

Implementation of a Multidisciplinary Bleeding and Transfusion Protocol Significantly Decreases Perioperative Blood Product Utilization and Improves Some Bleeding Outcomes

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Abstract: Perioperative transfusion of blood products is associated with increased morbidity and mortality after pediatric cardiac surgery. We report the results of a quality improvement project aimed at decreasing perioperative blood product administration and bleeding after pediatric cardiopulmonary bypass (CPB) surgery. A multidisciplinary team evaluated baseline data from 99 consecutive CPB patients, focusing on the variability in transfusion management and bleeding outcomes, to create a standardized bleeding and transfusion management protocol. A total of 62 subsequent patients were evaluated after implementation of the protocol: 17 with single pass hemoconcentrated (SPHC) blood transfusion and 45 with modified ultrafiltration (MUF). Implementation of the protocol with SPHC blood led to significant decrease in transfusion of every blood product in the cardiovascular operating room and first 6 hours in cardiovascular intensive care

unit ([CVICU] $p < .05$). Addition of MUF to the protocol led to further decrease in transfusion of all blood products compared to preprotocol. Patients <2 months old had 49% decrease in total blood product administration: 155 mL/kg preprotocol, 117 mL/kg protocol plus SPHC, and 79 mL/kg protocol plus MUF ($p < .01$). There were significant decreases in postoperative bleeding in the first hour after CVICU admission: 6 mL/kg preprotocol, 3.8 mL/kg protocol plus SPHC, and 2 mL/kg protocol plus MUF ($p = .02$). There was also significantly decreased incidence of severe postoperative bleeding (>10 mL/kg) in the first CVICU hour for protocol plus MUF patients ($p < .01$). Implementation of a multidisciplinary bleeding and transfusion protocol significantly decreases perioperative blood product transfusion and improves some bleeding outcomes. **Keywords:** transfusion, bleeding, pediatric, cardiac surgery, quality improvement, protocol. *JECT. 2016;48:11–18*

Perioperative transfusion of blood products is associated with increased morbidity after cardiac surgery, including prolonged mechanical ventilation, prolonged hospital length of stay, transfusion-related acute lung injury, increased incidence of infection, acute kidney injury, and mortality (1–5). Even with a trend toward minimizing the volume of cardiopulmonary bypass (CPB) circuits, priming volumes may still represent a significant percentage of a neonate's

and infant's circulating blood volume. The resultant hemodilution may lead to reduction of platelet and coagulation factor concentrations, which along with CPB-induced platelet dysfunction and coagulopathy, may contribute to persistent postoperative bleeding requiring significant blood product administration and its associated increased risk of complications.

A multidisciplinary approach to perioperative blood product management has been endorsed as best practice by the Society of Thoracic Surgeons (STS) in adult patients to minimize high transfusion rates associated with cardiovascular surgery (6). Adoption of perioperative transfusion algorithms may decrease blood product utilization after pediatric cardiac surgery and improve clinical outcomes (7,8). This study represents analysis of a multidisciplinary

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quality improvement (QI) project aimed at decreasing perioperative blood product administration and bleeding complications at our institution.

MATERIALS AND METHODS

This study represents a retrospective analysis of a QI database created to evaluate the effectiveness of a new perioperative bleeding management protocol. The study was approved by the University of Alabama at Birmingham institutional review board.

Planning of the QI Project

Excessive postoperative bleeding and blood product administration were identified as areas in need of clinical improvement during routine internal programmatic review at our institution; therefore, a QI project was planned to address these areas. A data collection form was created, and baseline data were prospectively collected by clinicians from August 2013 to February 2014 on 99 consecutive pediatric CPB patients; perioperative anticoagulation and transfusion management and bleeding outcomes were determined. Associations between demographics and practice patterns and volume of blood product transfusions were sought. The data analysis was presented to a multidisciplinary team including cardiac surgeons, anesthesiologists, perfusionists, cardiovascular intensive care unit (CVICU) physicians, and nurses. The general conclusions were that perioperative transfusion management was empiric and varied widely among the five pediatric cardiac anesthesiologists and some of the variable practices were associated with increased transfusions (see Results, below). Several opportunities for improvement were identified, and a perioperative "Bleeding and Transfusion Protocol," was created during several meetings to address these areas, to include implementation of modified ultrafiltration (MUF) into clinical practice (Figure 1).

QI Project

The aim of the protocol was to decrease bleeding and blood product transfusion in the perioperative period via reduction of variability in anticoagulation and transfusion management and introduction of MUF into intraoperative practice. A total of 62 patients were evaluated after implementation of the protocol from February 2014 to May 2014. While awaiting design changes of CPB circuit for MUF, 17 consecutive patients were managed with the new protocol, but in lieu of MUF, were transfused with blood after single pass hemoconcentration (SPHC) upon termination of CPB (9). The subsequent 45 patients were managed with the protocol plus MUF as the source of hemoconcentration.

Specific focus of the protocol was standardization and decreased variability in multiple areas. The team agreed to

precisely follow the Hepcon HMS (Medtronic, Minneapolis, MN) dosing recommendation for protamine and to administer protamine as an infusion over 5 minutes. When there was SPHC blood available post-CPB, it was administered prior to protamine and any other blood products. Laboratory results for clotting factors and thromboelastogram (TEG) were obtained before the transfusion of hemostatic donor products (platelets, fresh frozen plasma [FFP], or cryoprecipitate). If blood products were needed, the clinicians treated laboratory values "per protocol" transfusion thresholds only. In addition, autologous cell saver blood was used before allogenic red blood cells.

Demographic, surgical, transfusion, bleeding, and laboratory data were prospectively collected by clinicians on the postprotocol cohorts in the same manner as preprotocol patients. Blood product administration was followed for the first 6 hours in the CVICU to evaluate the impact of the protocol on CVICU outcomes and transfusion practices. The first analysis of data was conducted at 3 months, which demonstrated clear improvements in blood product utilization and some bleeding outcomes. At this point, prospective data collection was stopped, and the perioperative bleeding management protocol was adopted into daily practice without modifications.

Perfusion Management

CPB circuit consisted of a Terumo System 1 (Ann Arbor, MI), Terumo FX Oxygenators, Terumo Hemoconcentrator HC05, and a Sorin CSC-14 DelNido Cardioplegia Delivery Set (Arvada, CO). Packed red blood cells (PRBC; 100 mL) and FFP (100 mL) were utilized to prime the circuit for patients <5 kg, and the hemoconcentrator was used to reduce the volume to the minimum operating level prior to CPB (Table 1). In patients >5 kg, an estimated dilutional hematocrit (HCT) was determined and retrograde autologous priming was used. Once on CPB, blood products may be needed if the HCT goal set by surgeons for specific cardiac lesions were not met. All allogenic red blood cells used in the cardiovascular operating room (CVOR) were <7 days old and washed prior to use.

Prior to MUF institution, the residual circuit volume was hemoconcentrated using a SPHC technique (9) after completion of CPB, put into a labeled syringe, and then transfused before protamine administration. The arterio-venous MUF technique and modifications were based on previously published papers (10,11) and are depicted in Figure 2. The only modification to the previous CPB circuit for MUF was the addition of a 1/8" line and a luered connector. Our MUF circuit is unique in that we use stopcocks only (no clamps). The MUF circuit was started at 5 mL/kg/min to ensure hemodynamic stability before applying suction to the hemofilter at a pressure of negative 200 mmHg. Patient preload was supplemented with the arterial pump head as needed for targeted hemodynamics. When the volume of the circuit

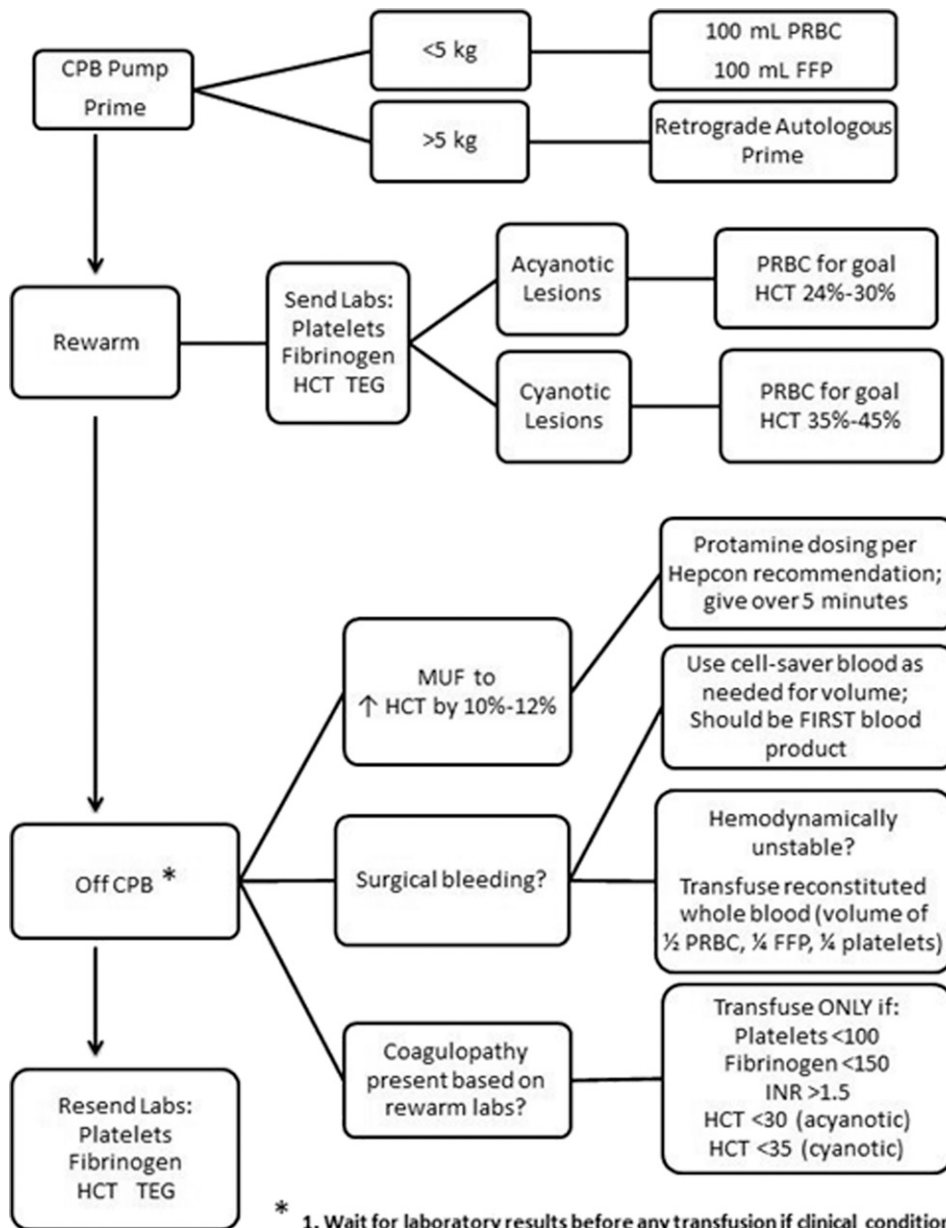


Figure 1. Bleeding and transfusion protocol.

- * 1. Wait for laboratory results before any transfusion if clinical condition permits.
- 2. Cell saver should be first blood product transfused in stable patients to raise HCT to goal or as needed for volume.
- 3. If hemodynamically unstable, use reconstituted whole blood (see above.)

was displaced with Plasmalyte-A, MUF was discontinued. This process usually took approximately 15 minutes.

After the completion of MUF, the anesthesiologist would administer the protamine infusion over 5 minutes. The dose

of protamine was determined using both the patient and circuit recommended protamine dose determined by the Hepcon HMS. Five minutes after the completion of protamine dose, a Hepcon HMS was used to confirm that there

Table 1. Cardiopulmonary bypass circuit sizes and corresponding flow rates.

Circuit size (inches)	$\frac{3}{16} \times \frac{3}{16}$	$\frac{3}{16} \times \frac{1}{4}$	$\frac{1}{4} \times \frac{1}{4}$	$\frac{1}{4} \times \frac{3}{8}$	$\frac{3}{8} \times \frac{3}{8}$	$\frac{3}{8} \times \frac{1}{2}$
Prime volume (mL)	175	200	$\frac{225}{375}$	450	$\frac{525}{650}$	850
Flow (L/min)	.00-.75	.76-1.30	1.31-2.00	2.01-3.00	3.01-4.50	>4.50

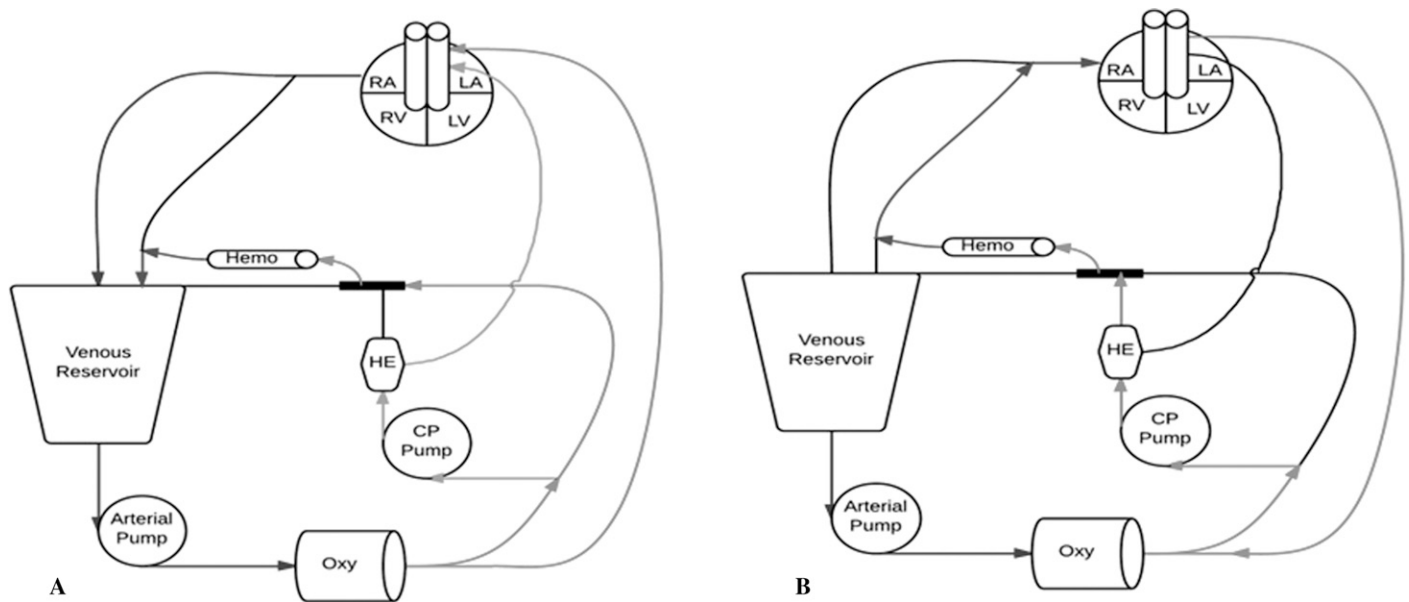


Figure 2. (A) Hemoconcentration during CPB. (B) Hemoconcentration during MUF. MUF is initiated by using the cardioplegia pump (CP) to provide retrograde flow down the arterial line, through the cardioplegia heat exchanger (HE), across the hemoconcentrator to a stopcock, and into a line that is connected to the venous line via luered connector. Hemo, hemofilter; LA, left atrium; LV, left ventricle; oxy, oxygenator; RA, right atrium; RV, right ventricle; blue line, venous blood; red line, oxygenated blood; green line, cardioplegia mix with blood; maroon, hemoconcentrated blood; arrows indicate direction of flow.

was full reversal of heparin. If there was residual heparin detected, the anesthesiologist would give the recommended dosage of protamine.

Statistical Analysis

All patient data were prospectively collected. SPSS[®] version 20 (IBM[®], Chicago, IL) was used for all analysis. Continuous variables that are not normally distributed were summarized as a median with interquartile range, with group comparison performed using the Mann–Whitney *U*-test. Continuous variables with a normal distribution were summarized as means with standard deviations and compared using the unpaired Student's *t*-test. One-way analysis of variance was performed when comparing variables across the three time periods. Pearson's correlation was performed to test for association of various risk factors and PRBC trans-

fusion during the preprotocol period. Categorical data were compared using Fisher's exact test. All tests were two tailed; *p* values of <.05 were considered statistically significant.

RESULTS

Patients and Baseline PRBC Transfusion Associations

A total of 161 consecutive pediatric patients <18 years old receiving cardiac surgery with CPB from August 2013 to May 2014 were included in this analysis. No patients were excluded. Demographics are shown in Table 2; median age, weight, and STS-European Association for Cardiothoracic Surgery Congenital Heart Surgery Mortality (STAT) category of entire study group were 140 days, 5.5 kg, and 3.1, respectively. There were no differences in demographics

Table 2. Demographics.

Characteristic	Preprotocol (<i>n</i> = 99)	Protocol Plus SPHC (<i>n</i> = 17)	Protocol Plus MUF (<i>n</i> = 45)	<i>p</i> Value
Age (days)	150 (90, 1181)	167 (97, 1249)	132 (74, 909)	.37
Weight (kg)	6 (5.5, 19)	5.3 (4.4, 17.6)	5.1 (4.4, 19.5)	.51
Under 2 months, <i>n</i> (%)	21 (21)	3 (18)	10 (22)	.92
STAT Category 5, <i>n</i> (%)	7 (7)	1 (6)	4 (9)	.90
STAT Category 4, <i>n</i> (%)	22 (22)	5 (29)	11 (24)	.80
STAT Category 3, <i>n</i> (%)	6 (6)	1 (6)	0 (0)	.24
CPB (minutes)	105 ± 41	109 ± 35	111 ± 39	.66
Aortic cross clamp (minutes)	45 ± 13	43 ± 12	47 ± 16	.74
Total heparin dose (U/kg)	870 ± 99	740 ± 101	808 ± 120	.49

Data represented as mean ± standard deviation or medians with interquartile ranges.

among the cohorts. There was no significant correlation between post-CPB PRBC administration and mean activating clotting time, total heparin dose, surgeon, international normalized ratio (INR), HCT, platelet count, or fibrinogen. In univariate analysis of preprotocol cohort, patient age ($r = .74, p < .01$), weight ($r = .63, p < .01$), CPB time ($r = .6, p < .01$), coldest temperature ($r = .55, p < .01$), and anesthesiologist ($r = .66, p < .01$) were all moderately correlated with total PRBC administration.

Variability in Bleeding Management

Preprotocol patients: There was important practice variability and risk factors for increased blood product transfusions identified in analysis of the 99 preprotocol patients. Mean blood product administration in this cohort can be seen in Figure 3. Protamine management, guided by Hepcon, was not consistent: 60/99 received the dose of protamine recommended by Hepcon ($\pm 10\%$), 30/99 received more protamine than recommended, while 9/99 received less protamine than recommended. This variability, however, was not associated with volume of PRBC transfusion. Receiving larger than recommended dose of heparin was associated with trend toward increased platelet transfusion 18 ± 16 mL/kg vs. 13 ± 11 mL/kg ($p = .07$). Of the 99 patients, 45 received protamine over 5 minutes, whereas 54/99 received a longer, continuous infusion of protamine. Protamine administered over 5 minutes was associated with decreased FFP transfusion in the CVOR when compared with prolonged infusions, 13 ± 12 mL/kg vs. 26 ± 29 mL/kg ($p = .01$). Of the 99 patients, 50 patients received fully

heparinized SPHC blood after separation from CPB. SPHC blood administration was variable with respect to timing associated with protamine and timing associated with other blood product administration; 20% of the time it was transfused prior to other blood products. Transfusion prior to other blood products was associated with decreased mean platelet transfusion, 7 ± 6 mL/kg vs. 19 ± 15 mL/kg ($p = .02$) and cryoprecipitate transfusion 4 ± 3 mL/kg vs. 11 ± 10 mL/kg ($p = .04$) in the CVOR. Of the 99 patients, 35 patients received washed blood from CPB circuit (cell saver), 26/64 of the patients that did not receive cell saver, had donor PRBC transfused in CVOR instead. Of the 99 patients, 67 patients received post-CPB FFP or platelets in the CVOR; 43 (64%) of which received FFP or platelets prior to results of coagulation studies.

Protocol patients: Variability in bleeding management was dramatically decreased after the protocol initiation. Compliance with Hepcon protamine dosing recommendations increased to 58/62 ($p < .01$); 47/62 received protamine infused over 5 minutes ($p < .01$). All the protocol plus SPHC patients (17/17) received SPHC blood prior to other blood products ($p < .01$). Transfusion of autologous cell saver increased to 52/62 after protocol initiation ($p < .01$); the 10 patients that did not receive cell saver were also not transfused with PRBC in the CVOR ($p < .01$). Among the 52 patients, 40 that received cell saver did not receive any other blood products. Only 8/30 patients that received platelets or FFP in the CVOR were transfused prior to availability of coagulation studies ($p < .01$).

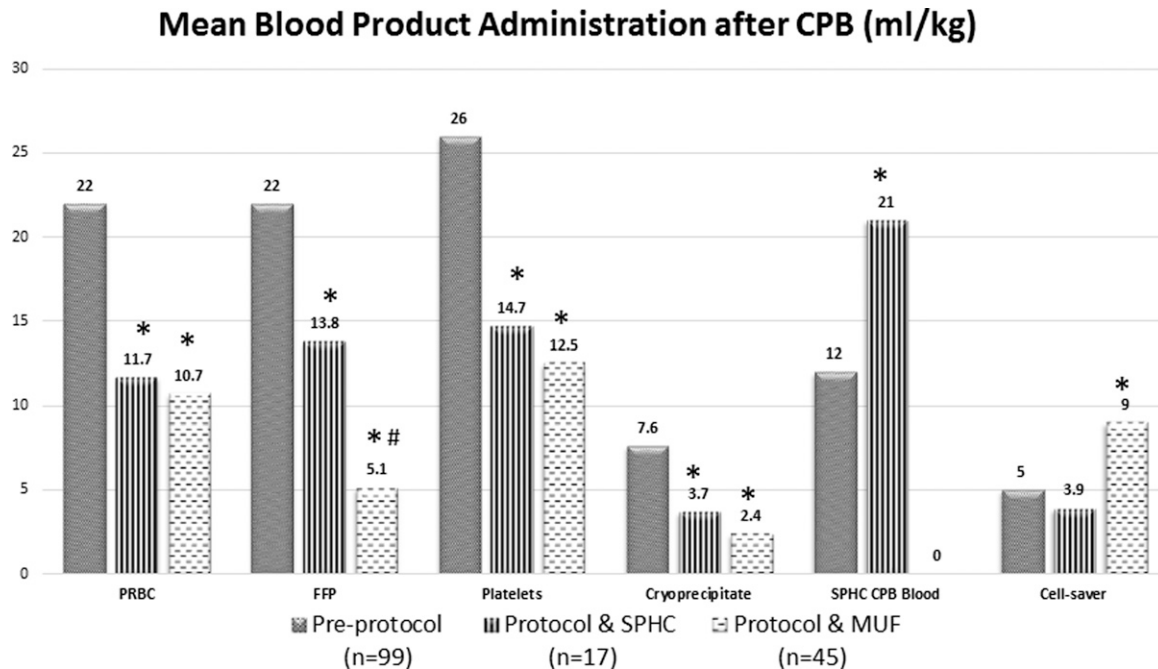


Figure 3. Blood product administration post-CPB. * $p < .05$ compared to baseline (preprotocol period). † $p < .01$ compared to protocol and SPHC.

Table 3. Laboratory values.

Laboratory Value	Preprotocol	Protocol Plus SPHC	Protocol Plus MUF
HCT post-CPB (%)	30 ± 7.8	33 ± 5.9*	35 ± 8.4*
HCT in CVICU (%)	33 ± 6.9	32 ± 7.5	42 ± 8.9*
INR post-CPB	2.2 ± .7	1.4 ± .3	1.6 ± .4
INR in CVICU	2.6 ± .5	1.3 ± .2	1.4 ± .4
Platelet count post-CPB (×10 ³ /μL)	143 ± 99	148 ± 101	131 ± 89
Platelet count in CVICU (×10 ³ /μL)	196 ± 111	237 ± 123	172 ± 109
Fibrinogen post-CPB (mg/dL)	230 ± 86	220 ± 79	168 ± 55
Fibrinogen in CVICU (mg/dL)	267 ± 95	270 ± 87	227 ± 65
ACT in operating room (seconds)	780 ± 132	703 ± 125	763 ± 147

Data presented as means ± standard deviation. All *p* values > .05, except * *p* < .01, when compared to preprotocol. ACT, activated clotting time.

Transfusion and Bleeding Outcomes

Table 3 compares the coagulation studies among the three cohorts. Not surprisingly, the HCT was significantly higher in protocol patients undergoing hemoconcentration with single pass or MUF. There was no difference in any of the other coagulation studies among cohorts.

Figure 3 compares blood product administration among the cohorts after separation from CPB. Implementation of the protocol led to decrease in transfusion of every donor blood product post-CPB through the first 6 hours in the CVICU. Transition of hemoconcentration technique to MUF maintained these transfusion benefits and also led to a further significant decrease in transfusion volume of FFP. Patients <2 months of age realized the greatest benefit of the protocol, with a 49% decrease in post-CPB total blood product administration; 155 ± 147 mL/kg preprotocol, 117 ± 74 mL/kg protocol plus SPHC, and 79 ± 71 mL/kg

protocol plus MUF (*p* = .01). Percent of patients that received cell saver increased in protocol patients, as did the average volume of cell saver transfused per patient. There was no difference in transfusion volume per patient of any blood product in the first 6 hours after CVICU admission with implementation of the protocol

Figure 4 compares bleeding outcomes. There was a non-significant increase in the number of surgeries that were not exposed to blood products after CPB with protocol implementation. The mean chest tube output was significantly decreased with protocol plus MUF patients in the first hour after CVICU admission: 6 ± 8 mL/kg preprotocol, 3.8 ± 6 mL/kg protocol plus SPHC, and 2 ± 4 mL/kg protocol plus MUF (*p* = .02); there was a significant decrease in incidence of postoperative bleeding >10 mL/kg in the first CVICU hour for protocol patients (Figure 4).

DISCUSSION

Postoperative bleeding is a common complication after CPB surgery and is independently associated with increased mortality in neonates (5). Blood product administration is associated with increased morbidity and cost after pediatric cardiac surgery, specifically increased mechanical ventilation and intensive care unit length of stay (1–4). As complication rates may increase with each PRBC unit transfused (12), efforts to decrease exposure to blood products will likely contribute to improved outcomes after pediatric cardiac surgery. Implementation of the transfusion and bleeding management protocol described herein was associated with over a 50% reduction in transfusion of every blood product post-CPB through the first 6 hours after CVICU admission. The highest risk population, children <2 months,

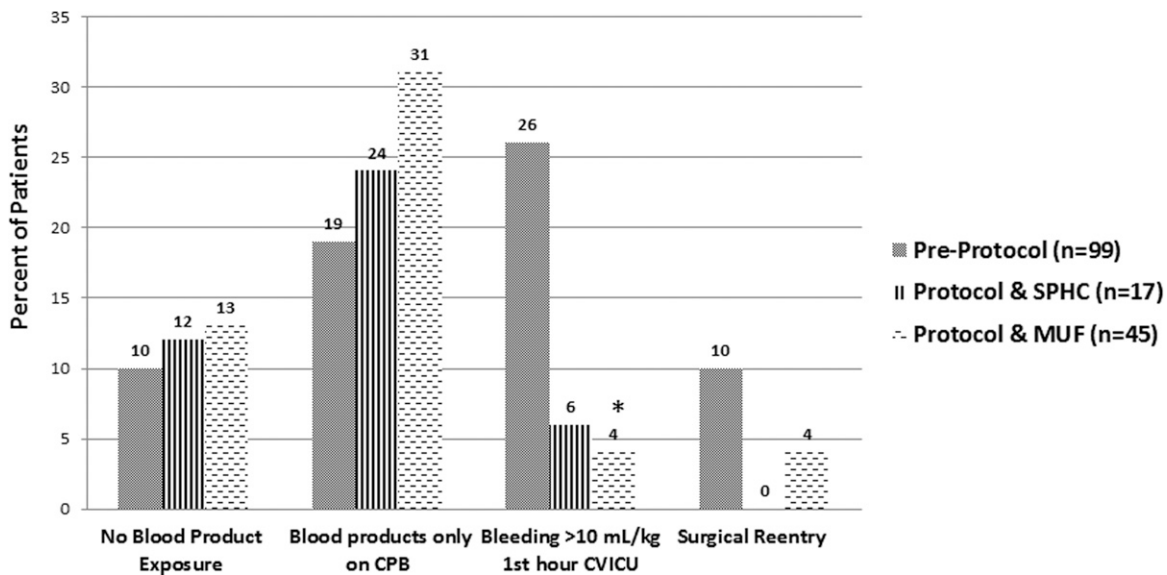


Figure 4. Blood product administration and bleeding complications. **p* = .001 compared to baseline (Preprotocol period).

benefited most from the protocol, with an average of almost 80 mL/kg reduction in blood product exposure. In addition, there was a significant reduction in heavy bleeding (>10 mL/kg) in the first hour of admission to the CVICU after protocol implementation.

STS Blood Conservation Clinical Practice Guidelines recommend a multidisciplinary approach for blood conservation during cardiac surgery using transfusion algorithms and point of care testing (6). Perioperative transfusion protocols decrease perioperative blood product administration after adult cardiac surgery (8,13,14), but there is limited evidence demonstrating benefit of transfusion algorithms after pediatric cardiac surgery. Whitney et al. (7), recently showed that a perioperative transfusion algorithm decreases blood product administration and mortality in pediatric patients after CPB surgery. Their study demonstrated a reduction in units of only PRBC and cryoprecipitate donor exposure after implementation of a laboratory-based transfusion algorithm, however, exact benefit in terms of volume of transfusion on a per patient basis could not be reported. With detailed prospective data collection, we were able to demonstrate that the volume of transfusion of every blood product was dramatically decreased with our protocol.

The benefit of our protocol in decreasing volume of transfusion was likely multifactorial. One important etiology was the implementation of a primarily laboratory-based transfusion protocol. Prior transfusion management was primarily empiric and variable by the attending anesthesiologist. The protocol encourages withholding blood products until laboratory results are available. Transfusion is only recommended if results are below transfusion thresholds or there is urgent need for transfusion in the setting of surgical bleeding with hemodynamic instability. This led to a reduction in incidence of transfusion of FFP, platelets, and cryoprecipitate prior to available laboratory results from 64.2% to 26.6%, creating a more restrictive transfusion practice without an increase in bleeding complications. In addition, restricting PRBC transfusion in nonhemorrhaging patients to only those with HCT below transfusion threshold likely led to a decreased dilution of clotting factors; potentially decreasing the subsequent need for platelet and/or coagulation factor administration for clinical bleeding. We saw a significant decrease in bleeding in the first CVICU hour after implementation of the protocol.

More protocolized utilization of autologous cell saver blood also likely contributed to our positive results. A recent randomized, controlled trial demonstrated, administration of cell saver blood significantly reduces PRBC and FFP exposure in the immediate postoperative period (14). Our protocol encouraged transfusion of cell saver as the first blood product when possible. Cell saver utilization increased from 35% to 84% and median cell saver volume per patient almost doubled with the protocol. Hodge et al. (8) also recently demonstrated that a multi-

disciplinary QI approach can significantly increase the utilization of cell saver transfusion after pediatric cardiac surgery. Protocol patients that received cell saver avoided donor PRBC transfusion 77% of the time.

Implementation of MUF also likely contributed to our positive findings. However, prior to the implementation of MUF, standardizing postoperative bleeding management and decreasing variability in coagulation and transfusion practices led to significant decrease in transfusion of all blood products (though this finding did represent only 17 patients). These 17 patients received the protocol plus SPHC blood; standardized transfusion of this hemocoagulated blood product, like MUF, may have also contributed to decreased blood product transfusion. When tested at our institution, SPHC blood was fully heparinized and approximates whole blood with the following values: HCT 65–70%; platelets $150\text{--}250 \times 10^3 \mu\text{L}$, fibrinogen 150–250 mg/dL, and clotting factors resulting in near-normal R time on TEG with heparinase (internal Q&I data initiative, unpublished data). The protocol encouraged transfusion of this autologous product prior to any other blood product and before protamine administration.

MUF has been associated with decreased morbidity after cardiac surgery including decreased mechanical ventilation, improved myocardial function, and decreased postoperative bleeding and blood product utilization (9). Once MUF was initiated with the protocol, we saw further nonsignificant decreases in transfusion of all blood products with a significant decrease in FFP transfusion and severe postoperative bleeding in the CVICU (>10 mL/kg/h) compared with protocol plus SPHC. This potentially suggested that MUF is more effective than SPHC at increasing the concentration of functional coagulation proteins.

This study has several limitations led by its small single center design and retrospective analysis in which unknown confounders may have contributed to the beneficial findings after implementation of this protocol. However, there were no other practice or personnel changes in addition to this protocol during this study period. Furthermore, surgical volume remained consistent and demographic risk factors for bleeding were similar in all three cohorts. The magnitude of improvement in transfusion of all blood products make it unlikely these findings were by chance. We cannot be sure which parts of our protocol contributed most to the beneficial findings, or if all parts were beneficial. In addition, our findings may not be reproducible at other centers to the same extent, which may be starting from different baselines of bleeding complications and postoperative transfusion practices, as well as have different institutional-specific risk factors for postoperative bleeding.

Despite these limitations, our study has demonstrated that a multidisciplinary approach to identifying a clinical problem and its associated risk factors with subsequent

design and implementation of an evidence-based QI effort can lead to improved clinical outcomes. Defining the exact impact of our protocol on specific transfusion and bleeding outcomes requires further prospective clinical trials.

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