICU, intensive care unit; KDIGO, Kidney Disease: Improving Global Outcomes; AKI, acute kidney injury.
and then gastrointestinal and infectious (non-gastroenteritis) (11% each). In patients without AKI, the most common reasons for readmission were somewhat similar, with cardiac issues or procedures (25%), other (25%), and then ear–nose–throat (16%), and respiratory (11%).

**Association of AKI With Readmission at 30 Days and 1-Year Postdischarge**

Kaplan–Meir curves in Figure 2 show that there was no statistically significant univariable association between AKI and readmission within 30 days or within 1 year of cardiac surgery. Table 4 shows that in adjusted analyses (adjusting for age, STAT surgical severity score ≥ 3, CPB time > 120 minutes, and cyanotic heart disease), the lack of statistically significant association of postoperative ≥ stage 1 AKI or ≥ stage 2 AKI with 30-day and 1-year readmission persisted. In the adjusted models, STAT score ≥ 3 was associated with 1-year readmission postcardiac surgery (adjusted hazard ratio [aHR], 11.68; 95% confidence interval [CI], 1.05–1.33; Appendix Table 4). In a sensitivity analysis including only children who survived to 30 days postcardiac surgery, there was again no statistically significant association between AKI and 1-year readmission (Appendix Table 5 and Appendix Figure 1).

**Association of AKI With Mortality at 30 Days and 1-Year Postdischarge**

Table 5 and Figure 3 show that postoperative ≥ stage 2 AKI was associated with time to mortality within 30 days of cardiac surgery (in adjusted analyses, aHR, 11.68; 95% CI, 1.17–3.43; Appendix Table 4). In a sensitivity analysis including only children who survived to 30 days postcardiac surgery, there was again no statistically significant association of AKI or stage 3 AKI with time to mortality at 30 days postdischarge. One-year mortality multivariable
results were not performed due to the low number of events (2 deaths) between 30 days and 1-year postdischarge.

**Evaluation of Effect Modification of the Association of AKI With Outcomes**

Appendix Table 7 shows that neither age >1 year, STAT surgical severity score ≥3, CPB >120 minutes, nor cyanotic heart disease modified the relationship between AKI with mortality or with hospitalizations (all interaction term P values >.1).

**DISCUSSION**

Decreasing readmission and mortality after cardiac surgery has been identified as a priority by government programs and bodies such as Medicare (United States) and Ontario Ministry of Health and Long Term Care (Canada) to improve patient outcomes and reduce health care costs.17,18 Currently, readmission rates after cardiac surgery are high, with approximately 10% to 20% of children being readmitted within 30 days of discharge.19,20 Identification of risk factors for long-term readmission and mortality would allow for close follow-up and targeted interventions in at-risk groups. In the present study, AKI during index admission was not associated with readmission to hospital within 30 days or 1 year of hospital discharge as shown in the Figure 4. Stage 2 AKI was associated with a greater risk of death within 30 days of discharge. Only a limited number of studies in children undergoing cardiac surgery have evaluated long-term readmission, and this is the first prospective cohort study to evaluate the association between postoperative AKI with readmission after pediatric cardiac surgery.

We found that 8% of our cohort was readmitted within 30 days, which does not differ significantly from other studies conducted on children after cardiac surgery.13,20 This study did not find an association

### TABLE 3. Patient characteristics by mortality status at 30 days postcardiac surgery

| Patient characteristics | Overall (n = 402) | No mortality at 30 d (n = 395) | Mortality at 30 d (n = 7) | P value |
|-------------------------|------------------|--------------------------------|--------------------------|---------|
| **Preoperative/baseline variables** |                  |                                |                          |         |
| Age, y – continuous     | 1.8 (0.44, 5.23) | 1.79 (0.44, 5.08)              | 8.54 (0.25, 17.54)       | .294    |
| Age – categorized       |                  |                                |                          |         |
| 31 d to 1 y             | 179 (45%)        | 176 (45%)                      | 3 (43%)                  | .929    |
| ≥1 to <18 y             | 223 (55%)        | 219 (55%)                      | 4 (57%)                  |         |
| Female sex              | 192 (48%)        | 188 (48%)                      | 4 (57%)                  | .616    |
| Cyanotic heart disease  | 134 (35%)        | 131 (35%)                      | 3 (43%)                  | .679    |
| Previous cardiothoracic operations | 165 (42%) | 162 (42%)                      | 3 (43%)                  | .953    |
| Noncardiac abnormalities | 101 (26%)        | 98 (25%)                       | 3 (43%)                  | .290    |
| **Surgery-related variables** |                  |                                |                          |         |
| STAT category (dichotomized) |                  |                                |                          |         |
| <3                      | 359 (90%)        | 355 (90%)                      | 4 (57%)                  | .004    |
| ≥3                      | 41 (10%)         | 38 (10%)                       | 3 (43%)                  |         |
| **Surgery type**        |                  |                                |                          |         |
| Septal defect repair    | 134 (35%)        | 134 (36%)                      | 0 (0%)                   | .101    |
| Inflow/outflow tract or valve procedure | 62 (16%) | 61 (16%)                      | 1 (14%)                  |         |
| Combined procedure      | 184 (48%)        | 178 (48%)                      | 6 (86%)                  |         |
| **Urgency of surgery**  |                  |                                |                          |         |
| Elective                | 368 (92%)        | 363 (92%)                      | 5 (71%)                  | .054    |
| Urgent                  | 34 (8%)          | 32 (8%)                        | 2 (29%)                  |         |
| **CPB time, min**       |                  |                                |                          |         |
| 105.78 (60.01)          | 104.15 (57.08)   | 197.57 (129.26)                | .023                     |
| CPB time >120 min       | 126 (31%)        | 120 (30%)                      | 6 (86%)                  | .002    |
| Crossclamp time, min    | 45.85 (44.08)    | 45.82 (43.93)                  | 47.86 (56.25)            | .901    |

Categorical variables are reported as n (%) and continuous variables are as reported mean (SD) or median (IQR). SD, Standard deviation; IQR, interquartile range; STAT, The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery risk adjustment tool; CPB, cardiopulmonary bypass; ICU, intensive care unit; KDIGO, Kidney Disease: Improving Global Outcomes; AKI, acute kidney injury.
between AKI and readmission outcomes at 30 days postcardiac surgery discharge. However, we did identify other predictors including STAT score ≥3, which may be potentially useful for conducting larger sample size studies and development of readmission risk prediction models. Postcardiac surgery AKI was also not associated with 1-year postdischarge hospital readmission. Therefore, reducing AKI postcardiac surgery would not likely result in reduced readmissions. These findings are consistent with our previous study among cardiac surgery patients that demonstrated no association between AKI and development of CKD and CKD.

### Table 4. Associations (HR [95% CI]) between ≥stage 1 AKI, ≥stage 2 AKI, and increasing AKI stage with 30-day and 1-year readmission

| AKI definitions | 30-d readmission | 1-y readmission |
|-----------------|------------------|-----------------|
|                  | Unadjusted | Adjusted* | Unadjusted | Adjusted* |
| No AKI vs AKI    |            |            |            |            |
| No AKI (n = 223) | 13 (6%)   | 1.0 (ref) | 1.0 (ref) | 55 (25%) | 1.0 (ref) | 1.0 (ref) |
| ≥Stage 1 AKI (n = 179) | 26 (15%) | 1.86 (0.92-3.76) | 1.57 (0.72-3.41) | 61 (34%) | 1.27 (0.87-1.85) | 1.06 (0.69-1.61) |
| No/stage 1 AKI vs ≥stage 2 AKI |            |            |            |            |
| No AKI/stage 1 AKI (n = 344) | 27 (8%) | 1.0 (ref) | 1.0 (ref) | 93 (27%) | 1.0 (ref) | 1.0 (ref) |
| ≥Stage 2 AKI (n = 58) | 12 (21%) | 1.68 (0.74-3.85) | 1.54 (0.62-3.81) | 23 (40%) | 1.21 (0.73-2.01) | 0.98 (0.55-1.74) |
| Increasing AKI stage |            |            |            |            |
| No AKI (n = 223) | 13 (6%) | 1.0 (ref) | 1.0 (ref) | 55 (25%) | 1.0 (ref) | 1.0 (ref) |
| Stage 1 AKI (n = 121) | 14 (12%) | 1.74 (0.8-3.81) | 1.44 (0.6-3.46) | 38 (31%) | 1.25 (0.82-1.9) | 1.07 (0.68-1.69) |
| Stage 2 AKI (n = 23) | 4 (17%) | 2.23 (0.66-7.51) | 2.1 (0.6-7.29) | 8 (35%) | 1.33 (0.6-2.93) | 1.16 (0.52-2.59) |
| Stage 3 AKI (n = 35) | 8 (23%) | 2.03 (0.66-6.25) | 1.67 (0.5-2.51) | 15 (43%) | 1.31 (0.69-2.49) | 0.91 (0.42-1.97) |

AKI, Acute kidney injury; HR, hazard ratio; CI, confidence interval; ref, reference group in the analysis. *Adjusted for age, STAT score ≥3, CPB time >120 min, and cyanotic heart disease.
hypertension 5 years postdischarge; however, this remains an area of controversy. In noncardiac surgery children admitted to the intensive care unit, AKI has been shown to be associated with increased health care use, including postdischarge hospitalizations, physician visits, and other important health outcomes. Therefore, given the known strong association of AKI with readmission and other outcomes in non-cardiac surgery populations, these findings are notable. Children undergoing cardiac surgery are at high risk of readmission, which prompts an urgent need to find easily identifiable, strong predictors that would allow for targeted interventions to reduce readmission. The high proportion of readmissions along with the lack of association between AKI and readmission calls on future research to identify other risk factors for readmission after cardiac surgery discharge. Previously identified 30-day risk factors should be further investigated at 1 year and may include sociodemographic risk factors (ethnicity) and clinical risk factors (complications during admission). In a 30-day

![Probability of Mortality by 30 days post-discharge](image)

**FIGURE 3.** Kaplan–Meier curves for mortality within 30 days by AKI status. The dotted red line represents patients with postoperative AKI and the blue line represents patients without postoperative AKI. There is a statistically significant difference between the two survival curves (log-rank test \( P = .0029 \)). AKI, Acute kidney injury.

![Probability of Readmission](image)

**FIGURE 4.** Kaplan–Meier curves for readmission within 30 days by AKI status. The dotted red line represents patients with postoperative AKI and the blue line represents patients without post-operative AKI. The red- and blue-shaded areas represent the confidence intervals for the AKI and non-AKI group, respectively. There is no statistically significant difference between the 2 survival curves (log-rank test \( P = .065 \)). AKI, Acute kidney injury.

### TABLE 5. Mortality rate at 30 days and 1 year postcardiac surgery by AKI status and associations (HR [95% CI]) between \( \geq \) stage 1 AKI, \( \geq \) stage 2 AKI, and increasing AKI stage with 30-day mortality

| AKI definitions                        | n (%) | 30-d mortality Unadjusted HR (95% CI) | Adjusted HR (95% CI) | 1-y mortality* n (%) |
|----------------------------------------|-------|--------------------------------------|----------------------|----------------------|
| No AKI vs AKI                          |       |                                      |                      |                      |
| No AKI (n = 223)                       | 0 (0%) | 1.0 (ref)                             | 1.0 (ref)            | 1 (0.5%)             |
| \( \geq \) Stage 1 AKI (n = 179)       | 7 (3.9%) | NA                                   | NA                   | 8 (4.5%)             |
| No/stage 1 AKI vs stage 2 AKI or greater|       |                                      |                      |                      |
| No AKI/stage 1 AKI (n = 344)           | 2 (0.6%) | 1.0 (ref)                             | 1.0 (ref)            | 4 (1.2%)             |
| \( \geq \) Stage 2 AKI (n = 58)        | 5 (8.6%) | 15.32 (2.97-78.99)                    | 11.68 (1.88-72.61)   | 5 (8.6%)             |
| Increasing AKI stage                   |       |                                      |                      |                      |
| No AKI (n = 223)                       | 0 (0%) | 1.0 (ref)                             | NA                   | 1 (0.5%)             |
| Stage 1 AKI (n = 121)                  | 2 (1.7%) | NA                                   | NA                   | 3 (2.5%)             |
| Stage 2 AKI (n = 23)                   | 1 (4.4%) | NA                                   | NA                   | 1 (4.4%)             |
| Stage 3 AKI (n = 35)                   | 4 (11.4%) | NA                                  | NA                   | 4 (11.4%)             |

AKI, Acute kidney injury; HR, hazard ratio; CI, confidence interval; ref, reference group in the analysis; NA, not applicable. *Total deaths from 0 to 365 days postcardiac surgery discharge. (Adjusted for age, STAT score \( \geq 3 \), CPB time \( > 120 \) min, and cyanotic heart disease. Adjusted and statistically significant at \( P < .05 \).
1-year mortality as there were only 2 deaths between discharge. It was not possible to assess the association between AKI and risk for mortality 30 days after cardiac surgery discharge. It is the first study that has assessed the relationship between AKI and mortality in long term (1-year readmission) studies.

We found that children with stage 2 AKI were at greater risk for mortality 30 days after cardiac surgery discharge. It was not possible to assess the association between AKI and 1-year mortality as there were only 2 deaths between 30 days and 365 days postcardiac surgery. Therefore, larger samples (≥400 children) are required to better understand AKI’s association with mortality. The current study’s results are congruent with a single-center study of 718 children where RIFLE (Pediatric Risk, Injury, Failure, Loss, End Stage Renal Disease) stage F (most comparable with stage 3 AKI defined using Kidney Disease: Improving Global Outcomes) was associated with greater long-term mortality (median follow-up of 4 years). However, to our knowledge, no study has assessed the adjusted association between AKI and mortality at 30 days post-pediatric cardiac surgery, a clinically relevant time point. In addition, we are aware of only 4 papers (including the study mentioned previously) that have studied this relationship beyond 30 days. Of these, one study focused solely on neonates and the remaining three were single centre studies and did not report on the association of AKI with 30-day mortality. Further research and development of care guidelines are warranted to improve peri and postoperative mortality.

Findings must be considered within the study’s context. Limitations of the study include lack of information regarding zip-code/postal code or nature of practice (local vs distant referral), resulting in loss of readmission information from hospitals other than our centres and potentially information bias in outcome ascertainment. However, the 30-day outcome is a relatively short-term postdischarge outcome, during which time close follow-up at the centre performing the index cardiac surgery was highly likely. There was also intercenter and interphysician variability in discharge criteria. Also, limited data were available regarding specific reasons for readmission and mortality, including whether readmissions for cardiac procedures were planned procedures. We were also limited in terms of the cyanotic heart disease designation and were unable to control for postdischarge variables such as new comorbidities or treatments due to limitations of collected data. The strengths of this study include the large prospective design with detailed index and readmission information up to a year postdischarge.

In conclusion, children with severe AKI (≥stage 2) after cardiac surgery are at a greater risk for mortality, but not readmission, within 30 days of discharge, compared with children without AKI. Future research should evaluate new factors that may predict readmission after pediatric cardiac surgery and interventions to reduce short-term mortality risk in children after cardiac surgery.

Conflict of Interest Statement
Dr Parikh receives consulting fees from Akebia Therapeutics, Inc, Genfit Biopharmaceutical Company, and Renalix AI. All other authors reported no conflicts of interest.

The Journal policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: acute kidney injury, pediatric cardiac surgery, readmission, mortality, postdischarge outcomes
APPENDIX FIGURE 1. Kaplan–Meier curve for 1-year readmission postcardiac surgery discharge in patients alive at 30 days only, by AKI status. Shown is a survival curve for the outcome of readmission within 1 year of cardiac surgery discharge by AKI versus no AKI status in patients alive at 30 days. The red dotted line represents patients with postoperative AKI and the blue line represents patients without post-operative AKI. The red- and blue-shaded areas represent the confidence intervals for the AKI and non-AKI group, respectively. There is no statistically significant difference between the 2 survival curves (log-rank test $P = .13$). AKI, Acute kidney injury.
**APPENDIX TABLE 1. Patient characteristics by AKI status**

| Patient characteristics | Total, n = 402 | Non-AKI, n = 223 | AKI, n = 179 | P value |
|-------------------------|---------------|------------------|--------------|---------|
| **Preoperative/baseline variables** | | | | |
| Age, y | 1.8 (0.4, 5.2) | 3.6 (0.5, 7.3) | 0.7 (0.4, 3.7) | <.001 |
| Age | | | | |
| 31 d to 1 y | 179 (45%) | 78 (35%) | 101 (56%) | <.001 |
| >1 to <18 y | 223 (55%) | 145 (65%) | 78 (44%) | |
| Female sex | 192 (48%) | 106 (48%) | 86 (48%) | <.001 |
| Previous cardiothoracic operations | 165 (42%) | 87 (40%) | 78 (44%) | .405 |
| Cyanotic heart disease | 134 (35%) | 86 (32%) | 48 (44%) | <.001 |
| **Surgery-related variables** | | | | |
| STAT category (dichotomized) | | | | |
| <3 | 359 (90%) | 210 (95%) | 149 (84%) | <.001 |
| ≥3 | 41 (10%) | 12 (5%) | 29 (16%) | |
| Surgery type | | | | |
| Septal defect repair | 134 (35%) | 98 (36%) | 36 (33%) | .004 |
| Inflow/outflow tract or valve procedure | 62 (16%) | 48 (18%) | 14 (13%) | |
| Combined procedure | 184 (48%) | 124 (46%) | 60 (55%) | |
| Urgency of surgery | | | | |
| Elective | 368 (92%) | 265 (93%) | 103 (89%) | .302 |
| Urgent | 34 (8%) | 21 (7%) | 13 (11%) | |
| CPB time, min | 105.78 (60.01) | 93.85 (52.51) | 120.65 (65.37) | <.001 |
| CPB time >120 min | 126 (31%) | 126 (31%) | 50 (22%) | <.001 |
| Crossclamp time, min | 45.85 (44.08) | 43.85 (42.35) | 48.34 (46.14) | .450 |
| **Postoperative variables** | | | | |
| Length of ICU stay, d | 2 (1, 4) | 2 (1, 3) | 3 (2, 6) | <.001 |
| Length of hospitaiy stay, d | 5 (4, 9) | 4 (3, 6) | 7 (5, 13) | <.001 |

Categorical variables are reported as n (%), and continuous variables are reported mean (SD), or median (IQR). SD, Standard deviation; IQR, interquartile range; AKI, acute kidney injury; STAT, The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery risk adjustment tool; CPB, cardiopulmonary bypass; ICU, intensive care unit.
APPENDIX TABLE 2. Patient characteristics by mortality at 1-year postcardiac surgery

| Patient characteristics                        | Total (N = 402) | No mortality within 1 y (N = 393) | Mortality within 1 y (N = 9) | P value |
|-----------------------------------------------|-----------------|-----------------------------------|-----------------------------|---------|
| **Preoperative/baseline variables**           |                 |                                   |                             |         |
| Age, y                                        | 1.8 (0.44, 5.23) | 1.71 (0.44, 5.05)                 | 8.54 (0.66, 13.88)          | .115    |
| Age                                           |                 |                                   |                             |         |
| 31 d to 1 y                                   | 179 (45%)       | 176 (45%)                         | 3 (33%)                     |         |
| >1 to <18 y                                   | 223 (55%)       | 217 (55%)                         | 6 (67%)                     | .494    |
| Female sex                                    | 192 (48%)       | 187 (48%)                         | 5 (56%)                     | .636    |
| Previous cardiothoracic operations            | 165 (42%)       | 160 (42%)                         | 5 (56%)                     | .396    |
| Cyanotic heart disease                        | 134 (35%)       | 129 (35%)                         | 5 (56%)                     | .202    |
| Noncardiac abnormalities                      | 101 (26%)       | 96 (25%)                          | 5 (56%)                     | .037    |
| **Surgery-related variables**                 |                 |                                   |                             |         |
| STAT score <3                                 | 359 (90%)       | 354 (91%)                         | 5 (56%)                     | <.001   |
| STAT score ≥3                                 | 41 (10%)        | 37 (9%)                           | 4 (44%)                     |         |
| Septal defect repair                          | 134 (35%)       | 134 (36%)                         | 0 (0%)                      | .038    |
| Inflow/outflow tract or valve procedure        | 62 (16%)        | 61 (16%)                          | 1 (11%)                     |         |
| Combined procedure                            | 184 (48%)       | 176 (47%)                         | 8 (89%)                     |         |
| Urgency of surgery                            |                 |                                   |                             |         |
| Elective                                      | 368 (92%)       | 361 (92%)                         | 7 (78%)                     | .133    |
| Urgent                                        | 34 (8%)         | 32 (8%)                           | 2 (22%)                     |         |
| CPB time, min                                 | 105.78          | 103.76 (56.55)                    | 194.11 (121.8)              | .013    |
| CPB time >120 min                             | 126 (31%)       | 119 (30%)                         | 7 (78%)                     | .002    |
| Crossclamp time, min                          | 45.85 (44.08)   | 45.72 (43.78)                     | 51.44 (58.72)               | .995    |
| **Postoperative variables**                   |                 |                                   |                             |         |
| Length of ICU stay, d                         | 2 (1, 4)        | 2 (1, 4)                          | 9.5 (2, 35.5)               | .023    |
| Length of hospital stay, d                    | 5 (4, 9)        | 5 (4, 9)                          | 7 (2, 31)                   | .851    |
| KDIGO AKI stages                              |                 |                                   |                             |         |
| No AKI                                        | 223 (55%)       | 222 (56%)                         | 1 (11%)                     | <.001   |
| Stage 1 AKI                                   | 121 (30%)       | 118 (30%)                         | 3 (33%)                     |         |
| Stage 2 AKI                                   | 23 (6%)         | 22 (6%)                           | 1 (11%)                     |         |
| Stage 3 AKI                                   | 35 (9%)         | 31 (8%)                           | 4 (44%)                     |         |

Categorical variables are reported as n (%) and continuous variables are reported as mean (SD) or median (IQR). SD, Standard deviation; IQR, interquartile range; STAT, The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery risk adjustment tool; CPB, cardiopulmonary bypass; ICU, intensive care unit; KDIGO, Kidney Disease: Improving Global Outcomes; AKI, acute kidney injury.
APPENDIX TABLE 3. Primary reasons for readmission 1-year postcardiac surgery discharge by AKI status

| Reason for readmission* | Total, n = 113 | Non-AKI patients, n = 55 | AKI patients, n = 58 |
|-------------------------|----------------|--------------------------|----------------------|
| Neurologic              | 3 (3%)         | 2 (4%)                   | 1 (2%)               |
| Seizure                 | 2 (1.77)       | 1 (1.82)                 | 1 (1.72)             |
| Unspecified             | 1 (0.88)       | 1 (1.82)                 | 0                    |
| Gastrointestinal        | 11 (9%)        | 4 (7%)                   | 7 (11%)              |
| Gastroenteritis         | 2 (1.77)       | 0                        | 2 (3.45)             |
| Gastrostomy             | 1 (0.88)       | 0                        | 1 (1.72)             |
| EGD                     | 1 (0.88)       | 1 (1.82)                 | 0                    |
| Bloody stool            | 1 (0.88)       | 0                        | 1 (1.72)             |
| Ultrasound of the abdomen | 1 (0.88)     | 0                        | 1 (1.72)             |
| Failure to thrive       | 1 (0.88)       | 1 (1.82)                 | 0                    |
| Gastronomy tube         | 2 (1.77)       | 0                        | 2 (3.45)             |
| Nausea                  | 1 (0.88)       | 1 (1.82)                 | 0                    |
| Unspecified             | 1 (0.88)       | 1 (1.82)                 | 0                    |
| Respiratory (noninfectious) | 12 (10%)     | 6 (11%)                  | 6 (10%)              |
| Pleural effusion        | 3 (2.65)       | 1 (1.82)                 | 2 (3.45)             |
| Pneumonectomy           | 1 (0.88)       | 1 (1.82)                 | 0                    |
| Respiratory failure     | 1 (0.88)       | 1 (1.82)                 | 0                    |
| Chest tube placement    | 1 (0.88)       | 1 (1.82)                 | 0                    |
| Chest radiograph        | 1 (0.88)       | 1 (1.82)                 | 0                    |
| Cough                   | 1 (0.88)       | 1 (1.82)                 | 0                    |
| Tracheomalacia          | 1 (0.88)       | 1 (1.82)                 | 0                    |
| Unspecified             | 4 (3.54)       | 0                        | 4 (6.90)             |
| Cardiac issue or procedure | 33 (28%)      | 14 (25%)                 | 19 (31%)             |
| Arrhythmia              | 4 (3.54)       | 1 (1.82)                 | 3 (5.17)             |
| Hypoplastic heart       | 1 (0.88)       | 0                        | 1 (1.72)             |
| Pacemaker placement     | 1 (0.88)       | 0                        | 1 (1.72)             |
| Heart failure           | 1 (0.88)       | 0                        | 1 (1.72)             |
| Endocarditis            | 2 (1.77)       | 1 (1.82)                 | 1 (1.72)             |
| Computed tomography angiogram | 1 (0.88) | 0                        | 1 (1.72)             |
| Cardiac catheterization | 11 (9.73)      | 6 (10.91)                | 5 (8.62)             |
| Echocardiogram          | 1 (0.88)       | 0                        | 1 (1.72)             |
| Cardiac surgical repair | 4 (3.54)       | 3 (5.45)                 | 1 (1.72)             |
| Pulmonary artery anomaly| 1 (0.88)       | 0                        | 1 (1.72)             |
| Pulmonary artery stenosis | 2 (1.77)     | 2 (3.64)                 | 0                    |
| Pericardial effusion    | 2 (1.77)       | 1 (1.82)                 | 1 (1.72)             |
| Not specified           | 2 (1.77)       | 0                        | 2 (3.45)             |
| Renal (noninfectious)   | 1 (1%)         | 1 (2%)                   | 0 (0%)               |
| Ureteral pelvic junction obstruction | 1 (0.88) | 1 (1.82) | 0 |
| Ear, nose, throat       | 12 (10%)       | 9 (16%)                  | 3 (5%)               |
| Otitis media myringotomy, tube placement in ears | 5 (4.42) | 5 (9.09) | 0 |
| Larynx stenosis         | 1 (0.88)       | 0                        | 1 (1.72)             |
| Nasolacrimal duct obstruction/probing | 2 (1.77) | 1 (1.82) | 1 (1.72) |
| Adenoidectomy           | 1 (0.88)       | 1 (1.82)                 | 0                    |
| Cleft palate            | 1 (0.88)       | 0                        | 1 (1.72)             |
| Micro laryngoscopy      | 1 (0.88)       | 1 (1.82)                 | 0                    |
| Infectious (non-gastroenteritis) | 12 (10%) | 5 (9%) | 7 (11%) |
| Respiratory infection   | 8 (7.08)       | 3 (5.45)                 | 5 (8.62)             |
| Fever                   | 1 (0.88)       | 0                        | 1 (1.72)             |
| UTI                     | 1 (0.88)       | 1 (1.82)                 | 0                    |
| Skin infection          | 1 (0.88)       | 1 (1.82)                 | 0                    |
| Unspecified             | 1 (0.88)       | 0                        | 1 (1.72)             |
| Other                   | 29 (26%)       | 14 (25%)                 | 15 (26%)             |

Categorical variables are reported as n (%). AKI, Acute kidney injury; EGD, esophagogastroduodenoscopy; UTI, urinary tract infection. *Primary reason for readmission was collected retrospectively during collection of the primary outcome. At the time of analysis, these were categorized (authors S.N. and H.T.P.) and then adjudicated (author M.Z.).
### APPENDIX TABLE 4. Associations (HR [95% CI]) between covariates and readmission postcardiac surgery discharge (full models)

| AKI definitions | 30-d readmission | 1-y readmission |
|-----------------|------------------|-----------------|
|                 | Adjusted* HR (95% CI) | Adjusted* HR (95% CI) |
| No AKI vs AKI   |                  |                  |
| No AKI (n = 223) | 1.0 (ref)        | 1.0 (ref)        |
| ≥Stage 1 AKI (n = 179) | 1.57 (0.72-3.41) | 1.06 (0.69-1.61) |
| Age             | 1.03 (0.94-1.12) | 0.97 (0.91-1.03) |
| STAT surgical severity score ≥3 | 0.75 (0.23-2.5) | 2 (1.17-3.43) |
| CPB time >120 min | 1.29 (0.62-2.66) | 1.01 (0.64-1.58) |
| Cyanotic heart disease | 0.49 (0.22-1.08) | 0.73 (0.47-1.12) |

No AKI vs stage 1 AKI

No AKI/stage 1 AKI (n = 344) | 1.0 (ref) | 1.0 (ref) |
| Age             | 1.02 (0.94-1.11) | 0.97 (0.91-1.03) |
| STAT surgical severity score ≥3 | 0.78 (0.23-2.65) | 2.02 (1.17-3.46) |
| CPB time >120 min | 1.24 (0.57-2.67) | 1.02 (0.64-1.64) |
| Cyanotic heart disease | 0.46 (0.21-1.01) | 0.72 (0.47-1.1) |

Increasing AKI stage

No AKI (n = 223) | 1.0 (ref) | 1.0 (ref) |
| Stage 1 AKI (n = 121) | 1.44 (0.6-3.46) | 1.07 (0.68-1.69) |
| Stage 2 AKI (n = 23) | 2.1 (0.6-7.29) | 1.16 (0.52-2.59) |
| Stage 3 AKI (n = 35) | 1.67 (0.52-5.41) | 0.91 (0.42-1.97) |
| Age             | 1.03 (0.94-1.12) | 0.97 (0.91-1.03) |
| STAT surgical severity score ≥3 | 0.76 (0.23-2.32) | 2.01 (1.17-3.43) |
| CPB time >120 min | 1.24 (0.59-2.6) | 1.03 (0.65-1.66) |
| Cyanotic heart disease | 0.49 (0.22-1.08) | 0.72 (0.47-1.12) |

### APPENDIX TABLE 5. Associations (HR [95% CI]) between ≥stage 1 AKI, ≥stage 2 AKI, and increasing AKI stage with 1-year readmission in patients alive at 30 days postcardiac surgery discharge

| AKI definitions | 1-y readmission |
|-----------------|-----------------|
|                 | n (%) | Unadjusted HR (95% CI) | Adjusted* HR (95% CI) |
| No AKI vs AKI   |        |                  |                  |
| No AKI          | 55 (25%) | 1.0 (ref) | 1.0 (ref) |
| ≥Stage 1 AKI    | 54 (31%) | 1.33 (0.92-1.94) | 1.11 (0.73-1.69) |

Increasing AKI stage

No/stage 1 AKI | 91 (27%) | 1.0 (ref) | 1.0 (ref) |
| Stage 2 AKI    | 18 (34%) | 1.34 (0.81-2.22) | 1.08 (0.62-1.9) |

HR, Hazard ratio; CI, confidence interval; AKI, acute kidney injury; ref, reference group in the analysis; STAT, The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery risk adjustment tool; CPB, cardiopulmonary bypass. *Adjusted for age, STAT surgical severity score ≥3, CPB time >120 min. | Adjusted and statistically significant at P < .05. |
APPENDIX TABLE 6. Associations (HR [95% CI]) between covariates and mortality postcardiac surgery discharge (full models)

| AKI definitions          | 30-d mortality | 1-y mortality |
|--------------------------|----------------|--------------|
|                          | Adjusted* HR (95% CI) | Adjusted* HR (95% CI) |
| No AKI vs AKI            |                |              |
| No AKI (n = 223)         | 1.0 (ref)      | 1.0 (ref)    |
| >Stage 1 AKI (n = 179)   | NA             | 6.73 (0.74-61.42) |
| Age                      | 1.18 (1.05-1.33) | 1.18 (1.06-1.31) |
| STAT surgical severity score ≥3 | 1.41 (0.23-8.51) | 1.88 (0.39-9.1) |
| CPB time >120 min        | 7.67 (0.87-67.53) | 4.51 (0.86-23.71) |
| Cyanotic heart disease   | 1.2 (0.24-5.86) | 0.57 (0.13-2.44) |
| No/stage 1 AKI vs ≥stage 2|                |              |
| No AKI/stage 1 AKI (n = 344) | 1.0 (ref) | 1.0 (ref) |
| >Stage 2 AKI (n = 58)    | 11.68 (1.88-72.61) | 4.51 (1-20.39) |
| Age                      | 1.16 (1.04-1.29) | 1.17 (1.06-1.29) |
| STAT surgical severity score ≥3 | 3.28 (0.51-21.01) | 2.96 (0.61-14.32) |
| CPB time >120 min        | 6.41 (0.68-60.11) | 3.88 (0.69-21.71) |
| Cyanotic heart disease   | 2.4 (0.36-16.16) | 0.74 (0.14-3.76) |
| Increasing AKI stage     |                |              |
| No AKI (n = 223)         | NA             | 1.0 (ref)    |
| Stage 1 AKI (n = 121)    | NA             | 4.61 (0.43-49.42) |
| Stage 2 AKI (n = 23)     | NA             | 10.05 (0.61-165.5) |
| Stage 3 AKI (n = 35)     | NA             | 13.56 (1.07-172.24) |
| Age                      | 1.17 (1.05-1.31) | 1.18 (1.06-1.3) |
| STAT surgical severity score ≥3 | 1.91 (0.28-11.89) | 2.12 (0.41-10.91) |
| CPB time >120 min        | 4.77 (0.46-49.73) | 3.43 (0.58-20.17) |
| Cyanotic heart disease   | 2.28 (0.37-13.86) | 0.8 (0.17-3.85) |

HR, Hazard ratio; CI, confidence interval; AKI, acute kidney injury; ref, reference group in the analysis; STAT, The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery risk adjustment tool; CPB, cardiopulmonary bypass; NA, not applicable. *Adjusted for age, STAT surgical severity score ≥3, CPB time >120 minutes. †Adjusted and statistically significant at P < .05.

APPENDIX TABLE 7. Assessment of effect modification of the AKI-outcome relationship by age, STAT surgical severity score, cardiopulmonary bypass time, and cyanotic heart disease

| Outcome                      | AKI stage                              | P value for interaction term of AKI and potential effect modifier |
|------------------------------|----------------------------------------|------------------------------------------------------------------|
|                              | Age >1                                 | STAT score ≥3          | CPB time >120 min | Cyanotic heart disease |
| Death within 30 d of surgery | No AKI vs >stage 1 AKI                  | .44                    | .99               | .99                   | .41 |
|                              | No/stage 1 AKI vs stage 2 or greater AKI| .93                    | .56               | .50                   | .15 |
| Readmission within 1 y of surgery | No AKI vs >stage 1 AKI                  | .65                    | .68               | .20                   | .71 |

AKI, Acute kidney injury; STAT, The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery risk adjustment tool; CPB, cardiopulmonary bypass; NA, not applicable.