J Extra Corpor Technol. 2017;49:241–248
The Journal of ExtraCorporeal Technology

The Influence of Intraoperative Autotransfusion on Postoperative Hematocrit after Cardiac Surgery: A Cross-Sectional Study

Andrew J. Stasko, MS, CCP; Alfred H. Stammers, MSA, CCP; Linda B. Mongero, BS, CCP; Eric A. Tesdahl, PhD; Samuel Weinstein, MD

SpecialtyCare, Inc., Nashville, Tennessee

Abstract: Utilization of intraoperative autotransfusion (IAT) during cardiac surgery with cardiopulmonary bypass (CPB) has been shown to reduce allogeneic red blood cell transfusion. Previous research has emphasized the benefits of using IAT in the intraoperative period. The present study was designed to evaluate the effects of using IAT on overall hematocrit (Hct) drift between initiation of CPB and the immediate postoperative period. We reviewed 3,225 adult cardiac procedures occurring between February 2016 and January 2017 at 84 hospitals throughout the United States. Data were collected prospectively from adult patients undergoing cardiac surgery with CPB, and stored in the SpecialtyCare Operative Procedural rEgistry (SCOPE), a large quality improvement database. Patients receiving allogeneic transfusion and those with missing covariate data were excluded from analysis. The effect of IAT volume returned to patients on the primary endpoint, hematocrit change from CPB initiation to intensive care unit (ICU) entry, was assessed using a multivariable linear mixed effects regression model controlling for patient demographics, operative characteristics, surgeon, and hospital. Descriptive analysis showed greater positive hematocrit change with increasing autotransfusate volume returned. Those patients with no IAT volume returned saw a median hematocrit change of +2.00%, whereas those with more than 380 mL/m^2 BSA had a median Hct drift of +5.00% ($p < .001$). After controlling for known confounds, our regression estimate of the effect of IAT volume returned on Hct drift was +.0045% per 1 mL/m^2 BSA ($p < .001$). For a patient with the median autotransfusate volume returned (273 mL/m^2 BSA), and all other covariate values at their respective medians, this translates to a predicted hematocrit change of +3.6% (95% CI +3.1 to +4.1). These findings lend further support to the notion that autotransfusate volume is positively associated with increases in postoperative hematocrit. **Keywords:** intraoperative autotransfusion, cell-salvage, cardiopulmonary bypass, post-operative hematocrit change, hematocrit-drift. *J Extra Corpor Technol. 2017;49:241–248*

The recovery of shed blood, its processing, and its re-infusion is termed "blood salvage." Generally the intraoperative standard is to wash the recovered blood, whereas the majority of post-operatively recovered blood is not washed before re-infusion. A combination of techniques is generally advised to decrease the need for allogeneic transfusion (1). A multidisciplinary approach to perioperative blood conservation and product management has been endorsed as best practice by the Society of Thoracic Surgeons in adult patients to minimize high transfusion rates associated with cardiovascular surgery (2). Clinical trials suggest that a restrictive approach to red blood cell transfusions (3) is associated with equivalent and potentially improved clinical outcomes in critically ill patients (4,5), with similar outcomes in post-operative cardiac surgery patients (6). Techniques have been reviewed, examined, and collaborated as components of a multimodality team and process to reduce the likelihood of receiving an allogeneic blood transfusion (7–10). Re-infusion of salvaged autologous blood after conventional cardiac surgical procedures using cardiopulmonary bypass (CPB) and the deployment of a cell-salvage device is termed intraoperative autotransfusion (IAT) (11,12). Benefits of IAT include reduced allogeneic blood exposure without an increase in adverse events or coagulopathy (13,14), the avoidance of immunosuppression, and the reduced transmission of infection (15). Residual CPB volume that is processed by the IAT device diminishes the amount of active inflammatory mediators (16,17). Preoperative anemia management in collaboration with practices focused at interventions during the surgical procedure may provide a more significant benefit in reducing transfusion risk (18,19). The purpose of this study was to assess the relative degree to which the re-infusion of IAT homologous red blood cells improves overall positive perioperative Hct drift between CPB initiation and entry to the intensive care unit.

Received for publication April 27, 2017; accepted July 10, 2017.
Address communications to: Andrew J. Stasko, MS, CCP, SpecialtyCare, Inc., 3100 West End Avenue, Suite 800, Nashville, TN 37203. E-mail: Andy.stasko@specialtycare.net
The senior author has stated that the authors have reported no material, financial, or other relationship with any healthcare-related business or other entity whose products or services are discussed in this paper.

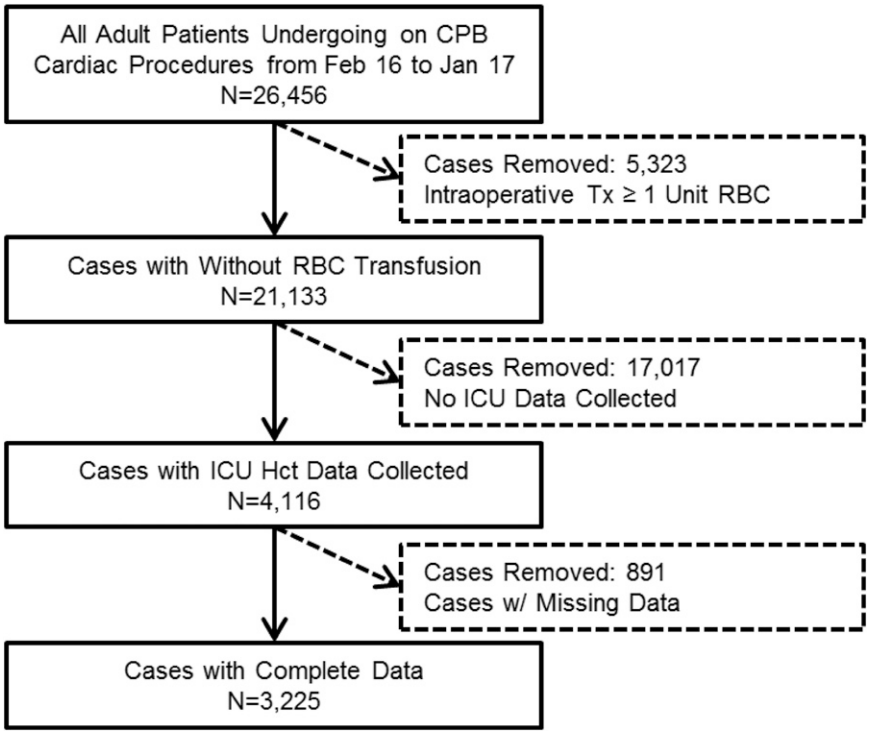

Figure 1. Sample inclusion/exclusion criteria caption.

METHODS

Data were collected prospectively from adult patients undergoing cardiac surgery on CPB with the use of a cell-salvage device, from February 2016 through January 2017 at 84 hospitals throughout the United States. Data entry and storage were carried out using the SpecialtyCare Operative Procedural rEgistry (SCOPE), a quality improvement database. The SCOPE registry was established in 2011 as a national quality control process for systematically collecting intraoperative data relevant cardiac surgical procedures. Data validation is assured by monthly auditing of random case records. The human subjects' research protocol for this study was reviewed and approved by an independent institutional review board.[1]

Sample inclusion and exclusion criteria are summarized in Figure 1. Patients with missing data on variables of interest and those receiving allogeneic red blood cells intraoperatively were excluded, yielding a final sample of 3,225 adult patients. The primary endpoint, Hct change, was calculated by subtracting each patient's Hct at CPB initiation from their later Hct at ICU entry such that positive figures represented increases in Hct, e.g., positive [+] Hct drift. In addition to information on each patient's Hct, we collected a broad range of relevant demographic and intraoperative variables, including factors related to procedure type and acuity and perfusion-relevant volumetric measures.

Descriptive statistics were calculated across five groups according to BSA-normalized autotransfusate volumes: No volume returned, less than 200 mL/m^2 BSA, 200–275 mL/m^2 BSA, 275–380 mL/m^2 BSA, and greater than 380 mL/m^2 BSA. Differences across these five groups were assessed using Kruskal–Wallis rank sum test for continuous variables and chi-squared tests for categorical variables.

We assessed the effect of autotransfusate volume returned to patients at the conclusion of surgery on our primary endpoint, Hct drift, using a multivariable linear mixed effects model. This particular regression modeling tool allows one to account for the correlation in outcomes that occurs for patients undergoing surgery at the same hospital, or with the same surgeon. In addition to these effects, we included statistical controls for age, gender, body surface area, diabetes status, procedure type, non-elective acuity, reoperation, net priming volume, asanguineous volume added during CPB, crystalloid cardioplegia volume, urine output on CPB, anesthesia asanguineous volume, ultrafiltration volume, total CPB time, cross-clamp time, first Hct on CPB, and total volume of acute normovolemic hemodilution collected and returned to the patient. All analyses were carried out using the R statistical

[1]Institutional ethics review board approval was obtained for the use of data from the SCOPE registry (Protocol #012017, Schulman IRB, 4445 Lake Forest Drive, Suite 300, Cincinnati, OH).

computing environment (20) in conjunction with the data. table (21), ggplot2 (22), lme4 (23), effects (24), and sjPlot (25) packages.

RESULTS

Table 1 gives demographic and procedural characteristics according to IAT volume returned groupings. Female patients represented relatively smaller proportions of all patients within the larger volumetric groupings ($p = .007$)—a pattern that was observed among patients with non-elective procedures ($p = .027$) and a history of diabetes ($p < .001$). Among patients undergoing reoperation, the majority fell into the higher volume returned categories ($p = .04$).

Intraoperative and volumetric characteristics of our sample are reported in Table 2. Median CPB time and cross-clamp times were longest in the largest volume returned group and shortest in the smallest volume returned group, respectively (both $p < .001$). Median ATS processed volume (as opposed to returned) was lowest in the "No Volume Returned" group at 329 mL, and highest in the 380 mL/m^2 BSA group at 3,616 mL ($p < .001$). Taken together, these descriptive findings suggest the importance of operative time as a predictor of IAT volume processed and eventually returned to the patient.

Descriptive analyses of Hct in the perioperative period are summarized in Table 3. Across the five groups patients did not vary greatly in median first Hct on CPB (although the small differences between groups were statistically significant); however, the median Hct drift from the initiation of CPB to the ICU entry was greatest in the largest IAT volume returned group and smallest in the no volume returned group (5.0% vs. 2.0%, $p < .001$). Data is expressed within Figure 2 as median with whiskers representing 1.5 times the interquartile range.

Our multivariable linear mixed model results are summarized in Figure 3 and Appendix Table 1. After controlling for known confounding variables, including hospital and surgeon, we estimated the effect of IAT volume returned to patients to be a .0045% increase in positive Hct drift per mL/m^2 BSA returned to the patient. For the median patient, with IAT returned volume of 273 mL/m^2 BSA, this equates to a predicted Hct drift between CPB initiation and ICU entry of 3.6% points (95% CI +3.1 to +4.1).

DISCUSSION

Intraoperative blood salvage should be the centerpiece of a cardiac surgical blood management program as it is the procedure that typically returns the greatest volume of red blood cells (RBC). Intraoperative autotransfusion was performed using various competitive cell-salvage units designed to collect, spin, and wash the salvaged RBC's with normal saline .9% and then suspending the processed volume in a transfusion bag in the perioperative setting with an approximate hematocrit of 55–60% (11,18,19,26). During the processing of IAT, these devices also remove functional platelets and clotting factors that can effect coagulation.

Re-infusion of the processed IAT volume was continuous and a seamless transition while the perfusionist

Table 1. Demographic and procedural characteristics.

	No Volume Returned	Less Than 200 mL/m^2	200–275 mL/m^2	275–380 mL/m^2	More Than 380 mL/m^2	*p*-Value
Observations	60	742	832	768	823	
Female gender—n (%)	17 (28.3)	194 (26.1)	198 (23.8)	170 (22.1)	154 (18.7)	.007
Patient age (years)—median [IQR]	62.50 [56.75, 73.00]	66.00 [59.00, 72.00]	66.00 [58.00, 73.00]	66.00 [58.00, 73.00]	65.00 [57.00, 72.50]	.344
Body surface area (m^2)—median [IQR]	2.00 [1.84, 2.13]	2.05 [1.89, 2.22]	2.03 [1.89, 2.14]	2.05 [1.89, 2.20]	2.04 [1.84, 2.19]	.011
Nadler est. blood volume (L)—median [IQR]	5.20 [4.68, 5.65]	5.38 [4.76, 6.04]	5.31 [4.84, 5.75]	5.41 [4.82, 6.00]	5.40 [4.67, 5.94]	.021
Diabetic patient—n (%)	24 (40.0)	320 (43.1)	304 (36.5)	257 (33.5)	226 (27.5)	<.001
Procedure type						<.001
Isolated CABG—n (%)	47 (78.3)	581 (78.3)	577 (69.4)	503 (65.5)	413 (50.2)	
Aortic surgery—n (%)	1 (1.7)	3 (.4)	16 (1.9)	14 (1.8)	36 (4.4)	
AV surgery + CABG—n (%)	2 (3.3)	47 (6.3)	68 (8.2)	66 (8.6)	70 (8.5)	
Combined AV/MV surgery—n (%)	1 (1.7)	2 (.3)	13 (1.6)	10 (1.3)	26 (3.2)	
Isolated AV surgery—n (%)	5 (8.3)	61 (8.2)	98 (11.8)	109 (14.2)	151 (18.3)	
Isolated MV surgery—n (%)	4 (6.7)	32 (4.3)	47 (5.6)	53 (6.9)	101 (12.3)	
MV surgery + CABG—n (%)	0 (.0)	16 (2.2)	13 (1.6)	13 (1.7)	26 (3.2)	
Non-elective procedure—n (%)	24 (40.0)	251 (33.8)	245 (29.4)	221 (28.8)	227 (27.6)	.027
Reoperation—n (%)	1 (1.7)	11 (1.5)	18 (2.2)	21 (2.7)	32 (3.9)	.040

mL/m^2, milliliters of ATS volume returned to patient per patient body surface area in meters-squared; CABG, cardiopulmonary bypass with graft; AV, aortic valve; MV, mitral valve.

J Extra Corpor Technol. 2017;49:241–248

Table 2. Intraoperative and volumetric characteristics.

	No Volume Returned	Less Than 200 mL/m^2	200–275 mL/m^2	275–380 mL/m^2	More Than 380 mL/m^2	*p*-Value
Observations	60	742	832	768	823	
Total ATS volume processed (mL)—median [IQR]	329.0 [.00, 2,305.8]	2,082.0 [1,305.0, 2,749.8]	2,628.0 [2,017.8, 3,284.8]	2,942.0 [2,357.8, 3,651.0]	3,616.0 [2,978.0, 4,602.5]	<.001
Net prime volume (mL)—median [IQR]	606.5 [410.0, 852.5]	680.0 [550.0, 800.0]	706.0 [550.0, 892.3]	700.0 [505.0, 900.0]	695.0 [342.5, 888.0]	<.001
CPB added volume (mL)—median [IQR]	635.0 [256.5, 823.8]	310.0 [150.0, 735.5]	255.0 [70.0, 672.5]	225.0 [80.0, 629.3]	215.0 [90.5, 633.0]	<.001
Crystalloid cardioplegia (mL)—median [IQR]	258.40 [72.3, 500.0]	360.0 [80.0, 536.8]	380.0 [100.0, 708.5]	330.0 [80.0, 591.6]	210.0 [70.0, 538.2]	<.001
Urine output on CPB (mL)—median [IQR]	287.50 [150.0, 450.0]	239.50 [130.0, 400.0]	245.0 [120.0, 400.0]	250.0 [150.0, 400.0]	255.0 [150.0, 475.0]	.001
Anesthesia crystalloid volume (mL)—median [IQR]	1,500 [1,488, 2,000]	1,500 [1,000, 1,900]	1,500 [1,100, 2,000]	1,500 [1,100, 2,000]	1,500 [1,100, 2,000]	.002
Ultrafiltration volume (mL)—median [IQR]	75.0 [.0, 1,550.0]	.0 [.0, 1,087.5]	.0 [.0, 800.0]	.0 [.0, 800.0]	.0 [.0, 1,000.0]	.013
Autologous blood harvest (mL)—median [IQR]	.0 [.0, 250.0]	.0 [.0, 200.0]	.0 [.0, .0]	.0 [.0, .0]	.0 [.0, .0]	<.001
CPB time (minutes)—median [IQR]	79.50 [59.0, 126.0]	97.0 [78.0, 121.0]	104.5 [83.0, 132.0]	107.0 [82.0, 137.0]	121.0 [90.0, 159.0]	<.001
Cross clamp time (minutes)—median [IQR]	64.0 [42.8, 97.0]	71.0 [54.0, 92.0]	76.0 [58.0, 100.0]	78.0 [59.0, 101.0]	87.0 [63.0, 119.0]	<.001

mL/m^2, milliliters of ATS volume returned to patient per patient body surface area in meters-squared; ATS, autotransfusion; CPB, cardiopulmonary bypass; IQR, inter-quartile range.

Table 3. Perioperative hematocrit readings.

	No Volume Returned	Less Than 200 mL/m^2	200–275 mL/m^2	275–380 mL/m^2	More Than 380 mL/m^2	*p*-Value
Observations	60	742	832	768	823	
First CPB Hct (%)—median [IQR]	30.20 [27.00, 33.00]	28.00 [25.00, 31.00]	28.00 [25.50, 31.00]	29.00 [26.00, 32.00]	30.00 [26.00, 33.65]	<.001
Lowest CPB Hct (%)—median [IQR]	28.50 [25.00, 31.00]	26.05 [24.00, 30.00]	26.00 [24.00, 30.00]	27.00 [25.00, 30.00]	28.00 [25.00, 31.00]	<.001
Last CPB Hct (%)—median [IQR]	30.00 [26.00, 34.92]	29.00 [26.00, 32.00]	29.00 [26.00, 32.00]	30.00 [27.00, 33.00]	31.10 [27.95, 35.00]	<.001
First ICU Hct (%)—median [IQR]	32.55 [28.65, 35.78]	31.70 [28.25, 35.00]	31.75 [29.00, 35.02]	33.00 [30.00, 36.60]	34.30 [30.80, 39.00]	<.001
Hct change: OR entry to first CPB (%)—median [IQR]	−8.00 [−11.00, −5.00]	−9.00 [−11.00, −7.00]	−9.00 [−11.00, −7.00]	−9.00 [−11.00, −6.00]	−9.00 [−11.00, −6.00]	.060
Hct change: first CPB to last OR (%)—median [IQR]	−1.00 [−3.00, .00]	.00 [−2.00, 1.00]	.00 [−2.00, 1.00]	.00 [−2.00, 1.00]	−1.00 [−2.45, 1.00]	<.001
Hct change: first CPB to first ICU (%)—median [IQR]	2.00 [−1.00, 5.00]	3.70 [1.20, 6.00]	4.00 [1.50, 6.00]	4.00 [2.00, 6.70]	5.00 [2.00, 7.40]	<.001

mL/m^2, milliliters of ATS volume returned to patient per patient body surface area in meters-squared; CPB, cardiopulmonary bypass; IQR, inter-quartile range; Hct, hematocrit; ICU, intensive care unit.

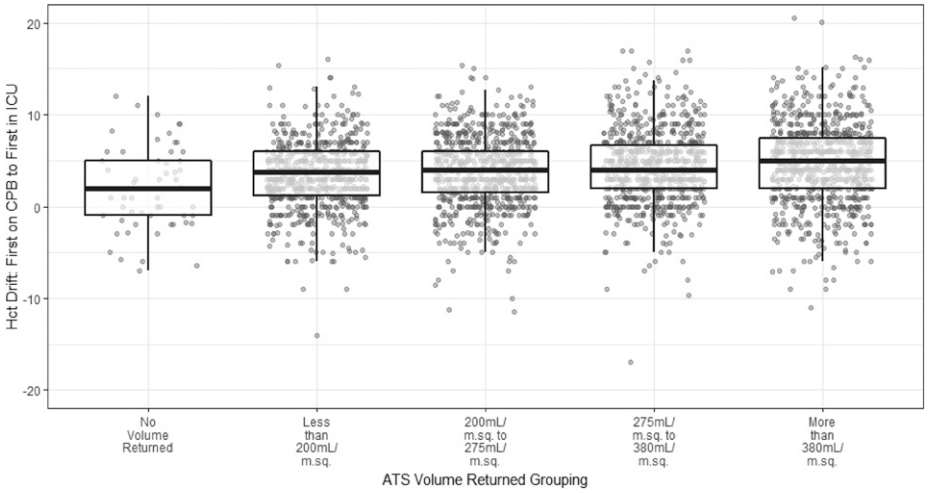

Figure 2. Hematocrit drift: first on CPB to ICU entry, by normalized autotransfusate volume returned. Boxplot interpretation: line at middle of box represents median, top and bottom of box are 25th and 75th percentiles, respectively. "Whiskers" extend to 1.5 times the inter-quartile range above the 75th and below the 25th percentiles. Dots represent individual data points. mL/m^2, milliliters of ATS volume returned to patient per patient body surface area in meters-squared; ATS, autotransfusate; Hct, hematocrit; CPB, cardiopulmonary bypass; ICU, intensive care unit.

emptied their post-CPB circuit volume; the concurrent recovery of mediastinal shed blood as hemostasis was achieved and the sternum approximated and closed. The monitoring of the hemodynamics for fluid assessment and filling pressures were managed by the anesthesiologist. They used our processed IAT, and physician choice of crystalloid and vascular expander colloids as needed. Once undraped, the transferring of the patient to their bed, with all their volume of IAT was completed either in the operating room suite or by the time the patient arrives at the ICU; was monitored by the team.

Anesthesia techniques and fluid administration are not standardized among the cardiac anesthesiologist (27). Before CPB, blood pressure is maintained with α-receptor-specific medications used to squeeze the vascular smooth muscle tone to elevate blood pressure (28) rather than fluid administration as long as monitoring parameters do not indicate a deleterious fluid deficit (29).

Conservation modalities that are frequently used in cardiac surgery are acute normovolemic hemodilution (ANH) and autologous priming (AP) (30) techniques of the extracorporeal bypass circuit performed by the perfusionists. Communication between the surgeon, perfusion, and anesthesia teams are coordinated to initiate and deploy their specific physician protocol methods for ANH and/or AP techniques before CPB

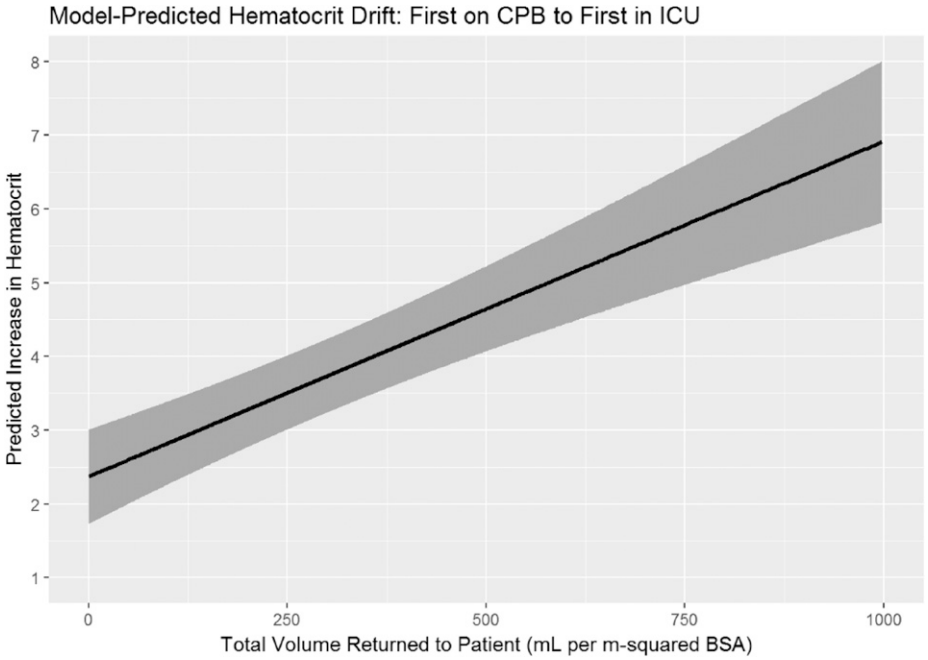

Figure 3. Effect of autotransfusate volume on hematocrit drift: regression-adjusted estimates and 95% confidence intervals. CPB, cardiopulmonary bypass; ICU, intensive care unit.

(8,31,32) to achieve the effect of a reduction in hemodilution.

As the patient's cardiac procedure reaches the point during the case where the chest wires are placed and hemostasis being evaluated before the wires being cinched closed and twisted, the washed and processed red cells shed from mediastinum, chest tube outflow, and from the post-CPB pump run have a survival which is equal to that of the patient's own blood, the morphology is unchanged, the levels of 2, 3-DPG are higher than allogeneic blood and the osmotic fragility is unchanged. All evidence suggests that the washed product from a cell salvage system is equal or superior to allogeneic blood. The ability of IAT to reduce the need for allogeneic blood transfusion after cardiac surgery has been well documented (33).

CPB has been associated with a significant systemic inflammatory response, which may lead to a capillary leak syndrome and a decrease in circulating blood volume (16,34,35). Studies have shown that this transfer of fluid into the third space within minutes of the initiation of CPB could result in an increase in the extravascular fluid volume of several liters during the first 24 hours (36,37). The inflammation caused by CPB may explain the post-operative pattern of hemoglobin shift and fluid mobilization occurring, with the circulating blood volume normalizing to include the volume re-infused. Their vascular compartment autoregulates as the core-temperature of 37°C is achieved with hemostasis, splenic bed release of the hibernating and sequestered RBC population, and the ongoing diuresing of kidney performance and monitoring urine outputs are key physiologic elements that afford discovery of the Hct drift (38–42) upward to demonstrate a positive Hct % change displayed on Table 3.

After controlling for known confounding variables normalized per BSA, effects of IAT volumes returned to our five cohort groups provided the evidence and analysis to build our model. This predictive-model displayed on Figure 3 expresses a [+] Hct % drift that demonstrates a positive slope trajectory correlating to greater increases in perioperative Hct recovery in the immediate post-operative setting. The median Hct drift from the initiation of CPB to the ICU entry was greatest in the largest IAT volume returned group and smallest in the no volume returned group (5.0% vs. 2.0%, $p < .001$). Our statistical analysis estimates a .0045% increase in positive Hct drift per mL/m^2 BSA returned for the patient. A patient falling within the median range of autotransfusate returned volume of 273 mL/m^2 BSA, this correlated to a predicted Hct drift between CPB initiation and ICU entry of 3.6% points (95% CI +3.1 to +4.1). The surprising findings fell within the initial group of 60 subjects studied. They had no volume transfused, and their median Hct % increased by 2.00 points. Spanning the subsequent 4 remaining IAT groups of 3,165 subjects, their respected median Hct % rise was statistically significant to create a positive sloped-axis with the regression analysis values delineated on Table 3. Data has identified a physiologic forecast to provide a benchmarking tool to be used within the cardiac surgical team members evaluating blood management objectives and outcome goals.

Limitations

There are several limitations to this study and include the analysis of data from a retrospective observational registry. This study was conducted using a national registry of data collected in a prospective, but non-randomized manner. Although the study comprised over 26,000 cases during the study period, only 3,225 patients were in the five cohort groups. Protocols for the timing of and the drip-rate used by the anesthesia team to deliver the processed and re-infusion of the IAT volumes were not standardized across centers. Therefore, differences in practice patterns do exist, and although we attempted to minimize these by multivariable logistic regression, we realize that variability may exist. Furthermore, blood management as well as transfusion protocols varied both across and within individual hospitals, so the administration of RBC may have been biased by clinical decisions.

CONCLUSION

As the patient's post-operative course achieves hemostasis, coagulopathies were corrected to maintain pre-operative hemodynamic parameters; this predicted Hct drift model may allow bedside team members and physician staff time to evaluate all critical factors knowing the Hct will elevate to a target range and thwart a potential allogeneic transfusion. Further research is warranted to examine and investigate the drivers of physiologic metrics that lead clinicians to understand Hct drift.

REFERENCES

1. Waters JH, Dyga RM, Waters JF, et al. The volume of returned red blood cells in a large blood salvage program: Where does it all go? Transfusion. 2011;51:2126–32.
2. Ferraris VA, Brown JR, Despotis GJ, et al. Update to the society of thoracic surgeons and the society of cardiovascular anesthesiologists blood conservation clinical practice guidelines. Ann Thorac Surg. 2011;91:944–82.
3. Avgerinos DV, DeBois W, Salemi A. Blood conservation strategies in cardiac surgery: More is better. Eur J Cardiothorac Surg. 2014;46: 865–70.
4. Hebert PC, Wells G, Blajchman MA, et al.; Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. N Engl J Med. 1999;340:409–17.
5. Ferraris VA, Ferraris SP, Saha SP, et al. Perioperative blood transfusion and blood conservation in cardiac surgery: The Society of

Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists Clinical Practice Guideline. Ann Thorac Surg. 2007;83:27–86.
6. Hajjar LA, Vincent JL, Galas FR, et al. Transfusion requirements after cardiac surgery: The TRACS randomized controlled trial. JAMA. 2010;304:1559–67.
7. 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.
8. Chu MW, Losenno KL, Moore K, et al. Blood conservation strategies reduce the need for transfusions in ascending and aortic arch surgery. Perfusion. 2013;28:315–21.
9. Vonk AB, Meesters MI, Garnier RP, et al. Intraoperative cell salvage is associated with reduced postoperative blood loss and transfusion requirements in cardiac surgery: A cohort study. Transfusion. 2013;53: 2782–9.
10. 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.
11. Murphy GJ, Rogers CS, Lansdowne WB, et al. Safety, efficacy, and cost of intraoperative cell salvage and autotransfusion after off-pump coronary artery bypass surgery: A randomized trial. J Thorac Cardiovasc Surg. 2005;130:20–8.
12. Bellone M, Pham HP, Shaz BH, et al. Retrospective analysis of community hospital red blood cell recovery procedures: Improved utilization needed for effectiveness. Transfusion. 2015;55:1972–9.
13. Murphy GJ, Allen SM, Unsworth-White J, et al. Safety and efficacy of perioperative cell salvage and autotransfusion after coronary artery bypass grafting: A randomized trial. Ann Thorac Surg. 2004;77: 1553–9.
14. Dalrymple-Hay MJ, Dawkins S, Pack L, et al. Autotransfusion decreases blood usage following cardiac surgery—A prospective randomized trial. Cardiovasc Surg. 2001;9:184–7.
15. Sirvinskas E, Lenkutis T, Raliene L, et al. Influence of residual blood autotransfused from cardiopulmonary bypass circuit on clinical outcome after cardiac surgery. Perfusion. 2005;20:71–5.
16. Amand T, Pincemail J, Blaffart F, et al. Levels of inflammatory markers in the blood processed by autotransfusion devices during cardiac surgery associated with cardiopulmonary bypass circuit. Perfusion. 2002;17:117–23.
17. Walpoth BH, Eggensperger N, Hauser SP, et al. Effects of unprocessed and processed cardiopulmonary bypass blood retransfused into patients after cardiac surgery. Int J Artif Organs. 1999;22:210–6.
18. Tran MH, Lin DM, Wilcox T, et al. Effects of a multimodality blood conservation schema toward improvement of intraoperative hemoglobin levels and off-pump transfusions in coronary artery bypass graft surgery. Transfusion. 2014;54:2769–74.
19. Ranucci M, Conti D, Castelvecchio S, et al. Hematocrit on cardiopulmonary bypass and outcome after coronary surgery in nontransfused patients. Ann Thorac Surg. 2010;89:11–7.
20. Team RCR. A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing; 2016.
21. Dowle M, Srinivasan A, Gorecki J, et al. Package 'data.table'. R package version 1(0); 2017.
22. Wickham H. ggplot2: Elegant Graphics for Data Analysis. New York, NY: Springer-Verlag; 2009:1–7.
23. Bates D, Mächler M, Bolker B, et al. Fitting linear mixed-effects models using lme4. J Stat Softw. 2015;67:1–48.
24. Fox J. Effect displays in R for generalised linear models. J Stat Softw. 2003;8:1–27.
25. Lüdecke D. Package sjPlot: data Visualization for Statistics in Social Science. R package version 1.9. 4; 2016.
26. Serrick CJ, Scholz M, Melo A, et al. Quality of red blood cells using autotransfusion devices: A comparative analysis. J Extra Corpor Technol. 2003;35:28–34.
27. Barry AE, Chaney MA, London MJ. Anesthetic management during cardiopulmonary bypass: A systematic review. Anesth Analg. 2015; 120:749–69.
28. Kalmar AF, Scheeren TW. Heart rate and the assessment of changes in venous return after phenylephrine. J Appl Physiol. 2013;114:1646.
29. Vretzakis G, Kleitsaki A, Aretha D, et al. Management of intraoperative fluid balance and blood conservation techniques in adult cardiac surgery. Heart Surg Forum. 2011;14:28–39.
30. Vandewiele K, Bove T, De Somer FM, et al. The effect of retrograde autologous priming volume on haemodilution and transfusion requirements during cardiac surgery. Interact Cardiovasc Thorac Surg. 2013;16:778–83.
31. Loubser PG, Morell RI, Loubser IA. Impact of extracorporeal circuit prime volume reduction on whole blood sequestration during acute normovolemic hemodilution for adult cardiac surgery patients. J Extra Corpor Technol. 2004;36:329–35.
32. Xydas S, Magovern CJ, Slater JP, et al. Implementation of a comprehensive blood conservation program can reduce blood use in a community cardiac surgery program. J Thorac Cardiovasc Surg. 2012;143:926–35.
33. Cross MH. Autotransfusion in cardiac surgery. Perfusion. 2001;16: 391–400.
34. Cremer J, Martin M, Redl H, et al. Systemic inflammatory response syndrome after cardiac operations. Ann Thorac Surg. 1996;61:1714–20.
35. Hamada Y, Kawachi K, Tsunooka N, et al. Capillary leakage in cardiac surgery with cardiopulmonary bypass. Asian Cardiovasc Thorac Ann. 2004;12:193–7.
36. Seghaye MC, Grabitz RG, Duchateau J, et al. Inflammatory reaction and capillary leak syndrome related to cardiopulmonary bypass in neonates undergoing cardiac operations. J Thorac Cardiovasc Surg. 1996;112:687–97.
37. Tschaikowsky K, Neddermeyer U, Pscheidl E, et al. Changes in circulating blood volume after cardiac surgery measured by a novel method using hydroxyethyl starch. Crit Care Med. 2000;28:336–41.
38. George TJ, Beaty CA, Kilic A, et al. Hemoglobin drift after cardiac surgery. Ann Thorac Surg. 2012;94:703–9.
39. Previsdomini M, Stocker R, Corti R, et al. Time course of hemoglobin concentrations in the intensive care unit in nonbleeding patients with acute coronary syndrome. Am J Cardiol. 2007;100:579–82.
40. Grant MC, Whitman GJ, Savage WJ, et al. Clinical predictors of postoperative hemoglobin drift. Transfusion. 2014;54:1460–8.
41. Scrascia G, Rotunno C, Nanna D, et al. Pump blood processing, salvage and re-transfusion improves hemoglobin levels after coronary artery bypass grafting, but affects coagulative and fibrinolytic systems. Perfusion. 2012;27:270–7.
42. Goldberg JB, Shann KG, Fitzgerald D, et al. The relationship between intra-operative transfusions and nadir hematocrit on post-operative outcomes after cardiac surgery. J Extra Corpor Technol. 2016;48: 188–93.

Appendix Table 1. Multivariable linear mixed model full results.

Linear Mixed Effects Model Full Results			
Fixed Effects	Parameter Estimate	95% Confidence Interval	*p*-Value
(Intercept)	13.576	10.67 to 16.48	<.001
Autotransfusion volume returned per m^2 BSA	.0045	.00 to .01	<.001
Gender (women)	−.3585	−.89 to .17	.186
Patient age	−.0144	−.03 to .00	.133
BSA	.9486	−.05 to 1.94	.062
Diabetes status (yes)	.2078	−.21 to .62	.329
Procedure: aortic surgery	−.0554	−1.47 to 1.36	.939
Procedure: AV surgery + CABG	−.1096	−.90 to .68	.785
Procedure: combined AV/MV surgery	.8209	−.81 to 2.45	.323
Procedure: isolated AV surgery	.211	−.42 to .84	.513
Procedure: isolated MV surgery	.4055	−.42 to 1.23	.334
Procedure: MV surgery + CABG	−.2475	−1.63 to 1.14	.726
Non-elective acuity	.3695	−.12 to .85	.135
Reoperation (yes)	−.4664	−1.69 to .76	.455
Net prime volume	0	−.00 to .00	.963
Asanguinous volume added on CPB	−.0004	−.00 to −.00	.039
Crystalloid cardioplegia volume	.0002	−.00 to .00	.476
Urine output volume on CPB	.0012	.00 to .00	.004
Anesthesia asanguineous volume	−.0006	−.00 to −.00	<.001
Ultrafiltration volume	.0001	−.00 to .00	.449
Total CPB time (minutes)	−.0253	−.04 to −.01	<.001
Cross clamp time (minutes)	.0068	−.01 to .02	.321
First hematocrit on CPB	−.3325	−.39 to −.28	<.001
Autologous blood harvest volume (mL)	.0026	.00 to .00	<.001
Random effects			
Residual variance		29.831	
Surgeon-level variance		0	
Hospital-level variance		2.924	
Number observations: surgeons		177	
Number observations: hospitals		84	
Intraclass correlation coefficient: surgeons		0	
Intraclass correlation coefficient: hospitals		.089	

p-Values and 95% confidence intervals obtained via the Kenward–Roger approximation as implemented in the R package "effects." mL/m^2, milliliters of ATS volume returned to patient per patient body surface area in meters-squared; CPB, cardiopulmonary bypass; IQR, inter-quartile range; Hct, hematocrit; ICU, intensive care unit; BSA, body surface area; CABG, cardiopulmonary bypass with graft; AV, aortic valve; MV, mitral valve.