Significant reduction in blood product usage, same early outcomes: Blood conservation in infants undergoing open heart surgery

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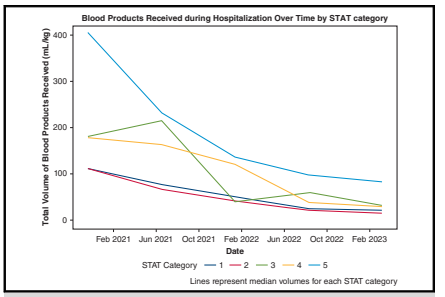
ABSTRACT

Objective: To evaluate the effect of a blood conservation program on trends in use of donor blood products and early clinical outcomes in infants undergoing open heart surgery.

Methods: Four hundred nine patients younger than age 1 year undergoing open-heart surgery between October 1, 2020, and June 30, 2023, were reviewed. The study period was divided into 4 eras with the first era as a before blood conservation baseline using traditional blood management. The following 3 eras comprised incremental implementation and evolution of blood conservation strategies. The total volume of blood products transfused for each surgical hospitalization was calculated and indexed to body weight at time of surgery.

Results: There was no significant difference in age at surgery, body weight, distribution of The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery categories, and in postoperative length of mechanical ventilation, intensive care unit or hospital length of stay, or postoperative mortality ($P > .05$ for all) across the 4 eras. Median total volume of blood products administered during hospitalization decreased from 128 mL/kg (range, 92-220 mL/kg) during the baseline period to 21 mL/kg (range, 6-44 mL/kg) during the last era ($P < .01$). Multivariate analysis demonstrated that later eras were associated with decreased odds of experiencing exposure to blood products during hospitalization.

Conclusions: Blood conservation is associated with significant reduction in usage of blood products during open heart surgery in infants with no significant effect on early outcomes. This trend is observed across all categories of surgical complexity. Additional studies are needed to prove consistency and to determine the longer-term clinical impact of this strategy. (JTCVS Open 2024;22:450-7)



Blood conservation allows to significantly reduce transfusion volumes.

CENTRAL MESSAGE

Programmatic blood conservation is associated with substantial reduction in blood product usage with no significant change in early clinical outcomes.

PERSPECTIVE

Existing evidence suggests that blood transfusions should be limited/avoided whenever possible. Blood conservation allowed us to reduce the median volume of transfused blood products 6-fold in just over 2 years with no change in early outcomes. These data suggest that many infants may be receiving excessive volumes of donor blood products without clear benefit.

Transfusion of donor blood products is common during open-heart surgery and/or postoperative recovery in infants.[1] Such practice had been established decades ago with little to no variability amongst different programs and only very limited effort to reduce volumes of transfused blood products effectively preserving the status quo in this

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Abbreviations and Acronyms
CPB = cardiopulmonary bypass
Hct = hematocrit
STAT = The Society of Thoracic Surgeons–European Association for Cardio-Thoracic Surgery Congenital Heart Surgery

important aspect of congenital cardiac surgery.[2] At the same time, risks associated with blood transfusions are well known.[3] Despite this, current transfusion practices in infants undergoing open heart surgeries remain unchanged other than that within several advanced blood conservation programs.[4] There is a growing body of evidence demonstrating feasibility and safety of blood conservation practices even in patients requiring complex cardiac surgery early in life.[5]

Programmatic approach to blood conservation was first started at Seattle Children's Hospital Heart Center in May 2021 to optimize patients' blood management. In this study, we present our experience and early outcomes of blood conservation in infants undergoing open heart surgery and compare those with before blood conservation baseline.

PATIENTS AND METHODS

Patient Population

Clinical data from consecutive patients who underwent open heart surgery in the first year of life at Seattle Children's Hospital between October 1, 2020, and June 30, 2023, were retrospectively reviewed after institutional review board approval (STUDY00003986; date of approval/exemption: September 9, 2022) and waiver of consent. Four hundred nine patients undergoing open heart surgery during the first year of life were included in this study. This cohort only includes patients which required single operation with cardiopulmonary bypass (CPB) during their admission. Twenty-seven patients who required more than 1 surgery with CPB per admission during the study period were excluded. The study period was divided into 4 eras with the first era as a pre-blood conservation baseline using traditional blood management. The following 3 eras comprised incremental implementation and evolution of blood conservation strategies throughout the study period (Table 1). Herein, we report our initial experience with blood conservation in a heterogeneous cohort of patients ranging from neonates undergoing urgent and complex repairs to infants requiring elective and relatively simple procedures. As with any new undertaking, our approaches to blood conservation evolved during the entire study period. Gradual stepwise advancement of various aspects of blood management was chosen to focus on patient's safety and to maintain provider discomfort at a low level.

Definitions

Attempted blood conservation is defined as clear primed CPB. Successful blood conservation is defined as a transfusion-free hospitalization. Non-red blood cell (RBC) blood products are defined as the components of blood such as fresh frozen plasma, cryoprecipitate, and platelets.

Perioperative Management

Preoperative management remained essentially unchanged throughout the study period. The only change included introduction of routine preoperative iron supplementation (2-4 mg/kg/day ferrous sulfate) in the latest era for all patients undergoing elective surgeries. It was initiated 3 months before a date of operation or as soon as the decision to proceed with surgery was made if past that time point. Iron indices and hemoglobin levels were not checked before or after initiation of supplementation unless there were additional considerations that would require it. Configuration of the CPB circuit underwent substantial optimization before initiation of blood conservation program and there is an ongoing gradual evolution of the circuit setup as areas for improvement are identified. We previously described CPB conduct in neonatal patients in detail and the same protocol is followed for older infants.[6] Two different circuits are currently used for patients younger than age 1 year. The first 1 is used in patients with a body weight <4 kg and has a prime volume of 126 mL, whereas the other is used for patients in the range of 4 to 12 kg with a prime volume of 141 mL. CPB prime contained balanced crystalloid solution with the addition of RBCs (180 mL) and fresh frozen plasma (100 mL) in vast majority of patients during the baseline era and in those patients during later eras who were not considered candidates for attempted blood conservation. In all other patients, no RBCs or fresh frozen plasma were added to the priming solution and autologous priming of the arterial and venous limbs of the CPB circuit was used. There was no protocolized cutoff for RBC transfusion during CPB and perioperative period before introduction of blood conservation. Starting from May 2021, we aimed to maintain hematocrit (Hct) level $\geq$24% while on CPB.[7] Intermittent decreases in Hct level to under 24% were tolerated if other markers of oxygen delivery remained within range and Hct level could be returned to $\geq$24% with ultrafiltration in fewer than 3 minutes. Both conventional and modified ultrafiltration were routinely performed. One or more non-RBC blood products were given routinely in vast majority of patients during the baseline era. With introduction and advancement of blood conserving approaches gradual transition was made from this practice to concept "no bleeding – no non-RBC blood products" (Table 1). Tromboelastography was not routinely used.

Since May 2021, we aimed to maintain Hct level $\geq$21% and $\geq$27% in hemodynamically stable patients with biventricular and single-ventricle physiology, respectively, in the post-CPB and postoperative periods.[8] The details of decision-making process regarding a need for RBC transfusion in the postoperative period were previously reported. In brief, no specific cutoffs within the multitude of parameters (heart rate, respiratory status, inotropic requirement, serum lactate level, near infrared spectroscopy, and diuresis) were used as triggers for RBC transfusion (except for Hct value) and trends and clinical judgement played primary role.[6] Criteria for RBC transfusion were the same for all patients during last 3 eras of this study period yet adherence to this policy at early stages of blood conservation was inconsistent.

Postoperative management followed the same principles in all patients. Early extubation, initiation of enteral feeds, and other components of enhanced recovery pathways were actively promoted whenever appropriate.[9] All patients who left the operating room without transfusion of RBCs were started on oral iron supplements when enteral feeding was established.

Statistical Analysis

Baseline characteristics, including demographics, perioperative characteristics, and outcomes after surgery, were collected and reported for each era. Furthermore, all blood products administered during the surgical hospitalization were totaled and indexed to body weight at time of surgery. Blood products were analyzed as total blood products, total non-RBC blood products and total RBCs, all indexed to weight at the time of surgery. We also examined the proportion of surgical admissions that did not receive any non-RBC blood products or RBCs for each era. Data are reported as proportions for categorical or ordinal variables and median with interquartile range for continuous variables. The χ^2 or Fisher exact test were used to examine associations between categorical variables. The Kruskal-Wallis or 1-way analysis of variance were used for continuous variables where appropriate. We also constructed multivariate regression models to

TABLE 1. Characteristics of blood management during various periods of the study

Time period	Dates	Blood management
Baseline	Oct 2020-Apr 2021	- Universal blood primed CPB for patients <12 kg with rare exceptions - Transfusion triggers for both RBC and non-RBC products based at the discretion of individual providers
Era 1	May 2021-Jan 2022	- Selective use of clear primed CPB (certain teams, higher baseline Hct, larger weight, lower surgical complexity) - Goal Hct level ≥24% while on bypass - Focus on surgical hemostasis - Structured RBC transfusion policy which instructs to maintain Hct level ≥21% for biventricular physiology and Hct level ≥27% for univentricular physiology in the postbypass period
Era 2	Feb 2022-Oct 2022	- Updated criteria for clear priming of CPB (weight >2.5 kg, baseline Hct level >35%, all complexities) - Group discussion of every transfusion unless emergency - Intraoperative surgical assessment of hemostasis as a primary guide for transfusion of non-RBC blood products
Era 3	Oct 2022-Jul 2023	- Preoperative iron supplementation for all patients undergoing elective surgeries - Selective use of blood primed CPB (very low baseline Hct level, severe hypotension, desaturation, or arrhythmia burden) - No non-RBC blood products if hemostasis is good on subjective surgical assessment, irrespective of bleeding panel values

CPB, Cardiopulmonary bypass; *RBC*, red blood cells; *non-RBC*, plasma/platelets/cryoprecipitate; *Hct*, hematocrit.

examine the association between subsequent eras of the conservation program and exposure to blood products, both as a continuous and dichotomous outcome. To examine the association between consecutive conservation eras, a quantile regression model, using the median, was constructed examining the total volume of all blood products per kilogram during the surgical admission, adjusting for weight at surgery and The Society of Thoracic Surgeons–European Association for Cardio-Thoracic Surgery Congenital Heart Surgery (STAT) mortality category. Similar models examining the total volume of donor RBCs per kilogram and non-RBC products per kilogram were also constructed. Finally, a logistic regression model examining exposure to any blood products during the surgical admission was constructed, adjusting for conservation era, STAT category and weight at time of surgery.

RESULTS

Blood conservation was attempted in 55.5% of patients (clear prime CPB n = 227) and was not attempted in 44.5% (blood prime CPB n = 182). Trends in bypass priming strategy over time stratified by surgical complexity are shown in Figure 1. Erythropoietin was not routinely used before or after surgery. Preoperative iron supplementation for all patients scheduled for elective open heart surgery was introduced in the third era. Significant variability was observed in duration of preoperative iron therapy due to patterns of clinical presentation and surgical listing. Patient characteristics are shown in Table 2. There was no significant difference in age at surgery ($P = .39$), preoperative weight ($P = .5$), or STAT category ($P = .79$) between different eras. Similarly, postoperative mechanical ventilation time ($P = .38$), intensive care unit length of stay ($P = .9$), hospital length of stay ($P = .16$), and mortality rate ($P = .8$) were not statistically different between the baseline period and various stages of blood conservation. Prothrombin complex or recombinant factor VII were used to assist with hemostasis in 3 patients with no use during the past 18 months of the study period.

Exposure to Blood Products

Downward trend in total volume of blood products received during surgical admission was seen across all categories of surgical complexity (Figure 2) throughout the study period. Statistically significant reduction in total volume of both non-RBC blood products and RBCs was identified ($P = .0001$ for both) when comparing blood conservation eras to pre-blood conservation baseline (Table 3). Freedom from exposure to any non-RBC blood product increased from 8.8% (n = 9) during era of traditional blood management to 82.5% (n = 85) during the latest era of blood conservation. However, achieving complete freedom from RBC transfusion is much harder and more than 75% of patients were still exposed to donor RBCs during the most recent blood conservation era. Although exposure to donor RBCs was still common, the volume of transfused blood was significantly lower than in the past. In multivariate quantile regression models that examined transfusion volumes adjusting for STAT category and weight, every later era of blood conservation, when compared with pre-blood conservation baseline, was associated with lower total volume of different blood products administered during hospitalization (Table 4). Not

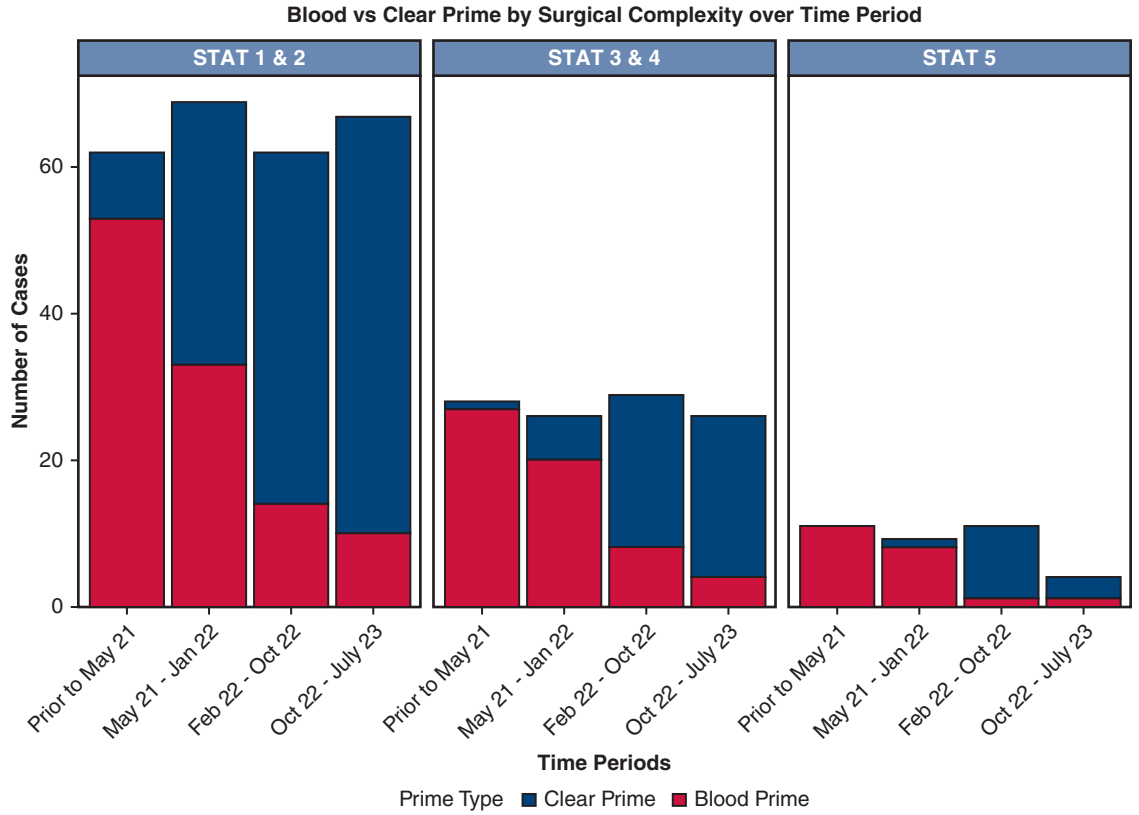

FIGURE 1. Evolution of the approach to blood conservation during the study period is demonstrated by progressive increase in application of clear prime bypass in patients undergoing open heart surgeries of all levels of complexity. *STAT*, The Society of Thoracic Surgeons–European Association for Cardio-Thoracic Surgery Congenital Heart Surgery Mortality Categories.

TABLE 2. Patient characteristics during different eras

Variable	Time period					*P* value
	Baseline (n = 101)	Era 1 (n = 104)	Era 2 (n = 102)	Era 3 (n = 102)	Total (N = 409)	
Patient characteristic						
Age at surgery (d)	84 (8-133)	80 (7-141)	72 (5-174)	79 (9-180)	79 (9-180)	.39
Weight (kg)	4.6 (3.5-5.8)	4.3 (3.5-5.7)	4.4 (3.4-6.3)	4.6 (3.4-6.8)	4.5 (3.4-6.2)	.5
Procedure-related characteristic						
STAT category						.79
1	29 (28.7)	36 (34.6)	35 (34.3)	28 (27.5)	128 (31.3)	
2	33 (32.7)	33 (31.7)	27 (26.5)	41 (40.2)	134 (32.8)	
3	19 (18.8)	17 (16.4)	18 (17.7)	20 (19.6)	74 (18.1)	
4	9 (8.9)	9 (8.7)	11 (10.8)	8 (7.8)	37 (9.1)	
5	11 (10.9)	9 (8.7)	11 (10.8)	5 (4.9)	36 (8.8)	
Postoperative characteristic						
Ventilation time (h)	29 (0-168)	28 (0-132)	31 (0-123)	28 (0-109)	28 (0-126)	.38
ICU LOS (d)	4 (2-12)	4 (2-13)	5 (2-11)	5 (2,9)	5 (2-11)	.9
Hospital LOS (d)	13 (7-38)	12 (6-31)	12 (6-20)	10 (6-21)	12 (6-26)	.16
Death	3 (2.9)	4 (3.9)	4 (3.9)	6 (5.8)	147 (4.1)	.8*

Values are presented as median (interquartile range) or frequency (%). *STAT*, The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery Congenital Heart Surgery Mortality Categories; *ICU*, intensive care unit; *LOS*, length of stay. *And .32 for trend.

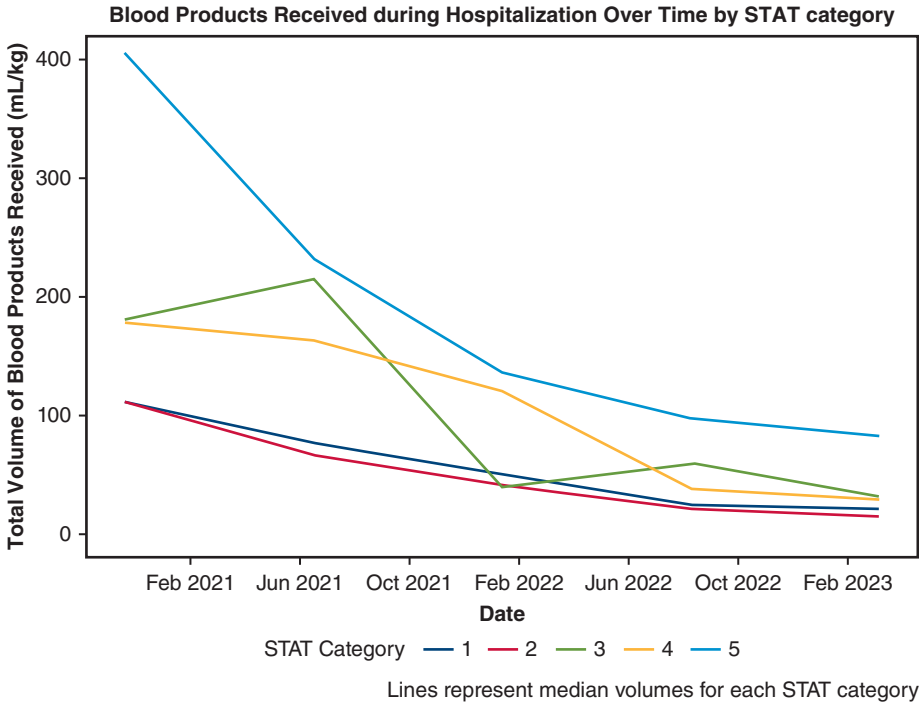

FIGURE 2. Downward trend in total volume of donor blood products transfused during surgical admission is observed throughout the study period. *STAT*, The Society of Thoracic Surgeons–European Association for Cardio-Thoracic Surgery Congenital Heart Surgery Mortality Categories.

surprisingly, increase in body weight was associated with lower transfusion requirement. Multivariate logistic regression models demonstrated that every later era of blood conservation, when compared with the era of traditional blood management, was associated with decreased odds of exposure to donor blood products during a surgical admission (Figure 3).

DISCUSSION

Blood products are believed to be required in essentially every infant undergoing open heart surgery[1,2] to prevent excessive hemodilution, facilitate hemostasis, increase oxygen delivery, and because "that's the way we have always been doing it." At the same time, risks and complications that are associated with blood transfusions are known and

TABLE 3. Transfusion characteristics during different eras

Variable	Time period					*P* value
	Baseline (n = 101)	Era 1 (n = 104)	Era 2 (n = 102)	Era 3 (n = 102)	Total (N = 409)	
Total volume of non-RBC products during admission (mL/kg)	60 (40-93)	35 (0-75)	2 (0-31)	0 (0-0)	19 (0-62)	<.01
Total volume of RBCs during admission (mL/kg)	70 (48-125)	55 (30-93)	33 (14-65)	21 (6-40)	44 (19-81)	<.01
Total volume of all blood products during admission (mL/kg)	128 (92-220)	92 (41-161)	42 (14-101)	21 (6-44)	60 (20-144)	<.01
No exposure to non-RBC products during hospitalization	9 (8.8)	28 (26.9)	51 (50.0)	85 (82.5)	173 (42.1)	<.01*
No exposure to RBCs during hospitalization	4 (3.9)	13 (12.5)	21 (20.6)	25 (24.3)	63 (15.3)	<.01*

Values are presented as median (interquartile range) or frequency (%). *non-RBC*, Plasma/platelets/cryoprecipitate; *RBC*, red blood cells. *For both χ^2 and trend.

TABLE 4. Quantile (median) linear regression models for exposure to blood products adjusted for surgical complexity

Variable	Coefficient*	95% CI
Total volume of non-RBC blood products per kilogram during admission		
Era 1	−25.8	−35.0, −16.7
Era 2	−53.1	−62.3, −44.0
Era 3	−56.7	−66.0, −47.5
Weight	−2.1	−4.1, −0.1
Total volume of donor RBCs per kilogram during admission		
Era 1	−12.1	−21.3, −2.9
Era 2	−36.3	−45.7, −27.1
Era 3	−40.3	−49.7, −31.1
Weight	−8.7	−10.7, −6.7
Total volume of all blood products per kilogram during admission		
Era 1	−35.9	−54.3, −17.5
Era 2	−81.5	−100.0, −63.0
Era 3	−94	−112.6, −75.4
Weight	−11.5	−15.5, −7.5

non-RBC, Plasma/platelets/cryoprecipitate; *RBC*, red blood cells. *Era 1, Era 2, and Era 3 are all compared with baseline era.

had been extensively reported.[3,4,6] Despite that, even in recent years, median transfusion rates in patients undergoing open heart surgery during the first year of life approach 100%.[2] The concept of blood conservation in pediatric cardiac surgery, irrespective of the patient's size/age, gained limited popularity and had been advanced by a small number of surgical programs worldwide.[5,6,10,11] However, even the leaders of blood conservation in pediatric heart surgery were able to achieve completely transfusion-free hospitalization in only 3.8% (19 out of 498) of patients weighing ≤7 kg.[5] In our current study, complete freedom from exposure to donor blood progressively increased with programmatic changes and reached 24.3% in the latest blood conservation era. It must be acknowledged that our cohort included patients up to age 1 year, so there was a small proportion of patients weighing more than 7 kg.

Identification and treatment of preoperative anemia has previously been noted to be an important component of blood conservation efforts.[12] Anemia was shown to increase risk of acute kidney injury among adult patients undergoing cardiac surgery.[13] Likewise, preoperative anemia independently predicts in-hospital mortality in young children and neonates undergoing noncardiac surgery.[14] At the same time, the relationship between preoperative anemia and postoperative outcomes/mortality in pediatric cardiac surgery patients has not been studied well yet.[12] In the latest era of the current study, we introduced routine low-dose iron supplementation for all patients scheduled for elective open heart surgery to alleviate preoperative anemia and to facilitate blood conservation. To streamline this process, we elected not to check iron panel values before or after initiation of supplementation unless there are additional considerations which would require it. Value, efficiency,

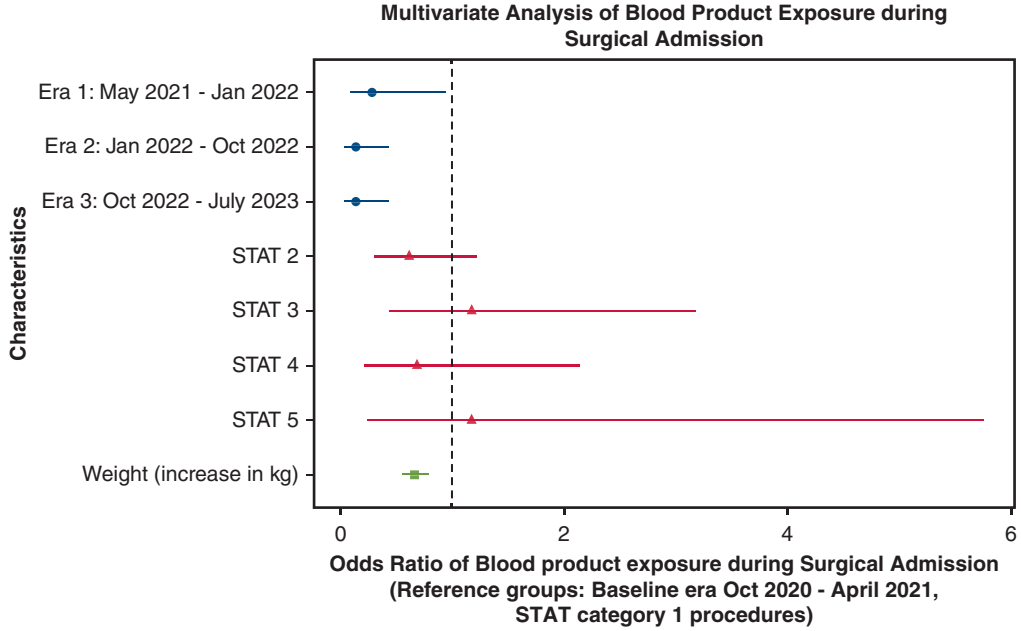

FIGURE 3. Multivariate logistic regression models demonstrate decreased odds of exposure to donor blood products during all eras of blood conservation, when compared with pre-blood conservation baseline. *STAT*, The Society of Thoracic Surgeons–European Association for Cardio-Thoracic Surgery Congenital Heart Surgery Mortality Categories.

and possible pitfalls of this approach are yet to be determined.

CPB and its circuit play integral role in blood conservation. The smaller the patient the more unfavorable is the ratio between circulating blood volume and CPB prime volume; therefore, optimization of circuit size and layout is very important. Various ways of organizing and priming of the CPB circuit, commencement, and conduct of bypass and volume management were described by blood conservation advocates.[6,10,15] Probably the smallest circuit thus far was designed by group from Berlin with a prime volume of only 73 mL.[15] We currently use 2 different circuits for patients younger than age 1 year based on a patient's weight. Patients weighing <4 kg receive a circuit with prime volume of 126 mL, whereas those in a range of 4 to 12 kg are assigned to a slightly larger circuit of 141 mL.

It has previously been demonstrated that not only the mere fact of patient's exposure to donor blood products is associated with a range of risks, but also that such risks can manifest in a dose-dependent fashion.[4] Total volume of transfused RBCs was shown to independently influence both the length of mechanical ventilation and the length of intensive care unit stay.[16] Similarly, a cross-sectional study from the Society of Thoracic Surgeons found that each 5% incremental increase in postoperative Hct level >38% was associated with 1.45-fold increase in the odds of operative mortality.[17] Cholette and colleagues[18] randomly assigned 162 infants after cardiac surgery to either a conservative or liberal transfusion strategy. Despite lower hemoglobin concentrations within the conservative group, serum lactate and clinical outcomes were similar. Current study aimed to evaluate the effect of programmatic blood conservation on trends in use of donor blood products and the influence of this change on early clinical outcomes in infants undergoing open heart surgery. There was no significant difference in early outcomes between the pre-blood conservation baseline and various eras of blood conservation. At the same time, downward trend was observed in total volume of transfused blood products throughout the study period (Figure 2). This data suggests that although majority of infants undergoing open-heart surgery are likely to require blood transfusion at some point during hospitalization, many of them may currently be exposed to excessive volumes of donor blood unnecessarily.

Limitations

This study has limitations that are typical to retrospective studies. The single-center nature of this study may limit generalizability of our results. Gradual change of multiple aspects of blood management over study period might have influenced the results. Patient selection criteria varied substantially among different eras, and this represents a source of selection bias.

CONCLUSIONS

Blood conservation is associated with significant reduction in usage of blood products during open heart surgery in infants with no significant effect on early outcomes. This trend is observed across all categories of surgical complexity. Non-RBC blood products are not required for adequate bleeding control in vast majority of patients. Additional studies are needed to determine the longer-term clinical influence of this strategy.

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.

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Key Words: blood conservation, infants, cardiopulmonary bypass