# Acute kidney injury and renal recovery following Fontan surgery

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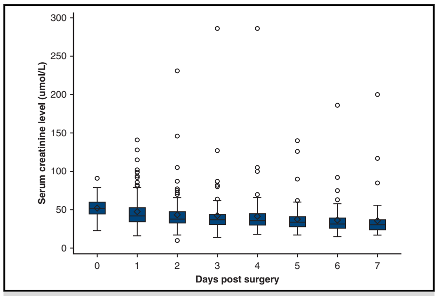
## ABSTRACT

**Objectives:** Acute kidney injury has been described after Fontan surgery, but the duration and outcomes are unknown. We sought to describe the incidence of and risk factors for acute kidney injury and the phenotype of renal recovery, and evaluate the impact of renal recovery phenotype on outcomes.

**Methods:** All children who underwent a Fontan operation at a single center between 2009 and 2022 were included. Data collected included Fontan characteristics, vasopressor use, all measures of creatinine, and postoperative outcomes. Logistic regression models were used to assess predictors of acute kidney injury and the association between acute kidney injury and outcomes.

**Results:** We enrolled 141 children (45% female). Acute kidney injury occurred in 100 patients (71%). Acute kidney injury duration was transient (<48 hours) in 77 patients (55%), persistent (2-7 days) in 15 patients (11%), more than 7 days in 4 patients (3%), and unknown in 4 patients (3%). Risk factors for acute kidney injury included higher preoperative indexed pulmonary vascular resistance (odds ratio, 3.90; $P = .004$) and higher postoperative inotrope score on day 0 (odds ratio, 1.13, $P = .047$). Risk factors for acute kidney injury duration more than 48 hours included absence of a fenestration (odds ratio, 3.43, $P = .03$) and longer duration of cardiopulmonary bypass (odds ratio, 1.22 per 15-minute interval, $P = .01$). Acute kidney injury duration more than 48 hours was associated with longer length of stay compared with transient acute kidney injury (median 18 days [interquartile range, 9-62] vs 10 days [interquartile range, 8-16], $P = .006$) and more sternal wound infections (17% vs 4%, $P = .049$).

**Conclusions:** Acute kidney injury after the Fontan operation is common. The occurrence and duration of acute kidney injury have significant implications for postoperative outcomes. (JTCVS Open 2024;17:248-56)




SCr (μmol/L) among the full study cohort during the first postoperative week.

**CENTRAL MESSAGE**

AKI after the Fontan operation is common. The occurrence and duration of AKI have significant implications for postoperative outcomes.

**PERSPECTIVE**

AKI is common after Fontan surgery; however, the duration of AKI has not previously been described. AKI duration more than 48 hours occurred in 16% of patients. The absence of a fenestration and longer duration of bypass were associated with AKI greater than 48 hours. Relative to patients having AKI for less than 48 hours, prolonged AKI increased hospital length of stay and risk of sternal wound infection.

The incidence of acute kidney injury (AKI) after Fontan surgery has been found to vary greatly in prior studies, with estimates ranging from 11% to 52%.[1-5] Risk factors for post-Fontan AKI include reduced renal perfusion pressure postoperatively, higher vasoactive-inotrope score, and longer duration of cardiopulmonary bypass (CPB).[1,3-5]

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**Abbreviations and Acronyms**

AKD = acute kidney disease
AKI = acute kidney injury
CPB = cardiopulmonary bypass
CVP = central venous pressure
ICU = intensive care unit
IQR = interquartile range
MAP = mean arterial pressure
OR = odds ratio
POD = postoperative day
SCr = serum creatinine

AKI post-Fontan is associated with longer duration of pleural drainage[5] and hospital length of stay,[4,5] and higher mortality[1] compared with those without AKI.

There is increasing focus on renal recovery after AKI, including the timing and degree of recovery and how these influence postoperative outcomes. Renal recovery is defined as no longer meeting criteria for AKI. "Transient" AKI is reversal of injury in 48 hours, compared with "persistent" AKI where reversal is in 2 to 7 days.[6] The term "acute kidney disease" (AKD) applies to kidney injury that does not improve within 7 days.[6] Gist and colleagues[7] reported that after the Norwood operation, persistent AKI was associated with greater mortality and among survivors a longer duration of mechanical ventilation compared with those having transient or no AKI.

Despite the common occurrence of AKI post-Fontan, the duration of AKI has not been described post-Fontan surgery, and the impact of persistent AKI, or AKD, on postoperative outcomes is unknown. Accordingly, we sought to determine the incidence and duration of cardiac surgery–associated AKI, determine the risk factors associated with AKI and renal recovery, and evaluate the impact of AKI and AKI duration on postoperative outcomes.

## MATERIAL AND METHODS

### Study Setting and Design

We conducted a retrospective, single-center cohort study at the Stollery Children's Hospital, a quaternary-care center in Edmonton, Alberta, Canada.

### Eligibility Criteria

We included patients who underwent Fontan surgery between May 2009 and April 2022 inclusive. We used the Western Canadian Single Ventricle Registry to identify eligible patients who underwent Fontan surgery. Exclusion criteria were absence of perioperative clinical data available for review, no serum creatinine (SCr) available within 90 days preceding the Fontan procedure, or need for preoperative dialysis. All data were collected from available electronic or written medical records and managed using Research Electronic Data Capture[8] electronic data capture tools hosted and supported by the Women and Children's Health Research Institute at the University of Alberta.

### Acute Kidney Injury Definition

AKI was determined using the Kidney Disease: Improving Global Outcomes definition: AKI stage 1 = SCr 1.5 to 1.9 × baseline, AKI stage 2 = SCr 2.0 to 2.9 × baseline, and AKI stage 3 = SCr 3.0 × baseline or need for renal replacement therapy.[9] Peak postoperative SCr was used to define AKI severity. Duration of AKI was categorized using the Acute Disease Quality Initiative 16 Workgroup definition: transient AKI (reversal of SCr < 1.5 × baseline within 48 hours), persistent AKI (SCr < 1.5 × baseline in 2-7 days), and AKD (SCr > 1.5 × baseline after day 7).[6] Baseline SCr was defined as the most recent preoperative value, typically obtained in the Preadmission Clinic 1 to 3 days before surgery. Only the first episode of AKI was included in the calculation of AKI duration; for patients who had resolution of AKI followed by a second occurrence of AKI, the second AKI event was not included.

### Data Collection

Medical records were reviewed for preoperative, intraoperative, and postoperative details. All SCr measurements were recorded from the most recent preoperative value to the time of discharge or postoperative day (POD) 30, whichever came sooner. Potential patient-specific risk factors included age at Fontan, sex, and primary cardiac diagnosis. Preoperative pulmonary artery pressure (mm Hg), averaged from right and left pulmonary artery pressures, and mean preoperative pulmonary vascular resistance (indexed Woods units × $m^2$) were acquired from the patient's pre-Fontan cardiac catheterization. Preoperative aortic valve regurgitation (none, trivial, trivial-mild, mild, mild-moderate, moderate, moderate-severe and severe) and preoperative ventricular function were obtained from the pre-Fontan echocardiogram reports.

Intraoperative information included type of Fontan (lateral tunnel, extracardiac, intra-extracardiac, hepatic vein inclusion post-Kawashima, and other), creation of fenestration (Y/N), whether additional surgery was performed during Fontan (and type of surgery performed), mean duration of CPB, and renal perfusion pressure at the end of the operation, which was calculated by subtracting central venous pressure (CVP) from the mean arterial pressure (MAP). Intraoperative flows were maintained at approximately 100 mL/kg/min to maintain age-appropriate blood pressure. Patients routinely underwent modified ultrafiltration. Renal near-infrared spectroscopy was not measured routinely. MAP and CVP were recorded in the operating room after separating from CPB, and the last 3 measurements of each were averaged for each patient. CVP was measured in the superior vena cava. Renal perfusion pressure was calculated as MAP-CVP. Fenestrations were created using a side-biting clamp on the atrial wall of the beating heart. The intended size of fenestrations was 3 to 4 mm. All patients underwent intraoperative transesophageal echocardiography to confirm patency of fenestrations and rule out Fontan pathway obstruction.

Postoperative MAP and CVP were collected every 4 hours, averaged over a 24-hour period for PODs 0, 1, and 2, and used to calculate the renal perfusion pressure. Inotrope doses (epinephrine, norepinephrine, milrinone, and vasopressin) were collected every 4 hours and then averaged for PODs 0, 1, and 2 to gain the vasoactive inotrope score for each day using the following formula: (100 × epinephrine μg/kg/min) + (100 × norepinephrine μg/kg/min) + (20 × milrinone μg/kg/min) + (10 × vasopressin units/kg/min) as modified from Wernovsky and colleagues.[10] The highest lactate was recorded for POD 0 to 2 inclusive. Additional postoperative information included length of stay in the intensive care unit (ICU), total hospital length of stay, postoperative sternal wound infection (Y/N), duration of pleural drainage, postoperative cardiac arrest (Y/N), and postoperative extracorporeal membrane oxygenation (Y/N). Ventilation time was not considered, because most patients at our institution are extubated in the operating room.

### Statistical Analysis

Descriptive analysis of baseline characteristics was undertaken, with continuous variables reported as mean and SD, or median with interquartile range (IQR) as appropriate, and categorical variables reported as total and relative frequencies. Fisher exact test was used for comparison of categorical variables, and the Mann–Whitney *U* test was used to compare continuous variables. Logistic regression was conducted to assess risk factors for AKI. Variables with *P* values less than .20 in univariate regression were included in the multivariable model. Likewise, logistic regression was used to identify risk factors for persistent AKI or AKD, relative to those with transient AKI. Analyses were performed using SAS Version 9.4 (SAS Institute Inc).

### Ethics Approval

The team gained approval for the study (Pro00118813; March 22, 2022) and approval to use the Western Canadian Single Ventricle Registry (Pro00107415) from the Ethics Board at the University of Alberta. Waiver of consent was provided.

## RESULTS

### Cohort Characteristics

A total of 143 patients met the inclusion criteria. Two patients were excluded because they had no SCr assessed within 90 days before their Fontan procedure. The remaining 141 patients were analyzed, among whom the baseline SCr was assessed within 3 days in 108 (77%). Mean age was 4.1 ± 1.9 years, and 45% were female. The most common primary cardiac diagnosis was hypoplastic left heart syndrome (38%). An extracardiac Fontan was performed in 95% of patients, and 77% had a fenestration. Baseline char-

**TABLE 1. Baseline characteristics**

| Variables | All patients N = 141 | AKI N = 100 | No AKI N = 41 |
|---|---|---|---|
| Mean age at Fontan | 4.1 ± 1.9 y | 4.1 ± 1.9 y | 4.1 ± 1.9 y |
| Female sex | 63 (45) | 45 (45) | 18 (44) |
| Primary cardiac diagnosis | | | |
| Hypoplastic left heart syndrome | 54 (38) | 41 (41) | 13 (32) |
| Double inlet left ventricle | 13 (9) | 11 (11) | 2 (5) |
| Tricuspid atresia | 16 (11) | 8 (8) | 8 (20) |
| Ebstein's anomaly | 2 (1) | 1 (1) | 1 (2) |
| DORV with mitral atresia | 4 (3) | 4 (4) | 0 (0) |
| Single ventricle, unbalanced AVSD | 20 (14) | 11 (11) | 9 (22) |
| Pulmonary atresia with intact ventricular septum | 12 (9) | 8 (8) | 4 (10) |
| Other | 20 (14) | 16 (16) | 4 (10) |
| Preoperative pulmonary artery pressure (mm Hg) (median, IQR) | 10 (8-13) | 10 (9-12) | 9 (8-11) |
| Preoperative PVR (indexed Woods units*m$^2$) (median, IQR) | 1.7 (1.2-2.0) | 1.8 (1.5-2.0) | 1.42 (1.0-1.7) |
| Preoperative ventricular end-diastolic pressure (mm Hg) (median, IQR) | 6.0 (4.0-8.0) | 6.0 (4.0-9.0) | 6.0 (3.5-7.5) |
| Preoperative aortic valve regurgitation (n = 125) | | | |
| None-mild | 112 (79) | 77 (77) | 35 (85) |
| Mild-moderate to severe | 13 (9) | 9 (9) | 4 (10) |
| Preoperative ventricular function (n = 138) | | | |
| Normal | 119 (86) | 85 (88) | 34 (83) |
| Reduced (mild, moderate, or severe) | 19 (14) | 12 (12) | 7 (17) |
| Type of Fontan | | | |
| Extracardiac | 134 (95) | 95 (95) | 39 (95) |
| Lateral tunnel | 4 (3) | 2 (2) | 2 (5) |
| Other | 3 (2) | 3 (3) | 0 (0) |
| Fenestrated | 109 (77) | 77 (77) | 32 (78) |
| Additional surgery performed at Fontan | | | |
| Aortic valve repair | 8 (6) | 7 (7) | 1 (2) |
| Arch reconstruction | 5 (4) | 4 (4) | 1 (2) |
| Duration of CPB (min) (median, IQR) | 80 (66-99) | 81 (66-105) | 80 (65-91) |

Results presented as N (%) unless otherwise specified. *AKI*, Acute kidney injury; *DORV*, double outlet right ventricle; *AVSD*, atrioventricular septal defect; *CPB*, cardiopulmonary bypass; *IQR*, interquartile range; *PVR*, pulmonary vascular resistance.

acteristics are summarized in Table 1. Postoperative data are detailed in Table 2. Median ICU length of stay was 2 days (IQR, 1-3), median duration of pleural drainage was 8 days (IQR, 6-11), and median hospital length of stay was 10 days (IQR, 8-16). Most patients (94%) were extubated in the operating room or on the same day of surgery. Postoperative SCr was highest on POD 0 and decreased during the first postoperative week (Figure 1). Two patients required postoperative renal replacement therapy (continuous renal replacement therapy in 1 and peritoneal dialysis in 1).

### Acute Kidney Injury Incidence and Duration

AKI occurred in 100 of 141 patients (71%). AKI first developed on the day of surgery (POD 0) in 81 patients, on POD 1 in 9 patients, on POD 2 in 5 patients, and by POD 7 in all 100 affected patients. Stage 1 AKI occurred in 63 patients (45%), stage 2 in 29 patients (21%), and stage 3 in 8 patients (6%). AKI was transient in 77 patients (55%), was persistent in 15 patients (11%), resulted in AKD in 4 patients (3%), and was of uncertain duration in 4 patients (3%). The occurrence and duration of AKI are outlined in Table 3. Among 63 children with stage 1 AKI, 56 (89%) had transient AKI. By comparison, 72% of stage 2 AKI was transient, and no cases of stage 3 AKI were transient.

Thirty patients had a second episode of AKI during the same hospitalization after SCr returned to less than 1.5× the baseline value. Among them, 16 of 30 (53%) had severe AKI (stages 2 or 3) during the first episode compared with 21 of 70 (30%) who had AKI only once ($P = .04$).

### Risk Factors Associated With Acute Kidney Injury

Table 4 shows the univariable analysis of risk factors for AKI. On multivariable analysis, higher preoperative

**TABLE 2. Postoperative outcomes**

| Variables | All patients N = 141 | AKI N = 100 | No AKI N = 41 |
|---|---|---|---|
| MAP (mm Hg) | | | |
| In operating room | 50 (42-58) | 50 (42-59) | 50 (43-56) |
| POD 0 | 64 (60-70) | 64 (60-71) | 65 (61-68) |
| POD 1 | 70 (65-76) | 70 (65-76) | 70 (64-77) |
| POD 2 | 70 (66-76) | 70 (67-78) | 66 (64-75) |
| CVP (mm Hg) | | | |
| In operating room | 18 (16-20) | 18 (16-21) | 18 (15-20) |
| POD 0 | 14 (12-17) | 15 (12-17) | 13 (12-15) |
| POD 1 | 13 (11-16) | 14 (12-16) | 13 (10-16) |
| POD 2 | 14 (12-16) | 15 (13-16) | 12 (10-15) |
| Renal perfusion pressure (mm Hg) | | | |
| In operating room | 32 (24-39) | 32 (24-39) | 32 (27-39) |
| POD 0 | 50 (46-55) | 50 (45-55) | 51 (47-55) |
| POD 1 | 57 (52-63) | 56 (52-62) | 59 (49-66) |
| POD 2 | 55 (51-58) | 55 (51-59) | 52 (49-55) |
| Length of stay in ICU (d) | 2 (1-3) | 2 (1-3) | 2 (1-3) |
| Hospital length of stay (d) | 10 (8-16) | 11 (8-19) | 8 (7-10) |
| Postoperative sternal wound infection N (%) | 7 (5) | 7 (7) | 0 (0) |
| Duration of pleural drainage (d) | 8 (6-11) | 8 (6-12) | 7 (5-9) |
| Postoperative cardiac arrest N (%) | 3 (2) | 2 (2) | 1 (2) |
| Postoperative ECMO N (%) | 3 (2) | 3 (3) | 0 (0) |
| Postoperative in-hospital death N (%) | 7 (5) | 6 (6) | 1 (2) |
| Postoperative vasoactive inotrope scores | | | |
| POD 0 | 5.4 (2.3-8.3) | 5.5 (2.3-9.2) | 4.0 (1.2-6.8) |
| POD 1 | 0.6 (0.0-2.8) | 0.7 (0.0-2.7) | 0.6 (0.0-3.0) |
| POD 2 | 0.0 (0.0-0.0) | 0.0 (0.0-0.0) | 0.0 (0.0-0.0) |
| Postoperative highest lactate (mmol/L) | | | |
| POD 0 | 3.2 (2.7-4.9) | 3.3 (2.7-5.0) | 3.0 (2.2-3.9) |
| POD 1 | 2.1 (1.4-3.1) | 2.3 (1.4-3.3) | 1.8 (1.4-2.5) |
| POD 2 (N = 65) | 1.4 (1.0-1.7) | 1.4 (1.1-1.8) | 1.2 (1.0-1.5) |

Results presented as median (IQR) unless otherwise specified. *AKI*, Acute kidney injury; *MAP*, mean arterial pressure; *POD*, postoperative day; *CVP*, central venous pressure; *ICU*, intensive care unit; *ECMO*, extracorporeal membrane oxygenator.

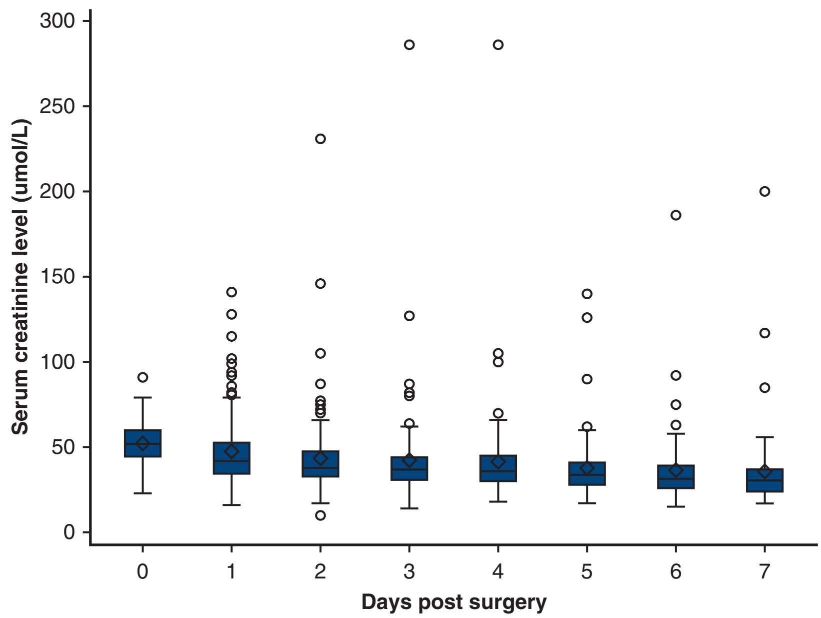


**FIGURE 1.** SCr (μmol/L) in the full study cohort during the first postoperative week.

indexed pulmonary vascular resistance (odds ratio [OR], 3.90 per 1.0 unit increase in indexed resistance, 95% CI, 1.54-9.92, $P = .004$) and higher inotrope score on POD 0 (OR, 1.13, 95% CI, 1.002-1.28, $P = .047$) were independent risk factors for the development of AKI. A subgroup analysis to identify risk factors for severe AKI (stages 2 or 3) demonstrated the same risk factors with nearly identical ORs (data not shown). Among patients requiring postoperative extracorporeal membrane oxygenation (n = 3), all developed AKI.

### Risk Factors for Prolonged Renal Recovery From Acute Kidney Injury

Table 5 shows the univariable analysis for risk factors for renal recovery more than 48 hours. Risk factors for persistent AKI or AKD were the absence of a fenestration (OR, 3.43, 95% CI, 1.11-10.63, $P = .03$) and longer duration of CPB (OR, 1.22 for each 15-minute increase, 95% CI, 1.04-1.43, $P = .01$).

### Impact of Acute Kidney Injury on Postoperative Outcomes

Duration of pleural drainage was significantly longer for those with AKI compared with those without AKI (8 days, IQR, 7-12 vs 7 days, IQR, 5-9, respectively, $P = .027$) (Table 6). Those experiencing AKI had a significantly longer total hospital length of stay when compared with patients with no AKI (11 days, IQR, 8-19 vs 8 days, IQR, 7-10, respectively, $P = .001$). Sternal wound infection occurred in 7% of patients with AKI versus no patients without AKI ($P = .192$).

### Impact of Acute Kidney Injury Duration on Postoperative Outcomes

Those with persistent AKI or AKD had a significantly longer hospital length of stay compared with those with transient AKI (18 days, IQR, 9-62 vs 10 days, IQR, 8-16, respectively, $P = .006$) (Table 6). There was a greater risk of sternal wound infection for those who experienced persistent AKI or AKD (n = 4, 7%) as opposed to those experiencing only transient AKI (n = 3, 4%) ($P = .049$). No significant difference was found for duration of pleural drainage or length of ICU stay for those with persistent AKI or AKD versus transient AKI.

## DISCUSSION

This study is the first to report the phenotypes of renal recovery post-Fontan. The key findings from this study are as follows: (1) AKI post-Fontan is common, with an incidence of 71%; (2) most patients had transient AKI, but 16% of the cohort experienced AKI lasting more than 48 hours; (3) the absence of a fenestration and longer duration of CPB were risk factors for having AKI duration more than 48 hours; and (4) AKI duration more than 48 hours was associated with a greater risk of sternal wound infection and longer hospital length of stay compared with those with transient AKI.

Our incidence of AKI was higher than reported in other post-Fontan studies.[1-5] The broad range of reported occurrences of AKI after the Fontan operation may be explained by the patient populations studied. Niaz and colleagues[1] found only 11.3% of their cohort developed AKI after Fontan completion or revision; however, the

**TABLE 3. Incidence of acute kidney injury and types of renal recovery**

| AKI stage | Length of AKI episode: Transient AKI | Length of AKI episode: Persistent AKI or AKD | Total |
|---|---|---|---|
| No AKI | 0<br>0.0% | 0<br>0.0% | 41 |
| AKI stage 1 | 56<br>88.9% | 7<br>11.1% | 63 |
| AKI stage 2 | 21<br>72.4% | 8<br>27.6% | 29 |
| AKI stage 3 | 0<br>0.0% | 8<br>100.0% | 8 |

Results presented as N (%). *AKI*, Acute kidney injury; *AKD*, acute kidney disease.

median age at surgery was several years older (7 years) than the median age observed in our study (4 years).[1] Moreover, the use of different criteria to define AKI can lead to discrepancies in AKI incidence and staging.[11] Niaz and colleagues[1] and Bai and colleagues[2] used the AKI Network and pediatric-modified risk, injury, failure, loss of function, and end-stage renal disease criteria, respectively, as opposed to the Kidney Disease: Improving Global Outcomes definition used in our study.[1,2] The severity of AKI in our cohort was consistent with a study by Algaze and colleagues,[3] which also found AKI stage 1 to be the most prevalent.

Our findings demonstrate that patient-specific factors are associated with the development of AKI. The independent risk factors of higher preoperative pulmonary vascular resistance and higher inotrope score on POD 0 are consistent with those found in other studies.[1,3,5] Niaz and colleagues[1] found elevated preoperative pulmonary artery pressure to be associated with developing AKI postoperatively in their multivariable analysis. Higher pulmonary vascular resistance and pulmonary artery pressure drive lower cardiac output and higher CVP post-Fontan, which likely contributes to the pathophysiology of AKI.[12] Routine preoperative management with pulmonary vasodilators may reduce the incidence of postoperative AKI, but this study was not designed to answer that question. Several studies observed that higher vasoactive-inotropic support, specifically on POD 0, translated to an increased risk of high-grade (stage 2 or 3) AKI after the Fontan, reinforcing our findings.[3-5]

Earlier studies have reported that reduced renal perfusion pressure on POD 0 is a significant predictor of AKI.[2-4] This did not come out as a risk factor in the current study, perhaps because we observed relatively little variability in renal perfusion pressure (Table 2). However, higher inotrope score on POD 0 was a risk factor for AKI; it is possible that higher inotrope score and lower renal perfusion pressure reflect a similar pathophysiological process.

Studies involving a more diverse group of cardiac surgical procedures in children have identified longer CPB time as a risk factor for AKI.[13,14] Although that did not apply in this study, possibly because there was not much diversity with respect to the duration of CPB among patients undergoing the same operation, we did find that a longer duration of CPB was associated with a greater risk of persistent AKI or AKD. Each 15-minute increase in duration of CPB was associated with a 22% increased risk of persistent AKI or AKD compared with those with transient AKI. This adds support to the hypothesis that ischemia, induced by the low-flow, low-pressure, and nonpulsatile perfusion in CPB, plays a central role in the etiology of AKI.[14]

The absence of a fenestration was associated with a 243% increased risk of persistent AKI or AKD. A fenestration in the Fontan circuit increases cardiac output and lowers systemic venous congestion, although at the expense of cyanosis.[12] It may be that the absence of a fenestration, resulting in sustained lower cardiac output postoperatively, drives the longer duration of AKI.

We found that the occurrence and increased duration of AKI were associated with worse postoperative outcomes when compared with patients with no or only transient AKI. Those with AKI had a longer duration of chest tube drainage and total hospital length of stay compared with those without AKI. Having persistent AKI or AKD was associated with a greater risk of sternal wound infection postoperatively and longer total hospital length of stay compared with those with only transient AKI. Patterson and colleagues[5] also observed longer duration of chest tube drainage and hospital length of stay for those with AKI. Other studies surveying the impact of AKI on postoperative outcomes found that patients with severe (stage 2-3) AKI fared worse.[3,4] Our study suggests that children post-Fontan with persistent AKI or AKD warrant additional attention in clinical practice.

Our program has shown that among neonates, cardiac surgery–associated AKI is associated with higher

**TABLE 4. Univariable analysis for risk factors of acute kidney injury post-Fontan**

| Independent variables | OR estimate | 95% CI for the OR Lower limit | 95% CI for the OR Upper limit | *P* value | AUC |
|---|---|---|---|---|---|
| Age at Fontan | 0.99 | 0.81 | 1.19 | .88 | 0.44 |
| Sex (male vs female) | 0.96 | 0.46 | 1.99 | .91 | 0.51 |
| Preoperative mean PAP (mm Hg) | 1.18 | 1.001 | 1.39 | .049 | 0.63 |
| Preoperative PVR index (units × $m^2$) | 3.53 | 1.51 | 8.25 | .004 | 0.68 |
| Preoperative ventricular end-diastolic pressure (mm Hg) | 1.03 | 0.93 | 1.14 | .63 | 0.53 |
| Preoperative aortic valve regurgitation (mild-moderate to severe) vs (none-mild) | 1.02 | 0.30 | 3.55 | .97 | 0.50 |
| Fenestration present (yes vs no) | 0.84 | 0.34 | 2.07 | .70 | 0.52 |
| Duration of bypass (min) | 1.01 | 0.997 | 1.02 | .14 | 0.55 |
| Renal perfusion pressure | | | | | |
| Renal perfusion pressure in operating room | 0.99 | 0.97 | 1.03 | .77 | 0.52 |
| POD 0 | 0.99 | 0.95 | 1.03 | .54 | 0.56 |
| POD 1 | 0.98 | 0.93 | 1.02 | .28 | 0.55 |
| Postoperative highest lactate | | | | | |
| POD 0 | 1.22 | 0.97 | 1.54 | .08 | 0.60 |
| POD 1 | 1.49 | 1.05 | 2.11 | .03 | 0.61 |
| Postoperative vasoactive inotrope score | | | | | |
| POD 0 | 1.09 | 0.996 | 1.18 | .06 | 0.60 |
| POD 1 | 1.01 | 0.97 | 1.05 | .68 | 0.50 |

*OR*, Odds ratio; *CI*, confidence interval; *AUC*, area under the curve; *PAP*, pulmonary artery pressure; *PVR*, pulmonary vascular resistance; *POD*, postoperative day.

mortality, longer duration of ventilation, and greater hospital length of stay.[15] Although mortality after the Fontan is significantly lower than after complex neonatal repairs, and most patients can be extubated safely in the operating room post-Fontan, the association between AKI and increased hospital length of stay is similar among both patient populations. The consistency of this observation suggested that the relationship between AKI and postoperative morbidity is likely causative and not simply reflective of illness severity.

We found that the severity of AKI was positively correlated with the duration of AKI. Among 63 children with stage 1 AKI, 56 (89%) had transient AKI (Table 3). By comparison, 72% of stage 2 AKI was transient, and no cases of stage 3 AKI were transient. This highlights that the duration of renal recovery may be influenced by the severity of the underlying renal injury, providing some new granularity to our understanding of evolving AKI phenotypes. The magnitude of injury to the kidney appears to have both severity and time components and has implications for clinical outcomes. In a large international study of critically ill children, the persistent AKI phenotype had the highest risk of failure of renal recovery at discharge and the worst outcome overall including mortality.[16] To optimize prevention of AKI occurrence and modify the disease course, further research evaluating the different trajectories toward AKD and implications of these trajectories for health outcomes has been identified as a critical research priority, and severity of AKI may predict this trajectory.[16]

## Limitations

This study had several limitations. The small sample size of our study limited statistical power. These results are from a single center and therefore may not be generalizable to other sites. Most patients were extubated in the operating room or on the same day of surgery; therefore, no relationship between the duration of mechanical ventilation and the development of AKI could be explored. We did not evaluate nephrotoxic drug use or diuretic use as possible additional risk factors for AKI, although diuretic use is routine in our center in the early postoperative period. Antibiotics such as vancomycin or aminoglycosides used to treat sternal wound infection may have contributed to AKI, although most cases of AKI occurred by POD 2, earlier than sternal wound infection typically manifests and requires treatment.

**TABLE 5. Univariable analysis for duration of acute kidney injury more than 48 hours**

| Independent variables | OR estimate | 95% CI for the OR Lower limit | 95% CI for the OR Upper limit | *P* value | AUC |
|---|---|---|---|---|---|
| Age at Fontan | 0.67 | 0.40 | 1.14 | .14 | 0.60 |
| Sex (male vs female) | 1.08 | 0.42 | 2.77 | .87 | 0.51 |
| Preoperative mean PAP (mm Hg) | 1.19 | 0.98 | 1.44 | .08 | 0.61 |
| Preoperative PVR index (units $\times$ m$^2$) | 2.70 | 0.75 | 9.72 | .13 | 0.64 |
| Preoperative ventricular end-diastolic pressure (mm Hg) | 0.98 | 0.87 | 1.11 | .80 | 0.51 |
| Fenestration present (no vs yes) | 2.20 | 0.79 | 6.16 | .13 | 0.58 |
| Duration of bypass (min) | 1.01 | 1.000 | 1.02 | .047 | 0.61 |
| Duration of bypass (in 15-min intervals, continuous) | 1.16 | 1.002 | 1.34 | .047 | 0.61 |
| Renal perfusion pressure | | | | | |
| Renal perfusion pressure in operating room | 0.99 | 0.95 | 1.03 | .52 | 0.53 |
| POD 0 | 1.01 | 0.97 | 1.06 | .68 | 0.49 |
| POD 1 | 0.97 | 0.91 | 1.03 | .34 | 0.55 |
| Postoperative highest lactate | | | | | |
| POD 0 | 1.01 | 0.79 | 1.30 | .92 | 0.48 |
| POD 1 | 0.86 | 0.62 | 1.19 | .36 | 0.56 |
| Postoperative vasoactive inotrope score | | | | | |
| POD 0 | 1.04 | 0.98 | 1.11 | .17 | 0.55 |
| POD 1 | 1.02 | 0.93 | 1.12 | .67 | 0.57 |

*OR*, Odds ratio; *CI*, confidence interval; *AUC*, area under the curve; *PAP*, pulmonary artery pressure; *PVR*, pulmonary vascular resistance; *POD*, postoperative day.

## CONCLUSIONS

AKI after the Fontan operation is common, and patient-specific factors, namely, higher preoperative pulmonary vascular resistance and higher inotrope score on POD 0, can predict the development of AKI. The absence of a fenestration and longer duration of CPB were risk factors for AKI duration more than 48 hours. The occurrence of AKI negatively impacts postoperative outcomes, including length of chest tube drainage, sternal wound infections, and total hospital length of stay. Likewise, duration of AKI more than 48 hours is associated with increased risk of sternal wound infection and total hospital length of stay. The shift from transient to persistent AKI represents an important transition period for children who have post-Fontan AKI, in whom the risk of negative outcomes increases. Critically important then are interventions before 48 hours of AKI to facilitate recovery and minimize extension of renal injury. Future studies should further explore this, including renal protective strategies that can be used preoperatively, intraoperatively, and early postoperatively in this patient population.

### Conflict of Interest Statement

The 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.

**TABLE 6. Impact of acute kidney injury and acute kidney injury duration on postoperative outcomes**

| Postoperative outcome | AKI Yes | AKI No | AKI *P* value | AKI duration Persistent or AKD | AKI duration Transient | AKI duration *P* value |
|---|---|---|---|---|---|---|
| N | 100 | 41 | | 23 | 77 | |
| Length of stay in ICU | 2 (1-3) | 2 (1-3) | .170 | 2 (1-4) | 2 (1-3) | .40 |
| Total hospital LOS | 11 (8-19) | 8 (7-10) | .001 | 18 (9-62) | 10 (8-16) | .006 |
| Infection (Y, %) | 7 (7) | 0 (0) | .192 | 4 (17) | 3 (4) | .049 |
| Duration of pleural drainage (d) | 8 (7-12) | 7 (5-9) | .027 | 8 (7-22) | 8 (6-12) | .16 |

Results are provided as median (IQR) unless otherwise specified. *AKI*, Acute kidney injury; *AKD*, acute kidney disease; *ICU*, intensive care unit; *LOS*, length of stay.

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