J Extra Corpor Technol. 2022;54:35–41
The Journal of ExtraCorporeal Technology

Blood and Blood Product Conservation: Results of Strategies to Improve Clinical Outcomes in Open Heart Surgery Patients at a Tertiary Hospital Are Maintained 4 Years after Initiation

Junaid H. Khan, MD; Marilyn S. Barkin, MPH, RN; Jeffrey Stanton, CCP; Asim Khan; Russell D. Stanten, MD

Sutter Health Alta Bates Summit Medical Center, Oakland, California

Abstract: Blood product usage is an important outcome for patients undergoing cardiac surgery. In 2015, our center made a concerted effort with multiple departments to focus on reducing transfusion rates in surgical patients requiring cardiopulmonary bypass (CPB). Specific changes included an upgrade of the oxygenator in mid-2015 and, in early 2016, implementation of a hemostasis management system (HMS) that used heparin dose-response titration assays for heparin and protamine management. A retrospective chart review demonstrated significant decreases in the quarterly average of patients receiving packed red blood cells (PRBCs) from a baseline of 26.7% to 22.7% following the oxygenator upgrade ($p = .021$) and from 22.7% to 8.8% following implementation of the HMS ($p = .0017$). Platelet usage decreased from an average of 50.5% during the baseline and oxygenator upgrade periods to 22.2% following implementation of the HMS ($p < .0001$). Usage of fresh frozen plasma (FFP) decreased from an average of 28.2% of cases during the baseline and oxygenator upgrade periods to 10.4% during 2016, and cryoprecipitate usage decreased from 38.5% to 15.4%. Heparin usage averaged 56,903 units before implementation of the HMS, decreasing to an average of 43,796 units following HMS implementation ($p < .0001$). During the same time periods, protamine usage averaged 340.3 mg and 183.2 mg, respectively. Because improvements achieved during quality initiatives may revert back to their pre-intervention state once the assessment period is over, we performed a second retrospective analysis to determine whether the improvements achieved were maintained during the 48 months following the initial study. During 2017–2020, quarterly average usage of blood products was as follows: PRBCs, 11.9%; platelets, 14.7%; FFP, 6.2%; and cryoprecipitate, 11.5%. Quarterly, average use of heparin and protamine were $31{,}556 \pm 2{,}757$ units and 189 ± 113 mg, respectively. These findings indicate that the improvements achieved were not limited to the duration of the initial quality initiative. **Keywords**: blood product conservation, cardiopulmonary bypass, heparin dose response, quality metrics. *J Extra Corpor Technol. 2022;54:35–41*

Patients undergoing open-heart surgeries requiring cardiopulmonary bypass (CPB) frequently receive transfusions of various blood products, such as packed red blood cells (PRBCs), platelets, fresh frozen plasma (FFP), and cryoprecipitate. Transfusions can be a life-saving necessity at times, but they also have been associated with perioperative complications and worse mortality and morbidity outcomes, even with low-volume (1–2 units) transfusions (1–5). Current clinical practice guidelines recommend a restrictive perioperative PRBC transfusion strategy over a liberal strategy to reduce both transfusion rates and units of allogenic RBCs without increasing the risks of mortality and morbidity (class I, level A) (6).

With the goal of improving clinical outcomes and anticipating that blood usage will soon become a Society of Thoracic Surgeons (STS) quality performance measure (7–9), blood conservation strategies were initiated at Alta Bates Summit Medical Center in Oakland, CA, in 2015. The existing CPB oxygenator was upgraded to one designed to be gentler on blood and blood

Received for publication April 15, 2021; accepted October 4, 2021.
Address correspondence to: Junaid H. Khan, MD, Director of CV Services, Sutter Health Alta Bates Summit Medical Center, 3300 Webster Street, Suite 500, Oakland, CA 94609. E-mail: khan94611@gmail.com
Presented at the 59th International Conference of the American Society of Extracorporeal Technology, Virtual, May 1–4, 2021.
Dr. Khan is a consultant for Medtronic. The other authors have no potential conflicts of interest to declare.

components (10), and in 2016, a new hemostasis management system (HMS) was implemented to enhance point-of-care anticoagulation monitoring during CPB (see Materials and Methods). We demonstrated a statistically significant reduction in the rate of PRBC transfusion from a baseline of 26.7% to 22.7% following the oxygenator upgrade ($p = .021$) and from 22.7% to 8.8% following implementation of the HMS ($p = .0017$) (11). Platelet usage decreased from an average of 50.5% during the baseline and oxygenator upgrade periods to 22.2% following implementation of the HMS ($p < .0001$). Usage of FFP decreased from an average of 28.2% of cases during the baseline and oxygenator upgrade periods to 10.4% during 2016, and cryoprecipitate usage decreased from 38.5% to 15.4% during the same period. Heparin usage averaged 56,903 units before implementation of the HMS, decreasing to an average of 43,796 units following HMS implementation ($p < .0001$). During the same time periods, protamine usage averaged 340.3 mg and 183.2 mg, respectively. Minimal change in intensive care unit (ICU) length of stay was observed, whereas hospital length of stay decreased from a quarterly average of 9–10 days to <7 days by the end of the study period (11). Improvements achieved during quality initiatives may revert back to their pre-intervention state once the assessment period is completed. To determine whether the improvements we observed in our first study were maintained long term, we analyzed all cardiac cases done between January 1, 2017 and December 31, 2020.

MATERIALS AND METHODS

This study compared blood product usage rates, heparin and protamine usage, and ICU and hospital length of stay during 2017–2020 with rates achieved during 2014–2016. A retrospective chart review of open-heart surgery patients was performed using the same methodology as the 2014–2016 study, which has been described in detail (11). Briefly, all adult open-heart surgery patients who underwent CPB from 2017 through 2020 were eligible for inclusion. Allowable open-heart procedures included aortic valve replacement (AVR), mitral valve replacement or repair, tricuspid valve repair, dual-valve surgery, valve replacement with coronary artery bypass graft (CABG), aneurysm repair, and CABG procedures. Both minimally invasive and full open surgical procedure were allowed. There were no off-pump cases done during this time. Exclusion criteria included a transcatheter AVR, emergency dissection/aneurysm repair, and cases requiring >12 units of blood products. Data were collected from the STS database and extracted from the patients' electronic medical records. Demographics, laboratory results, and PRBC, platelet, cryoprecipitate, and FFP usage data were analyzed to determine whether blood product usage rates changed during the 48 months following the initial quality initiative. We also compared heparin and protamine usage rates, as well as ICU and hospital length of stay, between the two study periods. Approval of the study was obtained from the institutional review board.

The CPB oxygenation system and HMS were the same as used in the previous study (Affinity Fusion and HMS Plus systems, Medtronic, Minneapolis, MN), and both were previously described in detail (11). Briefly, the CPB oxygenator was upgraded to the Affinity Fusion oxygenation system (Medtronic), which has a smaller integrated arterial filter and bubble trap than the previous system (Affinity NT, Medtronic). The new oxygenator had a shorter blood flow path length (3 cm compared with a previous length of 11 cm) and a smaller inlet tubing size (3/8″ compared with ½″), and the venous reservoir and oxygenator unit were redesigned to create slower velocity and smooth, uniform distribution to minimize turbulence and reduce static holdup (10).

Guidelines for blood transfusions during CPB did not change during the study period. Preoperative preparations included discontinuation of antiplatelet and anticoagulant therapies, antiplatelet function tests, and avoidance of excess fluid consumption. Transfusion triggers included out-of-range hematocrit levels associated with clinical sequelae. Non-invasive cerebral oximetry, which is associated with improved mortality outcomes and postoperative cognition, was used to monitor for cerebral hypoxia-ischemia (12–14). Oximetry triggers included a 20% decrease from baseline values or an absolute reading <50%. No transfusion triggers were changed over the period studied.

Before implementation of the HMS, heparin was administered at a dose of 3 mg/kg. After implementation, an activated clotting time (ACT) level of 550 seconds was targeted for all patients, and a threshold >480 seconds was achieved in all cases before the start of bypass. Patients whose heparinization was based on their heparin dose response were treated to that concentration throughout the case and reversed with the predicted protamine dose provided by the HMS. Protamine reversal was verified after dosing using a final heparin-protamine titration to ensure no circulating heparin remained. If any bleeding was noticed at the surgical field, another titration was run to determine the additional protamine dose needed for reversal. A return to baseline was achieved in all cases after protamine reversal.

Statistical Analysis

Categorical data are presented as frequencies, and continuous variables are reported as means with SDs. Blood product usage rates are reported as the quarterly average percentage of cases receiving a blood product. Heparin and protamine usage are reported as the average amounts administered during the baseline period (Q3–2014 through Q2–2015), oxygenator upgrade and HMS implementation period (Q3–2015 through Q4–2016), and current study period (Q1–2017 through Q4–2020). ICU and hospital length of stay are reported as average number of hours and days, respectively, during those same time periods. Data for analysis were extracted from electronic medical records and the STS database as aggregated data. Blood transfusion and blood product usage between the baseline period of observation and the current period of observation were compared using the Fisher exact test. Values $p < .05$ were considered statistically significant.

RESULTS

A total of 983 patients underwent a cardiac procedure requiring CPB during 2017–2020. Of these patients, 50 patients who had a type A dissection/aneurysm required >12 units of blood for non-cardiac reasons or were in a salvage category were excluded, as were three patients who received >12 units of blood products. Thus, 933 patients were included in the 2017–2020 study population. The populations for the two time periods were similar. The average age in each study was 65 years. The majority of patients in both time periods were male, and both study populations were ethnically diverse (Table 1). Less than 10% of the patients in both groups were on dialysis at the time of surgery, and serum creatinine and hematocrit levels were nearly identical.

Outcomes

The outcomes associated with the upgrade of the CPB oxygenator system and HMS observed in our previous study were maintained through 2020. The cross-clamp and perfusion times in both studies were relatively steady over time, with cross-clamp time averaging 1.0–1.3 hours and perfusion time averaging 1.3–1.8 hours (Figure 1). There was no change in average prime fluid volume used at the end of 2016 and the average used during the 2017–2020 time period (1,100 ± 50 mL). Our previous study showed a decrease in the rate of PRBC transfusion from a baseline of 26.7% to 8.8% by the end of 2016 ($p < .05$). As shown in Figure 2, the rate of intraoperative PRBC transfusion observed during 2017–2020 was maintained (8.8% vs. 11.9%, respectively, NS).

Our previous study showed a decrease in the average percentage of cases receiving platelets transfusion from a quarterly average of 50.5% when the ACT was used for anticoagulation monitoring to 22.2% following implementation of the HMS system. The rate of platelets transfusion continued to decrease to a quarterly average of 15.0% of cases during 2017–2020 (Figure 3) ($p < .05$). The percentage of cases requiring cryoprecipitate transfusion decreased from a quarterly average of 38.5% of cases during the baseline and oxygenator periods to 15.4% during 2016. This low percentage of cryoprecipitate transfusions was maintained during 2017–2018, although there was an increase to 22.6% at the end of 2019, followed by a steady decrease throughout 2020 (Figure 4) ($p < .05$); the quarterly average for the entirety of the study period was 11.5%. The decrease in FFP transfusions observed following implementation of the HMS in the initial study (10.4%) also was maintained during 2017–2020, with percentages of 10% or lower during all but two quarters of the study period (Figure 5) ($p < .05$).

Average heparin use decreased from 56,903 ± 16,543 units during 2014–2015 to 43,796 ± 13,629 units during 2016 following implementation of the HMS system (Figure 6). Heparin use continued to decrease throughout 2017–2020 with an average usage of 31,556 ± 2757 units during 2017–2020. Protamine usage decreased from 340 ± 119 mg during 2014–2015 to 183 ± 70 mg during 2016. During 2017–2020, protamine usage averaged 189 ± 113 mg (Figure 6).

The decreases in ICU and hospital length of stay observed in our previous study were maintained throughout the current study, with ICU stay averaging 59 hours during 2016 and 58 hours during 2017–2020. Similarly, hospital length of stay averaged 6.1 and 5.9 days during 2016 and 2017–2020, respectively (Figure 7).

Table 1. Baseline (preoperative) characteristics of patients in the initial and follow-up studies.

Characteristic	2014–2016 n = 718	2017–2020 n = 933
Age, years	65	65
Sex		
Male	68%	70%
Female	32%	30%
Race		
White	41%	38%
African American	18%	18%
Asian	20%	15%
Pacific Islander	2%	6%
Unknown	19%	23%
On dialysis	5%	8%
Body mass index, kg/m^2	28	28
Hematocrit, volume %	38	38
Serum creatinine, mg/dL	1.39	1.38

DISCUSSION

Blood and blood product transfusions are a critical part of care for patients who undergo open-heart

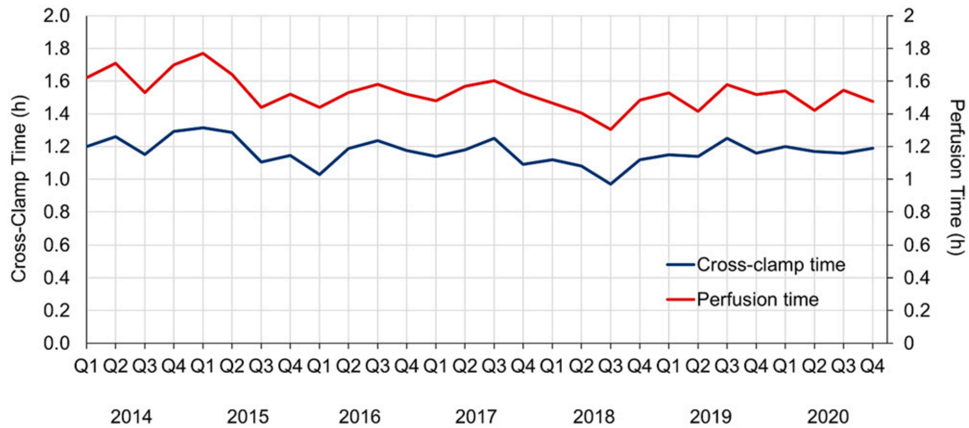

Figure 1. Cross-clamp and perfusion times for patients who underwent cardiac surgery with cardiopulmonary bypass from the first quarter of 2014 through the last quarter of 2020.

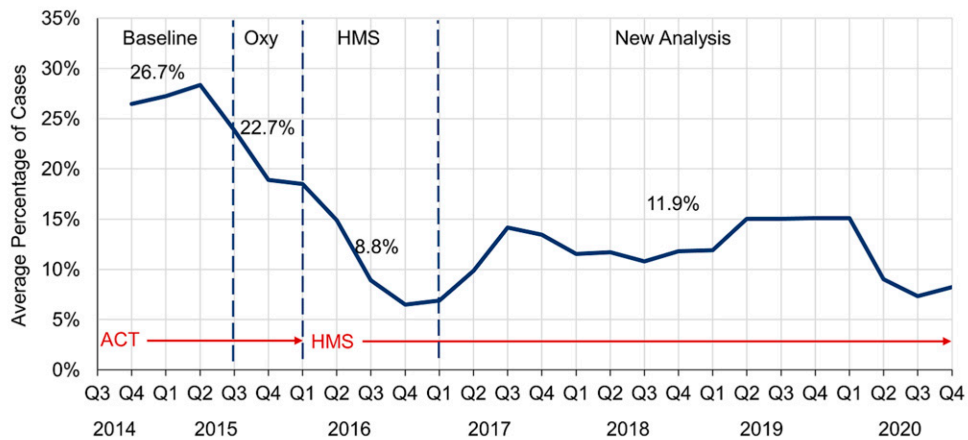

Figure 2. Average intraoperative packed red blood cell transfusions per quarter during the baseline period (Q3/2014 through the end of Q2/2015), during the oxygenator (oxy) upgrade (Q3/2015 through the end of Q4/2015), during implementation of the hemostasis management system (HMS; Q1/2016 through the end of Q4/2016), and during the long-term follow-up study (Q1/2017 through the end of Q4/2020).

surgery, yet they are also associated with worse mortality and morbidity outcomes (1–5). We previously analyzed blood and blood product usage in open-heart surgery patients who underwent CPB from 2014 through 2016 (11), showing significant reductions in transfusions over 27 months. The current analysis of the blood product usage in the subsequent 48 months demonstrates that the benefits observed after upgrading the CPB oxygenator and implementing an HMS were maintained long term.

The new 48-month follow-up period has a patient population very similar to the previous population with

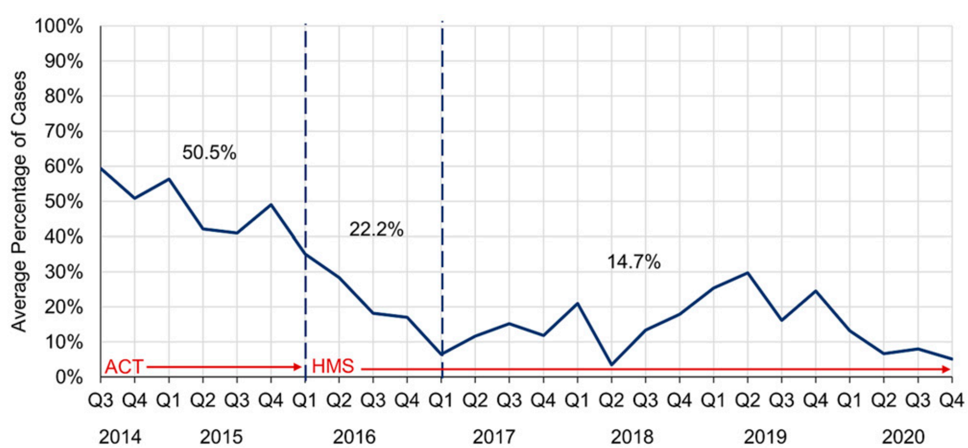

Figure 3. Average total platelets transfused during the initial study (Q3/2014 through Q4/2016) and the long-term follow-up study (Q1/2017 through Q4/2020).

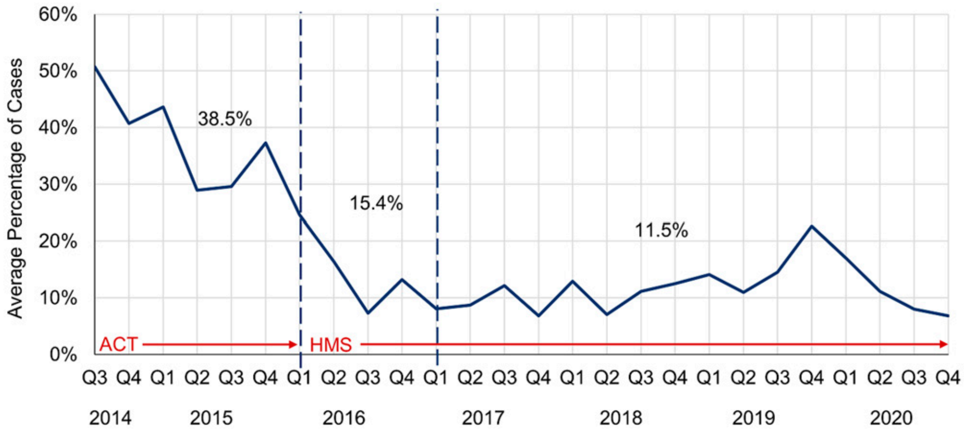

Figure 4. Average cryoprecipitate transfusions per quarter during the initial study (Q3/2014 through Q4/2016) and the long-term follow-up study (Q1/2017 through Q4/2020).

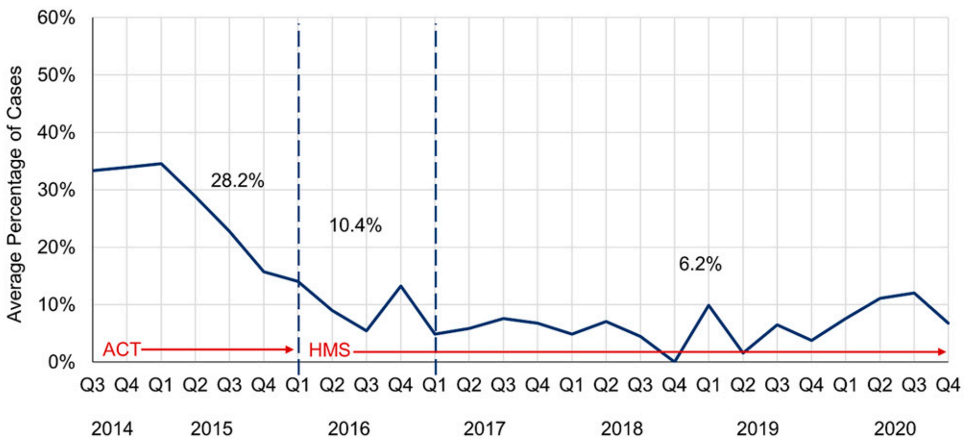

Figure 5. Fresh frozen plasma transfusions per quarter during the initial study (Q3/2014 through Q4/2016) and the long-term follow-up study (Q1/2017 through Q4/2020).

respect to age, comorbidities, and case complexities. Though there was a slight increase in intraoperative transfusion of blood from 8.8% to 11.9%—a change that was not statistically significant—a statistically significant reduction from the baseline transfusion rate of 26.7% was maintained during the most recent time period ($p < .05$). The benefits were also maintained for platelets, FFP, and cryoprecipitate ($p < .05$). These findings are consistent with those reported by other centers that have implemented patient blood management (PBM) programs. In a meta-analysis of 20 studies evaluating the

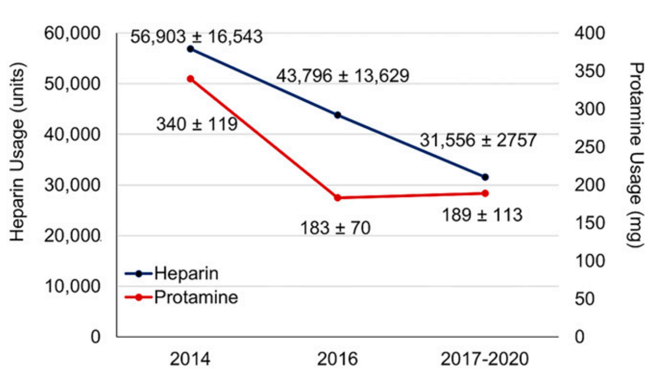

Figure 6. Average heparin and protamine dosing from mid-2014 through the end of 2020. The decrease in heparin dosing documented in 2016 continued during the long-term follow-up study (2017–2020), but the decrease in protamine dosing remained stable. Monitoring continues to better understand this observation.

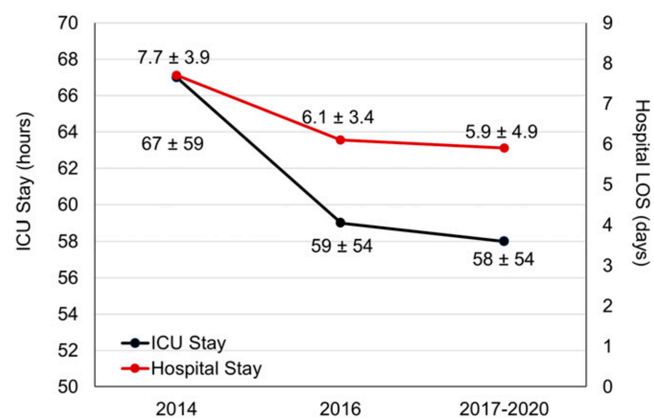

Figure 7. Average intensive care unit (ICU) and hospital length of stay (LOS). Both ICU and hospital stay decreased from 2014 through 2016. Although the reduction did not reach statistical significance, it was maintained during 2017–2020.

effectiveness of PBM programs, Mueller et al. (15) observed fewer RBC, platelet, and FFP transfusions, as well as a statistically significant decrease in the number of blood products per transfusion.

The previous reduction in protamine dosing was maintained during the current study. However, there was a further reduction in heparin dosing during 2017–2020 without a clear explanation. There were two vendor changes (from Sagent Pharmaceuticals to Fresenius-Kabi, and then back to Sagent) during 2017–2020, which we thought might be associated with the decreases in heparin usage. However, because we did not anticipate this finding, we did not track the specific dates of change, nor did we note the heparin vendor in patient records. Although we cannot adequately assess the relation between vendor and heparin usage, the decrease in heparin usage was continual, so we do not think they are correlated. We also considered that the bioactive coating on the circuitry of the HMS lessened the need for heparin. Again, however, the continuous decrease in heparin during 2017–2020 suggests this is not likely. We are continuing to monitor heparin usage in our CPB patients to better understand this finding.

With the long-term extension of the benefits of reduced blood and blood products for an additional 48 months, we are confident that the initial benefits seen were not only due to the enhanced focus of the quality initiative but also to the specific technology changes that were made (i.e., oxygenator upgrade, implementation of a HMS system). Length of hospital stay and ICU stay were decreased over the period of implementation of both the CPB circuit changes and HMS implementation (27 months) and continued to decrease during the latter 48 months. Though both measures are influenced by multiple factors, the decreases suggest the changes implemented may have influenced length of stay.

Confidence in the reduction in blood and blood product usage allowed us to decrease our par levels for PRBC and platelets for open-heart surgery cases from 4 and 2 units, respectively, to 2 and 1 units per case. Although we do not report acquisition cost or charge data in this manuscript, it is reasonable to assume that decreasing our par levels would lead to decreases in acquisition costs for these products. Added to those savings would be savings for typing and cross-matching of fewer units of PRBC per case. We did not estimate potential savings in hospitalization charges during the current study, and it is likely that hospitalization charges were greatly impacted by the COVID-19 pandemic (e.g., costs of traveler nurses). However, a savings in total hospitalization charges of 8% was estimated in our initial study (11), and other investigators have reported a reduction in hospitalization costs with reductions in intraoperative transfusions (16). Also of note, the reduced par level we achieved from 2017 through 2020 allowed us to maintain our operative schedule despite the decreased availability of blood during the COVID-19 crisis.

Limitations

This study used retrospective chart review to collect patient data, a method of data collection that may be limited by inaccurately entered or missing data. We were unable to access the raw data for the initial study, and the data we extracted were aggregated, which prevented us from performing inferential statistical analyses. The study was conducted at a single U.S. center, which limits the generalizability of these findings to countries with different healthcare systems.

Conclusions

The patients at Alta Bates Summit Medical Center are benefiting from the changes made intraoperatively with the HMS system. Usage of PRBCs, platelets, FFP, cryoprecipitate, heparin, protamine, and priming fluid were substantially reduced during the initial 27-month study, and those reductions either continued or were maintained for the following 48 months. These findings demonstrate that the benefits achieved with the upgrade of the CPB oxygenator and implementation of the HMS were not limited to the duration of the initial quality initiative.

ACKNOWLEDGMENTS

Julie A. Linick, an employee of Medtronic, drafted the Methods and Results sections and created figures for this manuscript. The initial study was sponsored by Medtronic, but no financial support was provided for the current study.

REFERENCES

1. Likosky DS, Dickinson TA, Paugh TA. Blood conservation—A team sport. J Extra Corpor Technol. 2016;48:99–104.
2. Yang JC, Sun Y, Xu CX, et al. Correlation between red blood cell transfusion volume and mortality in patients with massive blood transfusion: A large multicenter retrospective study. Exp Ther Med. 2015;9:137–42.
3. Surgenor SD, DeFoe GR, Fillinger MP, et al. Intraoperative red blood cell transfusion during coronary artery bypass graft surgery increases the risk of postoperative low-output heart failure. Circulation. 2006;114:143–8.
4. Surgenor SD, Kramer RS, Olmstead EM, et al. The association of perioperative red blood cell transfusions and decreased long-term survival after cardiac surgery. Anesth Analg. 2009;108:1741–6.
5. Moskowitz DM, McCullough JN, Shander A, et al. The impact of blood conservation on outcomes in cardiac surgery: Is it safe and effective? Ann Thorac Surg. 2010;90:451–8.
6. Tibi P, McClure RS, Huang J, et al. STS/SCA/AmSECT/SABM update to the clinical practice guidelines on patient blood management. Ann Thorac Surg. 2021;112:981–1004.

7. Ertugay S, Kudsioglu T, Sen T, Patient Blood Management Study Group Members. Consensus report on patient blood management in cardiac surgery by Turkish Society of Cardiovascular Surgery (TSCVS), Turkish Society of Cardiology (TSC), and Society of Cardio-Vascular-Thoracic Anaesthesia and Intensive Care (SCTAIC). Turk Gogus Kalp Damar Cerrahisi Derg. 2019;27:429–50.
8. Raphael J, Mazer CD, Subramani S, et al. Society of Cardiovascular Anesthesiologists clinical practice improvement advisory for management of perioperative bleeding and hemostasis in cardiac surgery patients. J Cardiothorac Vasc Anesth. 2019;33:2887–99.
9. Stammers AH, Tesdahl EA, Mongero LB, Stasko A. The effect of various blood management strategies on intraoperative red blood cell transfusion in first-time coronary artery bypass graft patients. Perfusion. 2020;35:217–26.
10. Zecchillo F. Hemolysis in vivo on fusion. Options and Outcomes, Rome, Italy, 2014.
11. Khan JH, Green EA, Chang J, et al. Blood and blood product conservation: results of strategies to improve clinical outcomes in open heart surgery patients at a tertiary hospital. J Extra Corpor Technol. 2017;49:273–82.
12. Schon J, Serien V, Hanke T, et al. Cerebral oxygen saturation monitoring in on-pump cardiac surgery–A 1-year experience. Appl Cardiopulm Pathophysiol. 2009;13:243–52.
13. Monhandas BS, Jagadeesh AM, Vikram SB. Impact of monitoring cerebral oxygen saturation on the outcome of patients undergoing open heart surgery. Ann Card Anaesth. 2013;16:102–6.
14. Colak Z, Borojevic M, Bogovic A, Ivancan V, Biocina B, Majeric-Kogler V. Influence of intraoperative cerebral oximetry monitoring on neurocognitive function after coronary artery bypass surgery: A randomized, prospective study. Eur J Cardiothorac Surg. 2015;47:447–54.
15. Mueller MM, Van Remoortel H, Meybohm P, et al. Patient blood management: recommendations from the 2018 Frankfurt consensus conference. JAMA. 2019;321:983–97.
16. LaPar DJ, Crosby IK, Ailawadi G, et al. Blood product conservation is associated with improved outcomes and reduced costs after cardiac surgery. J Thorac Cardiovasc Surg. 2013;145:796–803, discussion 803–4.