

Albumin 5% Versus Crystalloids for Fluid Resuscitation in Children After Cardiac Surgery*

Adil R. Dingankar, DNB¹; Dominic A. Cave, MD¹⁻³; Vijay Anand, MD^{1,2}; V. Ben Sivarajan, MD, MS^{1,2}; Susan Nahirniak, MD⁴; Cathy Sheppard, RN²; Jan Hanot, MD⁵; Gonzalo Garcia Guerra, MD, MSc^{1,2}

Objectives: To determine the clinical benefit of using colloids versus crystalloids for volume resuscitation in children admitted after cardiac surgery.

Design: Retrospective pre-/postintervention cohort study.

Setting: Stollery Children's Hospital tertiary care pediatric cardiac ICU.

Patients: Children admitted to the pediatric cardiac ICU after cardiac surgery.

Interventions: Fluid resuscitation policy change in which crystalloids replaced albumin 5% as the primary fluid strategy for resuscitation after cardiac surgery.

Measurements and Main Results: Children who underwent cardiac surgery in the 6 months prior to the policy change (5% albumin group) were compared with children admitted during the 6 months after (crystalloid group). Demographic, perioperative, and outcome variables (fluid intake days 1–4 postoperative, vasoactive therapy, blood products, time to negative fluid

balance, renal replacement therapies, mechanical ventilation, pediatric cardiac ICU, and length of stay) were collected. Data were analyzed using linear and logistic multivariate analysis. The study included 360 children. There was no association between fluid group and fluid intake (mL/kg) on day 1 postoperatively (coefficient, 2.84; 95% CI, 5.37–11.05; $p = 0.497$). However, crystalloid group was associated with significantly less fluid intake on day 2 (coefficient, -12.8; 95% CI, -22.0 to -3.65; $p = 0.006$), day 3 (coefficient, -14.9; 95% CI, -24.3 to -5.57; $p = 0.002$), and on the first 48 hours postoperative (coefficient, 10.1; 95% CI, -27.9 to -1.29; $p = 0.032$). Pediatric cardiac ICU stay (coefficient, -1.29; 95% CI, -2.50 to -0.08; $p = 0.036$) was shorter for the crystalloid group. There were no significant differences in the time to negative balance, need for renal replacement therapy, mechanical ventilation days, hospital stay, or pediatric cardiac ICU survival.

Conclusions: In our study, the use of albumin 5% for resuscitation after cardiac surgery was not associated with less fluid intake but rather the opposite. Albumin administration did not provide measured clinical benefit while exposing children to side effects and generating higher costs to the healthcare system. (*Pediatr Crit Care Med* 2018; 19:846–853)

Key Words: cardiac surgery; fluid resuscitation; pediatrics

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¹Department of Pediatrics, University of Alberta, Edmonton, AB, Canada.

²Pediatric Cardiac Intensive Care Unit, Stollery Children's Hospital, Edmonton, AB, Canada.

³Department of Anesthesiology and Pain Medicine, University of Alberta, Edmonton, AB, Canada.

⁴Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, AB, Canada.

⁵Department of Pediatrics, Pediatric Critical Care, MUMC+, Maastricht, The Netherlands.

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For information regarding this article, E-mail: gonzalo.guerra@ahs.ca

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Volume resuscitation is extensively used in children after cardiac surgery for a variety of reasons. The postoperative course can be complicated by low cardiac output and hemodynamic instability (1). Cardiopulmonary bypass (CPB) induces an immune-mediated systemic inflammatory response, coagulation-fibrinolytic cascades, and ischemia-reperfusion injury (2). Hypothermia, ventriculotomy, and bleeding in the perioperative period can further contribute to hemodynamic instability necessitating fluid resuscitation and vasoactive support (3). Endothelial damage during critical illness, including in post-CPB states, has been described as a cause of interstitial edema and a reason for the reduced volume-expanding effects of exogenous fluid administration during resuscitation (4).

Despite being one of the most common interventions in ICUs, there is ongoing debate as to whether colloids or crystalloids should be used for volume resuscitation of critically ill

patients. Generally, colloid solutions are thought to be more efficient than crystalloids in terms of volume expansion and intravascular persistence creating an expectation that less fluid would be required when using colloids versus crystalloids to achieve similar hemodynamic goals (5). This characteristic of colloids could be of benefit in situations where capillary leak syndrome is present, for example, after CPB. However, randomized controlled trials (RCTs) and systematic reviews comparing crystalloids and colloids across various clinical conditions in critically ill adults have not demonstrated any advantages in using colloids for resuscitation (6, 7). Despite this lack of evidence demonstrating superiority, colloids are still widely used for resuscitation of critically ill adults (8). A recent survey conducted by our group revealed that colloids are frequently used for volume resuscitation of children admitted to the ICU after cardiac surgery (27% respondents) and are often the treatment of choice for those needing ongoing resuscitation due to low cardiac output in the postoperative phase (76% respondents).

Despite being used based on theoretical benefits, there is no evidence supporting the use of colloids for volume resuscitation after cardiac surgery in children. At our institution, a blood bank policy change led to the discontinuation of 5% albumin as the main fluid used for resuscitation after cardiac surgery with CPB. On December 17, 2012, the blood bank discontinued the ward stock supply of 5% albumin to the pediatric cardiac ICU (PCICU), so it was only available as a patient-specific request. Hence, using this change in practice, we conducted a preintervention and postintervention cohort study to determine the clinical benefit of using 5% albumin versus crystalloids for volume resuscitation in critically ill children admitted to PCICU after cardiac surgery. We hypothesize that volume resuscitation using albumin 5% will be associated with less fluid intake on day 1 postoperatively and better clinical outcomes after pediatric cardiac surgery.

METHODS

This is a pre-postintervention retrospective cohort study conducted at a tertiary care PCICU in Edmonton, AB, Canada. The Stollery Children's Hospital has the second most active pediatric cardiac program in Canada and is the major referral center for four western provinces. The program performs more than approximately 450 index cardiac surgeries a year and has an active Extracorporeal Life Support (ECLS) and ventricular assist device program. On December 17, 2012, 5% albumin was discontinued as the main resuscitation fluid used after open cardiac surgery (using CPB) and substituted with crystalloid solutions (NaCl 0.9% and Plasmalyte, Deerfield, IL). This change gave us the unique opportunity to compare the effects of colloids versus crystalloids in the postoperative management of two similar groups of children with cardiac disease. Eligible participants were children admitted to PCICU following open cardiac surgery between June 2012 and June 2013. We constructed two cohorts, a 5% albumin group (AG) which included children admitted from June 1, 2012, to November 30, 2012, and a crystalloid group (CG) including children admitted between January 1, 2013, and June 30, 2013. Patients

admitted during December 2012 were not included to allow a washout period during the transition. The attending intensivist and the care team determined volume and frequency of fluid administration (maintenance and resuscitation) based on the patients' clinical condition and their hemodynamic status. There were no other significant changes or new staff (intensivist or surgeons) hired during the study period. Data were collected retrospectively from the patients' electronic chart records and transferred to a custom-made database.

Demographic data, cardiac diagnosis, single/biventricular physiology, the Risk Adjustment for Congenital Heart Surgery-1, CPB and cross-clamp times, early extubation in the operating room, and Pediatric Risk of Mortality (PRISM) III scores were collected as independent variables (9, 10).

Outcomes

The primary outcome was the total fluid intake (mL/kg/d) on day 1 postoperatively. The total fluid intake was calculated including maintenance fluid, enteral and/or parenteral nutrition, medications, blood products, and fluids used for volume resuscitation. Prescribed fluids in our practice are usually around 50 mL/kg/d for 24–48 hours after surgery and include maintenance fluid, nutrition, continuous infusions, and medications. Day 1 began at the time of admission until 7 AM the next day; day 2 and onwards were calculated from 7 AM to 7 AM on subsequent days. Data on fluid administration and fluid balance were recorded for the first 4 days following admission.

Secondary outcomes included total fluid intake (mL/kg/d) on days 2, 3, 4, time to negative fluid balance, blood products administration, need for renal replacement therapy (continuous renal replacement therapy and/or peritoneal dialysis), cardiovascular support, daily lowest mixed venous oxygen saturation (Svo_2), lowest daily hemoglobin, peak daily arterial lactate and creatinine levels, mechanical ventilation days, PCICU and hospital length of stay (LOS), and PCICU survival. Negative fluid balance was defined as the day on which the total fluid output exceeded the input when this time exceeded 4 days negative fluid balance was arbitrarily designated as 7 days; cardiovascular support was quantified using the Vasoactive Inotrope Score (VIS) (11). The study protocol was approved by the University of Alberta ethics review board.

Statistical Methods

Categorical variables are described as frequencies (%), and continuous variables are described as means (SD) or median (interquartile range [IQR]) as appropriate. Demographic, baseline characteristics, and univariate comparisons between the AG and the CG were conducted using Wilcoxon rank-sum and Fisher exact tests. Multiple linear and logistic regression analysis was performed to explore the association between fluid group (AG vs CG) and the different outcomes after adjusting for potential confounders. This analysis consisted of all variables from Table 1 that were found significant at p value of less than or equal to 0.10 in the univariate analysis, after screening for multicollinearity. Because PRISM scores, and hence the mortality risk, were significantly different between AG and CG,

TABLE 1. Demographic and Baseline Patients' Characteristics

Variables	Albumin 5% Group, n = 208	Crystalloids Group, n = 158	p
Age, yr, median (IQR)	0.53 (0.19–3.34)	0.64 (0.2–3.9)	0.519
Sex, male, n (%)	117 (56)	97 (61)	0.337
Weight, kg, median (IQR)	6.4 (4.2–14.3)	7.0 (4.2–15.0)	0.640
Pediatric Risk of Mortality-III, median (IQR)	10.0 (5.5–13.0)	7.0 (4.0–11.0)	0.002
Risk Adjustment for Congenital Heart Disease-1, median (IQR)	2.0 (1.0–4.0)	2.0 (2.0–4.0)	0.086
Cardiopulmonary bypass, min, median (IQR)	87.5 (64.0–121.0)	97.0 (58.0–130.0)	0.631
Cross-clamp time, min, median (IQR)	42.0 (20.0–64.0)	49.0 (20.0–67.0)	0.188
Single ventricle, yes, n (%)	42 (20)	28 (18)	0.593
Extubated in operating room, yes, n (%)	37 (18)	48 (30)	0.005
Extubated in pediatric cardiac ICU within 24 hr, yes, n (%)	37 (18)	35 (22)	0.298

IQR = interquartile range.

we took a conservative approach and PRISM was forced in the multivariable analysis due to its clinical relevance and despite its level significance at the univariate analysis. Extubation in the operating room was also different across fluid group. However, the decision to extubate before arrival to PCICU is related not only to the severity of illness but also to the anesthetist preference, number of cases on that day, and time of the day. Hence, extubation in the operating room was only included in the multivariable analysis if its association with the different outcomes was significant at the univariate level. Results are presented as coefficients or odds ratio (OR) along with 95% CI and two-sided p values. No corrections were made for multiple comparisons. We considered statistically significant those variables that have a p value of less than 0.05 in the multiple regression analysis. Statistical analyses were performed using Stata Version 10.0 software (Stata Corporation, College Station, TX).

RESULTS

During the study period, 366 patients were admitted to the PCICU after cardiac surgery with CPB; of these, 208 patients were in the AG and 158 on the CG. Demographic and baseline characteristics of both groups are shown in Table 1. Both groups were similar in most aspects except for a higher PRISM III score in the AG (median [IQR], 10.0 [5.5–13.0] vs 7.0 [4.0–11.0]; p = 0.002), a higher proportion of patients extubated in the operating room in the CG (n [%], 37 [18] vs 48 [30]; p = 0.005), and the type of fluid administered for volume resuscitation. There was a clear separation in the fluid choice between the AG and the CG after the policy change. Patients in the CG rarely received 5% albumin, and Plasmalyte was the fluid most commonly used for resuscitation; on the other hand, prior to the policy change (AG), children received mainly 5% albumin for volume expansion (**Supplemental Table 1**, Supplemental Digital Content 1, <http://links.lww.com/PCC/A704>).

Multilinear regression analysis showed no difference in total fluid intake on day 1 postoperatively between the AG and the CG

(coefficient, 2.84; 95% CI, -5.37 to 11.05; p = 0.497). However, fluid intake for the CG was significantly lower on day 2 (coefficient, -12.8; 95% CI, -22.0 to -3.65; p = 0.006), day 3 (coefficient, -14.9; 95% CI, -24.3 to -5.57; p = 0.002), and in the first 48 hours after surgery (coefficient, -3.99; 95% CI, -27.6 to -1.29; p = 0.032). There was no difference in fluid intake during day 4 (**Table 2**). There was no difference in blood products administration, peak lactate, Svo₂, lowest hemoglobin between groups (**Supplemental Table 2**, Supplemental Digital Content 2, <http://links.lww.com/PCC/A705>; and **Supplemental Table 3**, Supplemental Digital Content 3, <http://links.lww.com/CCM/D725>). There was a statistically significant difference in VIS on day 1 (coefficient, 1.71; 95% CI, 0.51–2.90; p = 0.005) and day 2 postoperatively (coefficient, -1.14; 95% CI, -2.57 to -0.38; p = 0.008) (**Supplemental Table 3**, Supplemental Digital Content 3, <http://links.lww.com/CCM/D725>). However, this difference was small and probably clinically irrelevant. The AG and CG showed no significant difference in the time (d) to achieve negative fluid balance (coefficient, 0.00; 95% CI, -0.48 to 0.50; p = 0.930) nor in peak creatinine levels (**Table 3**). Similarly, there was no difference between groups in terms of renal replacement therapy (OR, 0.02; 95% CI, 0.06–0.01; p = 0.212) or ECLS support (OR, 1.26; 95% CI, 0.19–8.27; p = 0.803) (**Table 3**). After adjusting for confounders, mechanical ventilation days were similar across groups (coefficient, -0.74; 95% CI, -1.80 to 0.32; p = 0.170). However, PCICU LOS was significantly shorter in the CG versus the AG (coefficient, -1.29; 95% CI, -2.50 to 0.08; p = 0.036). There was no difference in hospital LOS (OR, 1.22; 95% CI, -6.93 to 9.37; p = 0.253) or PCICU survival (OR, 2.49; 95% CI, 0.25–24.0; p = 0.429) (**Table 4**). The description of outcome characteristics can be seen in Supplemental Table 1 (Supplemental Digital Content 1, <http://links.lww.com/PCC/A704>).

DISCUSSION

Our retrospective cohort study comparing the use of 5% albumin versus crystalloids for volume resuscitation after open pediatric cardiac surgery showed no significant difference in

TABLE 2. Multiple Linear Regression Analysis for Fluid Intake by Day

Variables	Coefficient (95% CI)	p
Day 1 postoperative		
Age, yr	-2.26 (-3.18 to -1.34)	< 0.001
PRISM III	0.93 (0.09–1.76)	0.029
RACHS-1	4.57 (0.97–8.17)	0.013
Open chest, yes	35.4 (16.9–54.0)	< 0.001
Fluid group, crystalloid	2.84 (-5.37 to 11.05)	0.497
Day 2 postoperative		
Age, yr	-3.45 (-4.48 to -2.42)	< 0.001
PRISM III	1.29 (0.36–2.22)	0.006
RACHS-1	7.13 (3.13–11.1)	0.001
Open chest, yes	36.6 (16.2–57.1)	< 0.001
Extubation operating room, yes	-19.3 (-30.6 to -8.06)	0.001
Fluid group, crystalloid	-12.8 (-22.0 to -3.65)	0.006
Day 3 postoperative		
Age, yr	-3.96 (-5.00 to -2.94)	< 0.0001
PRISM III	1.59 (0.64–2.54)	0.001
RACHS-1	10.6 (6.83–14.4)	< 0.0001
Fluid group, crystalloid	-14.9 (-24.3 to -5.57)	0.002
Day 4 postoperative		
Age, yr	-4.43 (-7.17 to -1.70)	0.002
PRISM III	0.39 (-1.07 to 1.86)	0.595
RACHS-1	9.56 (3.89–15.2)	0.001
Fluid group, crystalloid	-15.8 (-1.6 to 33.2)	0.075
First 48 hr postoperative		
Age, yr	-7.78 (-9.64 to -5.90)	< 0.001
PRISM III	4.64 (2.98–6.31)	< 0.001
RACHS-1	25.3 (18.8–31.8)	< 0.001
Cardiopulmonary bypass, min	0.49 (0.34–0.65)	< 0.001
Open chest, yes	122.1 (86.3–157.8)	< 0.001
Fluid group, crystalloid	-10.13 (-27.9 to -1.29)	0.032

PRISM III = Pediatric Risk of Mortality-III, RACHS-1 = Risk Adjustment for Congenital Heart Disease-1.

total fluid intake on day 1 postoperatively but, against our hypothesis, found significantly lower fluid intake on days 2 and 3 after surgery. This difference was not associated with increased blood product utilization or with surrogate markers of low cardiac output (lactate levels and SvO_2) or need for mechanical cardiovascular support. Although a statistically significant association between fluid group and VIS was present in the first 2 days after surgery, the direction of this association changed between days 1 and 2 and is probably clinically irrelevant since it is equivalent to a dose difference of 0.01 $\mu\text{g}/\text{kg}/\text{min}$ of epinephrine. An association between 5% albumin

administration and more days on mechanical ventilation was observed, but this difference was not statistically significant after adjusting for early extubation in the operating room. The use of crystalloids was associated with shorter PCICU LOS. All other outcomes were similar between those who received crystalloids and 5% albumin for fluid resuscitation.

Hypovolemia due to fluid loss and/or capillary leak and consequent fluid shifts are common after cardiac surgery (12). In this context, volume resuscitation can increase cardiac output and improve acute care outcomes (13, 14). There has been an ongoing debate within the critical care community regarding

TABLE 3. Multiple Linear Regression Analysis for Negative Balance, Peak Creatinine, Renal Replacement Therapy, and Extracorporeal Membrane Oxygenation

Variables	Coefficient (95% CI)	p
Time negative fluid balance		
PRISM III	-0.29 (-0.07 to 0.02)	0.242
CPB, min	-0.01 (-0.01 to -0.00)	< 0.001
Extubation operating room, yes	0.60 (0.00–1.20)	0.049
Fluid group, crystalloid	0.00 (-0.48 to 0.50)	0.930
Peak creatinine day 1 postoperative		
Age, yr	2.75 (2.17–3.34)	< 0.0001
PRISM III	0.39 (-0.12 to 0.92)	0.135
Fluid group, crystalloid	2.84 (0.20–5.29)	0.996
Peak creatinine day 2 postoperative		
Age, yr	2.45 (1.90–3.00)	< 0.0001
PRISM III	0.48 (-0.00 to 0.98)	0.133
CPB, min	0.11 (0.06–0.17)	< 0.001
Fluid group, crystalloid	0.90 (-3.93 to 5.75)	0.712
Peak creatinine day 3 postoperative		
Age, yr	2.27 (1.34–3.21)	< 0.0001
PRISM III	0.71 (0.07–1.34)	0.029
Cross clamp, min	0.17 (0.07–0.27)	0.001
Fluid group, crystalloid	-0.84 (-8.06 to 6.36)	0.817
Peak creatinine day 4 postoperative		
Age, yr	3.47 (1.55–5.40)	0.001
PRISM III	0.85 (-0.26 to 1.97)	0.132
Cross clamp, min	0.34 (0.15–0.53)	< 0.001
Fluid group, crystalloid	0.90 (-15.2 to 10.3)	0.707
Renal replacement therapy		
PRISM III	1.06 (0.95–1.19)	0.247
Cross clamp, min	0.00 (0.00–0.01)	0.005
Open chest, yes	0.13 (0.05–0.22)	0.001
Fluid group, crystalloid	0.02 (0.06–0.01)	0.212
Extracorporeal membrane oxygenation		
PRISM III	1.43 (1.14–1.80)	0.002
Open chest, yes	10.2 (1.74–60.7)	0.010
Fluid group, crystalloid	1.26 (0.19–8.27)	0.803

CPB = cardiopulmonary bypass, PRISM III = Pediatric Risk of Mortality-III.

which type of fluid is, in fact, more effective and the best choice for resuscitation. Optimal outcomes after pediatric cardiac surgery depend on adequate preoperative care, timely and appropriate surgical repair, followed by postoperative management with special attention to details. IV fluid administration forms part of

every patient's postoperative care at one point or another. Fluids administered for volume resuscitation are drugs, and, as such, the type, dose, rate of administration, and timing of their administration should be carefully considered (15). Excessive fluid administration has been associated with worse outcomes (16, 17).

TABLE 4. Multiple Linear Regression Analysis for Mechanical Ventilation Days, Pediatric Cardiac ICU Length of Stay, Hospital Length of Stay, and Pediatric Cardiac ICU Survival

Variables	Coefficient (95% CI)	p
Mechanical ventilation days		
Age, yr	-0.15 (-0.27 to -0.03)	0.014
PRISM III	-0.04 (-0.15 to 0.06)	0.393
CPB, min	0.02 (0.00–0.03)	0.001
Open chest, yes	3.59 (1.22–5.95)	0.003
Extubation operating room, yes	-2.12 (-3.46 to -0.78)	0.002
Fluid group, crystalloid	-0.74 (-1.80 to 0.32)	0.170
PCICU LOS, d		
Age, yr	-0.26 (-0.47 to -0.59)	0.012
Sex, male	1.76 (-0.10 to 3.62)	0.064
PRISM III	0.14 (0.02–0.26)	0.018
CPB, min	0.07 (0.05–0.09)	< 0.001
Fluid group, crystalloid	-1.29 (-2.50 to -0.08)	0.036
Hospital LOS, d		
Age, yr	-1.19 (-2.10 to -0.28)	0.010
PRISM III	0.93 (0.14–1.73)	0.020
Risk Adjustment for Congenital Heart Disease	6.13 (2.99–9.27)	< 0.001
Fluid group, crystalloid	1.10 (-7.07 to 9.29)	0.790
Variables	OR (95% CI)	p
PCICU survival		
PRISM III	0.93 (0.78–1.11)	0.440
Open chest, yes	0.10 (0.01–0.80)	0.030
Fluid group, crystalloid	2.49 (0.25–24.0)	0.429

CPB = cardiopulmonary bypass, LOS = length of stay, OR = odds ratio, PCICU = pediatric cardiac ICU, PRISM III = Pediatric Risk of Mortality-III.

Commonly, two types of fluid are considered for volume expansion, colloids, and crystalloids. Crystalloids are rapidly redistributed and contribute to 20–25% of plasma volume after administration (18–20). On the other hand, it is presumed that the effects of albumin (with a higher molecular weight) would make it more efficacious than crystalloids for volume replacement both in terms of volume required and clinical effects (21, 22). Based on the conventional Starling model, it is believed that two to three times more crystalloids are needed to have the same effect as colloids during volume resuscitation (12, 23). This would make the use of colloids ideal after pediatric cardiac surgery (24). However, this theory is contradicted by data from several RCTs in which crystalloids have shown similar efficacy when compared with colloids with a ratio for volume expansion of approximately 1:1.2–1.14 (15). The revised model recognizes the importance of the endothelial glycocalyx as the key determinant of vascular permeability which in turn influences efficacy of volume expanders (23, 25). In this scenario, the use of albumin or

other colloids for volume resuscitation may not have any advantage over the administration of crystalloids (24, 26, 27).

Even if colloids and crystalloids are equally effective, there are potential negative consequences of colloid administration to critically ill patients. Protein-based collides can have a negative inotropic effect by binding circulating calcium (28). On the other hand, synthetic colloid solutions have been associated with acute kidney injury and higher risk of bleeding (7, 29). Albumin is derived from pooled plasma collection and carries theoretical risk of infection and allergic effects (30, 31). Also, albumin has been shown to be associated with adverse outcomes in patient's posttraumatic brain injury (32). Importantly, critically ill patients following cardiac surgery with CPB may also have impairment of the blood-brain barrier and could be subjected to the same negative consequences (33).

Our results are contrary to those by Verheij et al (12). In this relatively small RCT, the authors showed that

volume administration with either albumin or starches was associated with an increase in oncotic pressure and greater increase in cardiac index while using lower volumes. However, this study was conducted in adult patients, and a single volume load and its immediate hemodynamic response were evaluated rather than clinical endpoints in the first days after surgery. Several studies including systematic reviews of RCTs have shown no benefit in the use of colloids for fluid resuscitation even in condition where albumin levels are low (7, 34–36). Despite the available evidence against the use of colloids for resuscitation, the use of colloids is still recommended for refractory shock (37, 38). The Pediatric Cardiac Intensive Care Society recently published a consensus statement reviewing fluid management in pediatric cardiac critical care (39). This article highlights the lack of evidence and evidence-based recommendations surrounding the choice of fluid for volume expansion after cardiac surgery in children. A recent survey conducted by our group revealed that colloids are frequently used for volume resuscitation of children admitted to the ICU after cardiac surgery and are the treatment of choice for those needing ongoing resuscitation due to low cardiac output on the postoperative phase (unpublished data). The current retrospective study not only demonstrates lack of benefit for the use of 5% albumin in fluid resuscitation but shows an association between crystalloid use and shorter LOS and higher survival. It could be hypothesized that in the context of glycocalyx injury and capillary leak syndrome, the 5% albumin does not remain in the intravascular space and becomes even more difficult to mobilize after. The well-described side effects of albumin could also be responsible for this association. Although not definitive, our study adds pediatric data to the pool of evidence against the routine use of colloids for volume resuscitation in this patient population.

From a cost perspective, there is an additional advantage in using crystalloids versus colloids. As has been mentioned in previous studies, the cost of colloids is significantly higher than crystalloids. In Canada, 250 mL of 5% albumin costs approximately \$29 Canadian dollars (\$114 per liter) versus \$2 and \$2.5 for a liter of Plasmalyte and NaCl 0.9%, respectively. Hence, using 5% albumin is 50 times more expensive than using crystalloids.

This study has the following strengths. First, it is the first study to compare the use of 5% albumin to crystalloids for volume resuscitation after pediatric cardiac surgery with CPB, providing evidence in a research area where consensus remains elusive. Second, this study was conducted in a large cohort of patients before and after a policy change; the similarity within groups is reflected in the patient characteristics. An adjusted analysis was conducted for variables that were slightly different. After the adjustment, the study showed no benefit for using 5% albumin. Third, despite being an observational study, there was a clear separation between groups with very small volumes of crystalloids given to the AG and almost no albumin given to the CG. The nature of the external

policy change meant there was no evident risk for selection and/or indication bias.

The study also has some limitations. Although unlikely, the type of design may have not captured other modifications in practice over the observed time period. However, during the study, there were no changes in perioperative patient management or in our staff composition. The short timeline (13 mo) also reduces the risk that some undetected factor changed during the period. Second, due to the observational nature of our study, we could not adjust for unknown confounders. Despite adjusting for surgical risk, PRISM, severity of illness, and early extubation in the operating room, we have found a significant association between crystalloid use and shorter PCICU LOS. Although unlikely, it is possible that unmeasured variable is responsible for this association. Also, the association between CG and shorter PCICU LOS does not imply causation. These results should be taken with caution, and future studies with a different design should confirm the results. Third, the study compares the use of albumin versus crystalloids. Although the majority of patients in the CG received Plasmalyte, this study was not able to assess whether balanced or unbalanced solutions are superior. Finally, the study was conducted in a single center, and its results may not apply to other environments; further research is needed to prove its generalizability.

CONCLUSIONS

This retrospective cohort study provides evidence that the use of crystalloids for volume resuscitation after pediatric cardiac surgery is superior to 5% albumin. In our study, the use of crystalloids was associated with reduced fluid administration despite the theoretical oncotic advantage of albumin. Even more, the study found an association between crystalloid use and shorter PCICU LOS. Using crystalloids is safer as it does not have the inherited risk of a blood products administration and has significantly lower cost. Considering the frequent use of colloids in pediatric cardiac critical care, further research may be necessary to confirm these results.

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