Acute kidney injury after Fontan completion: Risk factors and outcomes

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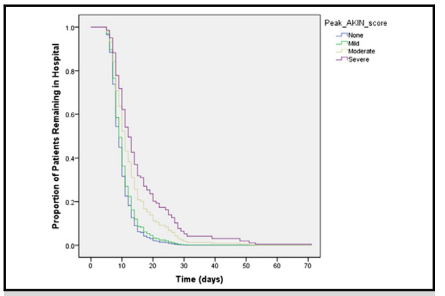
ABSTRACT

Objective: Acute kidney injury (AKI) is a predictor of outcomes in heterogeneous populations of children undergoing cardiac surgery. We investigated its causes and consequences in a cohort undergoing Fontan completion, hypothesizing that central venous pressure is independently associated with development of AKI.

Methods: In this retrospective cohort study of patients undergoing Fontan (n = 211), univariable and multivariable analyses identified factors associated with AKI within 3 days of surgery. Secondary analyses identified factors associated with hospital length of stay, and examined effects of perioperative kidney injury on follow-up renal function.

Results: Acute kidney injury occurred in 42% of cases (n = 89), with the following independent risk factors: mean renal perfusion (mean arterial minus central venous) pressure on postoperative day zero (per mm Hg; adjusted odds ratio [AOR] 0.83; $P < .001$); preoperative atrioventricular valve regurgitation > mild (AOR 6.78; $P = .02$); bypass time (per 10 minutes, AOR 1.08; $P = .04$); peak inotrope score on postoperative day zero (per point, AOR 1.17; $P < .001$); and preoperative pulmonary vascular resistance (per Wood unit, AOR 1.69; $P = .04$). Central venous pressure was not independently associated with AKI. Moderate and severe (but not mild) AKI were independently associated with prolonged hospital length of stay (adjusted hazard ratios, 0.56; $P = .004$, and .41; $P = .006$, respectively). Perioperative injury was not associated with longer-term renal dysfunction.

Conclusions: Acute kidney injury is common after Fontan completion and has several potentially modifiable risk factors. Moderate-to-severe injury is associated with longer hospital length of stay but not with renal dysfunction at follow-up. (J Thorac Cardiovasc Surg 2015;150:190-7)



Effect of acute kidney injury on length of stay after Fontan completion.

Central Message

Acute kidney injury is common after Fontan completion, and moderate-to-severe AKI predicts longer hospital length of stay. Injury seems to be mediated more by systemic hypotension than by central venous hypertension. Maintaining postoperative renal perfusion pressure while moderating inotrope use might reduce risk of injury and thus length of stay.

Perspective

Acute kidney injury in adults undergoing cardiac surgery is strongly associated with adverse outcomes. The importance of cardiac surgery–associated AKI in children is less clear. Patients undergoing Fontan completion face an acute rise in renal venous pressure and thus comprise an appealing model population. Acute kidney injury is common after the Fontan procedure, and moderate-to-severe AKI predicts longer hospital length of stay. Lower renal perfusion pressure and higher peak inotrope score are independent risk factors for AKI, whereas higher central venous pressure is not. This study provides important insight on the pathophysiology of AKI, and suggests strategies to mitigate AKI in this population.

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Acute kidney injury (AKI) in adults undergoing cardiac surgery is strongly associated with adverse outcomes, including death, and the development of chronic kidney disease (CKD).[1,2] The importance of cardiac surgery–associated AKI in children is more controversial, and the epidemiology is not as well characterized, a fact reflected by the wide range of reported[3,4] incidences (15%-52%). Available evidence in children suggests that moderate to

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Abbreviations and Acronyms
AHR = adjusted hazard ratio
AKI = acute kidney injury
AOR = adjusted odds ratio
CAP = common atrial pressure
CI = confidence interval
CKD = chronic kidney disease
IQR = interquartile range
MAP = mean arterial pressure
POD = postoperative day

severe AKI prolongs mechanical ventilation time, need for inotropic support, and lengths of stay in both the intensive care unit and hospital,[3-6] although the implications for mortality and development of CKD are less clear.[3,7] Whether risk factors for cardiac surgery–associated AKI in children are modifiable, and whether preventing AKI would result in improved outcomes, remain open questions.

Several investigators have begun to explore risk factors for the development of AKI and its implications for children undergoing congenital heart surgery[3,4,8,9]; data are sparse regarding the relationship between specific surgical procedures and AKI. Patients undergoing Fontan completion comprise an appealing study population from which to improve our understanding of AKI. Incorporation of the inferior vena cava into the pulmonary arteries results in an abrupt increase in renal vein pressure that provides a unique window into the effects of systemic venous hypertension on the development of AKI. Moreover, these patients face a significant lifetime risk of developing CKD, the presence of which is an important risk factor for late death and need for cardiac transplantation.[10]

We sought to identify risk factors for the development of AKI in patients undergoing Fontan completion. We hypothesized that higher postoperative Fontan (ie, central venous) pressure is an independent risk factor for AKI. Second, we investigated the implications of AKI for hospital length of stay and longer-term renal function.

METHODS

This retrospective, single-center cohort study included all patients undergoing Fontan completion at Boston Children's Hospital, between October 2003 and June 2009, in whom a recent (within 30 days) preoperative serum creatinine value was available. These dates were selected based on availability of an electronic medical record with granular intra- and post-operative hemodynamic data, along with a pre-existing Fontan database. A priori exclusion criteria were: (1) Fontan revision rather than completion; (2) Fontan comprising only incorporation of hepatic veins (ie, previous Kawashima operation); (3) dependence on renal replacement therapy at the time of the Fontan procedure; (4) early postoperative extracorporeal membrane oxygenation (within 48 hours) or death (within 30 days); and (5) absence of invasive central venous pressure monitoring on postoperative day (POD) 0. The protocol was approved by the Boston Children's Hospital Committee on Clinical Investigation.

Data Collection

Medical records were reviewed for demographic, anatomic, and physiologic details. Baseline creatinine was defined as the most recent serum creatinine level (mg/dL) within 30 days of Fontan completion. The coefficient of variation for the Roche (Mannheim, Germany) mass spectroscopy-traceable enzymatic creatinine assay used in the Boston Children's Hospital chemistry laboratory was 1.8% during the study period. Estimated creatinine clearance was calculated using the modified Schwartz and colleagues' formula[11]: 0.413 × Height (cm)/creatinine (mg/dL). The estimated creatinine clearance was used as a surrogate for glomerular filtration rate, with 80 mL/minute/1.73 m^2 used as the lower limit of normal to define renal dysfunction.[12]

The preoperative data collected comprised echocardiographic indices (degree of atrioventricular valve regurgitation and systemic ventricular dysfunction), hemodynamic data from pre-Fontan catheterization (mean pulmonary artery and atrial pressures, transpulmonary gradient, systemic ventricular end diastolic pressure, pulmonary vascular resistance), and preoperative use of potential nephrotoxins (diuretics, angiotensin-converting enzyme inhibitors, aminoglycoside antibiotics). To consider the potential effects of intravenous contrast agents on kidney function, the time interval between pre-Fontan catheterization and surgery was recorded. Intraoperative data collected comprised type of Fontan (lateral tunnel vs extracardiac), fenestration creation, additional surgical maneuvers performed (eg, valvuloplasty), total cardiopulmonary bypass time, total aortic crossclamp time, lowest intraoperative bypass flow rate, intraoperative urine output, lowest intraoperative hematocrit, lowest intraoperative rectal temperature, peak intraoperative lactate, and use of aprotinin.

Postoperative data were summarized by day: POD0 was defined as the period from postoperative admission to the cardiac intensive care unit until 7:00 PM the following morning; POD1, POD2, and POD3 were defined as sequential 24-hour intervals thereafter. Mean arterial pressure (MAP; mm Hg) was analyzed using arterial line data when available and cuff blood pressure once the arterial line was removed. Fontan pressure (mm Hg) was measured from a central line in the internal jugular vein. Common atrial pressure (CAP; mm Hg) was measured from a transthoracic catheter placed in the operating room. Renal perfusion pressure (mm Hg) at any point in time was defined as MAP minus Fontan pressure. Review of the medical record by the investigators—blinded to AKI status—allowed documentation of a representative MAP, Fontan pressure, CAP, and renal perfusion pressure for each hour of monitoring (median after excluding data points that were clearly "noise"—for example, pressures while infusing through the line). For each POD, median MAP, Fontan pressure, CAP, and renal perfusion pressure were calculated using hourly values. Additionally, daily nadirs of MAP and renal perfusion pressure were recorded, as were daily peak Fontan pressures. Inotrope score was defined as[13]: [dose of dopamine in mcg/kg/minute] + [dose of milrinone in mcg/kg/minute] × 10 + [dose of epinephrine in mcg/kg/minute] × 100. For each POD, peak inotrope score was recorded.

Peak postoperative lactate was defined as the highest lactate measured in the cardiac intensive care unit before the end of POD3. Daily fluid intake, volume of packed red blood cell transfusion, urine output, and total output were indexed to patient weight. Absolute daily fluid balance was recorded. For each day, "diuretic intensity" was determined by counting the number of distinct diuretics used (furosemide, bumetanide, chlorothiazide, spironolactone). Use of nephrotoxins (aminoglycosides, vancomycin, angiotensin-converting enzyme inhibitors, amphotericin) was recorded. Additional postoperative data collected included "significant arrhythmia" (defined as any rhythm other than sinus rhythm or junctional rhythm paced AAI or DDD), use of cooling, and echocardiographic measures of systemic ventricular dysfunction and atrioventricular valve regurgitation (defined using postoperative transesophageal echocardiogram, if available, and otherwise, using predischarge transthoracic echocardiogram). Each patient's most recent serum creatinine (with paired height) was used to