

The influence of cardiopulmonary bypass residual volume processing technique on blood management in cardiac surgical patients

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Abstract

Background: Post-cardiopulmonary bypass (CPB) blood processing is an important component of blood management during cardiac surgery.

Purpose: The purpose of this study is to evaluate several methods of processing post-CPB residual blood.

Research Design: Using a multi-institutional national database (SpecialtyCare Operative Procedural rEgistry [SCOPE]), 77,591 cardiac surgical operations performed in adults (>18 years) between January 2017 and September 2022 were reviewed.

Study Sample: Blood processing methods included: Cell washing (CW, $n = 63,592$), Ultrafiltration (UF, $n = 6286$), Whole blood (WB, $n = 3749$), Hemobag (HB, $n = 2480$), and No processing (NO, $n = 1484$). The primary outcome was intraoperative post-CPB allogenic red blood cell (RBC) transfusion.

Data Analysis: Group differences in RBC transfusion were assessed using a Bayesian mixed-effects logistic regression model controlling for multiple operative variables.

Results: Across blood processing groups, patients had similar ages, body mass index and surgical procedures performed as well as preoperative hematocrit and nadir operative hematocrit. Median hematocrit change from last-in-operating room to first-in-ICU were highest in UF and HB groups (3.0 [IQR = 2.0–4.8] and 2.5 [IQR = 0.4–5.0]), respectively. The model-predicted probability of intraoperative post-CPB RBC transfusion was lowest in the HB group (0.79% [95% CrI = 0.37%–1.26%]), and highest in NO group (2.12% [95% CrI = 1.47%–2.82%]). Relative to CW, the odds of RBC transfusion for HB cases were reduced by half (OR = 0.5 [95% CrI = 0.28–0.89], statistical reliability = 99.1%), while odds for NO were 1.41 greater (OR = 1.41 [95% CrI = 1.03–1.93], statistical reliability = 98.2%).

Conclusions: Post-CPB blood processing affects the likelihood for both receiving an intraoperative post-CPB RBC transfusion and for hematocrit change, with HB use resulting in the lowest predicted risk for transfusion, and NO the highest.

Keywords

blood processing techniques, blood management (adult), cardiopulmonary bypass

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Introduction

In the field of transfusion medicine, an unequivocal recommendation is to administer blood products in a judicious manner to achieve maximum patient benefit. Patients exposed to allogeneic blood have been shown to have longer hospital length of stay, increased pulmonary dysfunction and postoperative infections, and higher morbidity and mortality in a dose-dependent manner.¹⁻³ Patients who undergo cardiac surgery with the use of cardiopulmonary bypass (CPB) are one of the highest consumers of intraoperative transfusion of red blood cells (RBCs).⁴

The process of CPB requires the priming of extracorporeal circuitry, most often with asanguineous fluids, which results in hemodilution. Additionally, during CPB and cardiac surgery, the volume of resuscitative fluids administered to maintain hemodynamics may frequently worsen hemodilution and result in circulatory overload. As such, maintaining appropriate fluid balance requires processes that are focused on reducing the risk for iatrogenic anemia and the loss of the formed elements of blood, which may require replacement with allogeneic products. Despite this risk, strategies are available to reduce blood loss during open heart surgery; these strategies utilize different technologies and may offer specific benefits to patients undergoing CPB.^{5,6}

Clinical practice guidelines have been developed and endorsed by multiple professional societies to assess the benefit and risks of various perioperative blood management strategies for adult cardiac surgical patients.⁷ While these guidelines address the processing of post-CPB salvaged pump blood with centrifugation and cell washing (CW), other important interventions not discussed include ultrafiltration (UF), whole blood (WB) administration, and the use of commercial systems for hemoconcentration (Hemobag® [HB], Global Blood Resources, Somers, CT, USA). Several studies have examined one or more of these processes, but no comprehensive evaluation of all of these techniques has been reported.⁸⁻¹¹

Therefore, the purpose of this study is to evaluate commonly used techniques for processing post-CPB pump blood and to compare their effect on intraoperative post-CPB RBC transfusion rates and hematocrit (HCT) change in adult patients undergoing isolated coronary artery bypass grafting (CABG), isolated valve repair or replacement, or CABG with valve repair or replacement.

Methods

The human subjects research protocol for this study was reviewed and approved by an independent

Institutional Review Board with a waiver of the need for consent (Protocol #012017, ADVARRA Center for IRB Intelligence, 6100 Merriweather Dr, Suite 600, Columbia, MD 21,044). Before exclusions, 91,560 cardiac surgical operations performed in adults (>18 years) between January 2017 and September 2022 were reviewed utilizing a multi-institutional national database (SpecialtyCare Operative Procedural rEgistry (SCOPE), <https://specialtycareus.com>). Cases included isolated CABG, isolated cardiac valve repair or replacement, and combined CABG and valvar procedures. Patients who received an RBC transfusion prior to initiation of CPB were excluded. This resulted in a final analytic sample of 77,591 cases (Figure 1). The primary outcome measure was intraoperative post-CPB allogeneic RBC transfusion, with secondary endpoints of intraoperative and postoperative changes in HCT. Post-CPB blood processing methods included: CW ($n = 63,592$), UF ($n = 6286$), WB ($n = 3749$), HB ($n = 2480$), and No processing (NO, $n = 1484$):

- The CW blood processing technique utilized several different manufacturer models for collection, filtration, and centrifugation of shed blood used in the process of intraoperative cell salvage (ICS). While different devices were utilized, the techniques of ICS were standardized across all centers using policies and procedures established by a national perfusion service provider (SpecialtyCare, Cell Washing Practice Guidelines, CLIN GUI 0600, 3 Maryland Farms, Suite 200, Brentwood, TN, USA). All of the returned autotransfusate was reinfused through a 40-micron blood filter.
- In the UF technique, the remaining CPB volume was processed and concentrated by using a multi-pass technique removing excess plasma water. Thereafter, the UF volume was transferred from the CPB circuit to a collection bag for patient reinfusion. The technique of UF was standardized by the use of clinical practice guidelines (SpecialtyCare, Cardiopulmonary bypass practice guidelines on fluid management, CLIN GUI 0802, Brentwood, TN, USA). No effort was made to standardize the quantity of plasma water volume removed across centers, which was determined by the attending perfusionist as a function of both the quantity of residual CPB volume and the hemodynamic requirements of the patient. The choice of the UF manufacturer and model was not standardized and was let to the discretion of each center.

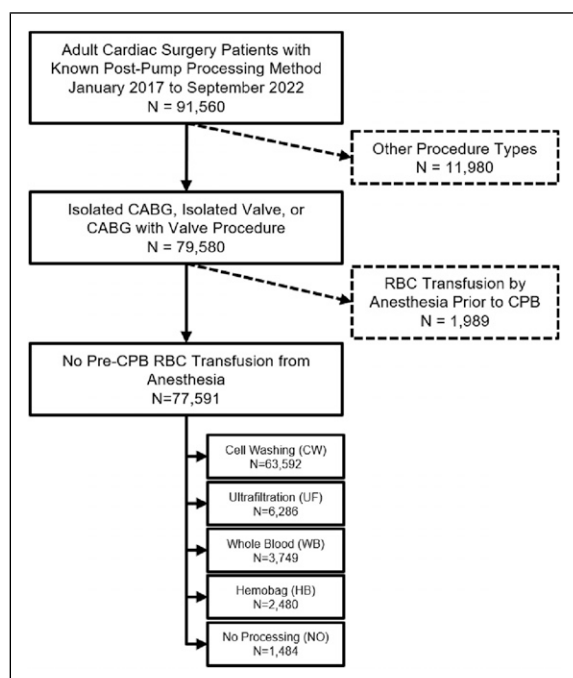


Figure 1. CONSORT flow diagram depicting the distribution of all patients not receiving a red blood cell transfusion prior to cardiopulmonary bypass. Abbreviations: CABG: coronary artery bypass graft; CPB: cardiopulmonary bypass; RBC: red blood cells.

- The WB technique, also known as a direct infusion technique, reinfused the residual CPB volume directly into the patient either through the arterial cannula or by placing the volume into a reinfusion bag that is then given to the anesthesia personnel for infusion.
- The HB technique is known as off-line modified ultrafiltration (MUF); the HB technique differs from in-line MUF because in-line MUF occurs while the patient remains heparinized with vascular cannulae still in place.¹⁰ The HB technique utilizes an isolated reservoir collection bag connected to an ultrafiltrator. All the residual blood volume in the CPB circuit is displaced with clear fluid into a reservoir collection bag and is then hemoconcentrated until a desired volume is achieved according to the manufacturer's instructions for use.¹² The reservoir collection bag and volume are then reinfused into the patient, typically by anesthesia personnel.
- For the NO technique, the remaining pump volume contents were not processed and were discarded post-CPB.

When processing residual CPB blood using UF, WB or HB techniques, all formed elements of blood

(platelets and RBCs) along with the plasma component and coagulation factors are reinfused. These systems all require that the collected volume remains heparinized to prevent clotting. When the volume for any of these methods was infused after heparin reversal with protamine, additional protamine was administered if re-heparinization was suspected. In contrast, when residual blood is processed by the CW technique, the RBC fraction is returned devoid of plasma and platelets, with the majority of heparin removed by the washing process. However, if the surgeon or anesthesiologist suspected that residual heparin may have been retained in the autotransfusate, additional protamine may have been given. No effort was made to standardize this treatment and protamine doses were not recorded.

Statistical analysis

Unadjusted descriptive statistics were calculated by group using median and interquartile range for continuous variables, and count with percentage for categorical variables. Group differences in the probability of post-CPB RBC transfusion were assessed using Bayesian mixed-effects logistic regression controlling for patient age, body mass index (BMI), gender, procedure type, first HCT upon admission to the operating room (OR), lowest HCT on CPB, CPB duration, fluid balance, and RBC transfusion during CPB. A random effect was included to adjust for variability in outcomes by perfusionist. Missingness was assessed for each study variable and was found to be highest for "total asanguineous volume given" (6% missing). Per established statistical practice, cases with missing data were not removed, but instead a total of ten data sets were imputed from original using the chained equations method; the regression model was fit to all ten data sets, and the results were combined into a single model summary using the Bayesian model stacking method. All data preparation and analysis were carried out within the R statistical computing environment (version 4.3.1),¹³ in conjunction with the packages 'data.table',¹⁴ 'compareGroups',¹⁵ and 'rmsb'.¹⁶

Results

The CW technique was utilized in 81.9% of all cases with only 1.9% using the NO method (Table 1). Patient age and BMI were similar across the five processing techniques. The UF method was more commonly used in both isolated valve and CABG with valve procedures than other techniques. The CW technique resulted in the highest volume of autotransfusate returned which was more than double that seen with the UF and HB

Table 1. Descriptive summary of demographic and baseline characteristics by blood processing group.

	All	CW	UF	WB	HB	NO	N
	N = 77591	N = 63592	N = 6286	N = 3749	N = 2480	N = 1484	
Age (years)	67 [59;73]	67 [59;73]	67 [60;74]	66 [59;72]	67 [59;74]	67 [60;73]	77,591
Sex, N (%)							77,591
Men	56694 (73.1%)	46318 (72.8%)	4672 (74.3%)	2828 (75.4%)	1765 (71.2%)	1111 (74.9%)	
Women	20897 (26.9%)	17274 (27.2%)	1614 (25.7%)	921 (24.6%)	715 (28.8%)	373 (25.1%)	
BMI (kg/m ²)	29.1 [25.8;33.2]	29.3 [25.8;33.3]	28.4 [25.2;32.4]	29.1 [25.7;33.1]	29.7 [26.0;34.0]	29.1 [25.7;33.0]	77,257
Procedure type							77,515
Isolated CABG	56120 (72.4%)	46447 (73.1%)	3840 (61.1%)	2805 (74.9%)	1877 (75.7%)	1151 (78.5%)	
Isolated valve	14110 (18.2%)	11304 (17.8%)	1611 (25.6%)	619 (16.5%)	379 (15.3%)	197 (13.4%)	
CABG and valve	7285 (9.40%)	5792 (9.12%)	832 (13.2%)	319 (8.52%)	223 (9.00%)	119 (8.11%)	
Autotransfusate volume returned (mL)	471 [300;680]	500 [403;710]	225 [210;314]	270 [0;453]	180 [72;265]	0 [0;250]	76,837
Autotransfusate sufficient for return	74266 (96.7%)	63592 (100%)	6286 (100%)	2338 (68.0%)	1607 (76.2%)	443 (31.3%)	76,837
Urine output on CPB (mL)	225 [125;375]	235 [125;400]	200 [100;300]	250 [140;400]	232 [140;350]	225 [130;376]	77,591

Note. Measures are presented as number (percentage) or median [25th and 75th] percentiles.

Abbreviations: BMI: body mass index; CABG: coronary artery bypass graft; CPB: cardiopulmonary bypass; CW: cell washing; HB: hemobag; NO: no processing; UF: ultrafiltration; WB: whole blood.

Table 2. Descriptive summary of operative characteristics by blood processing group.

	All	CW	UF	WB	HB	NO	N
	N = 77,591	N = 63,592	N = 6286	N = 3749	N = 2480	N = 1484	
First HCT in OR	37.0 [33.0;40.0]	37.0 [33.0;40.0]	37.0 [33.0;40.3]	37.0 [33.5;41.0]	37.0 [33.0;41.0]	36.8 [32.6;40.5]	77,591
Nadir HCT on CPB	26.0 [23.0;29.0]	26.0 [23.0;29.0]	26.0 [22.6;28.2]	26.0 [23.0;30.0]	26.0 [23.0;30.0]	26.0 [23.0;29.0]	77,591
Last HCT in OR	28.2 [25.8;32.0]	29.0 [26.0;32.0]	27.0 [25.0;31.0]	29.0 [26.0;32.7]	29.0 [26.0;33.0]	28.0 [25.0;31.0]	77,580
First HCT in ICU	32.0 [28.8;36.0]	32.0 [28.6;36.0]	31.0 [29.0;35.0]	32.0 [28.5;36.0]	33.0 [29.0;36.2]	31.0 [27.2;35.7]	8246
HCT change: First in OR to last in OR	-8.0 [-11.0;-5.0]	-8.0 [-11.0;-5.0]	-9.0 [-12.0;-6.0]	-7.8 [-10.0;-5.0]	-7.0 [-10.0;-5.0]	-8.1 [-11.0;-5.1]	77,580
HCT change: Last in OR to first in ICU	2.3 [0.3;4.7]	2.2 [0.0;4.7]	3.0 [2.0;4.8]	2.1 [0.1;4.1]	2.5 [0.4;5.0]	1.0 [0.0;3.0]	8246
RBC added during CPB, N (%)	9081 (11.7%)	7422 (11.7%)	800 (12.7%)	359 (9.6%)	302 (12.2%)	198 (13.3%)	77,590

Note. Measures are presented as number (percentage) or median [25th and 75th] percentiles.

Abbreviations: CPB: cardiopulmonary bypass; CW: cell washing; HB: hemobag; HCT: hematocrit; ICU: intensive care unit; NO: no processing; OR: operating room; RBC: red blood cells; UF: ultrafiltration; WB: whole blood.

processing modes. To assess whether or not sufficient autotransfusate was available for return, a minimum return volume of 250 mL was used as this is the approximate volume found in one unit of RBCs. Both the CW and UF techniques resulted in 100% availability of that target volume, while the other techniques had lower rates of achieving that value. All cases utilized ICS throughout the operative procedure so collected blood would have been processed regardless of the post-CPB salvaged blood processing technique.

The first HCT in OR and nadir HCT on CPB were also similar amongst groups (Table 2). The last HCT in OR was lowest in the UF group and was approximately two percentage points lower than CW. However, this may have been a function of the timing of HCT assessment since all the processed volume may not have been transfused prior to the sample being drawn for analysis. The first HCT in the ICU was slightly lower for UF and NO compared to other groups, though all groups had a three to four percentage point increase in

HCT from the last HCT in OR. The percentage of patients with any units of RBC added during CPB was highest in the NO group and lowest in the WB group.

The median HCT change from first in the OR to last in OR differed marginally, ranging from a low of -7.0% [IQR = -10.0 ; -5.0] in the HB group to -9.0% [IQR = -12.0 ; -6.0] in UF group (Table 2). The median HCT change from last in OR to first in ICU was highest in the UF and HB groups, (3.0% [IQR = 2.0 ; 4.8] and 2.5% [0.4 ; 5.0]), respectively while the NO group had the lowest change (1.0% [IQR = 0.00 ; 3.00]). The auto-transfusate returned volume was highest when the CW and WB techniques were used, and lowest in the NO and HB groups.

The predicted probability of intraoperative post-CPB RBC transfusion was lowest in the HB group (0.78% , [95% Credible Interval {CrI} = 0.30% – 1.25%]) and highest in NO group (1.90% [CrI = 1.19% – 2.69%]) (Figure 2). Relative to CW, the odds of intraoperative post-CPB transfusion for HB cases were reduced by half (OR = 0.5 [CrI = 0.28 – 0.89], statistical reliability of decrease: 99.1%), while the odds of transfusion in cases using NO were 1.41 times greater (OR = 1.41 [CrI = 1.03 – 1.93], statistical reliability of decrease: 98.2%) (Table 3).

Discussion

The present study demonstrated that use of the HB compared to all other techniques had the lowest predicted risk of RBC transfusion, and that not reinfusing any of the post-CPB volume resulted in the highest likelihood for transfusion. In cardiac surgery, numerous blood conservation techniques have been established to help reduce the risk for allogeneic blood product transfusion.^{5,6} Updated recommendations that target CPB interventions that are effective blood conservation strategies include the use of cell salvage with centrifugation, retrograde priming of the CPB circuit, reducing circuit prime volumes, using ‘mini-circuits’ during CPB, acute normovolemic hemodilution, and established blood transfusion triggers.⁷ While cell salvage with centrifugation has been identified as a Class I, Level A recommendation, its use in concentrating pump-salvaged blood has received a lower ranking of available evidence (Class IIa, Level A).

Following a cardiac surgical procedure where extracorporeal circulation has been utilized, residual volume remains within the CPB circuit that contains the patient’s own blood as well as a mixture of solutions that have been added during surgery. These solutions can either be sanguineous or asanguineous with the latter most often being balanced electrolyte solutions. Colloid

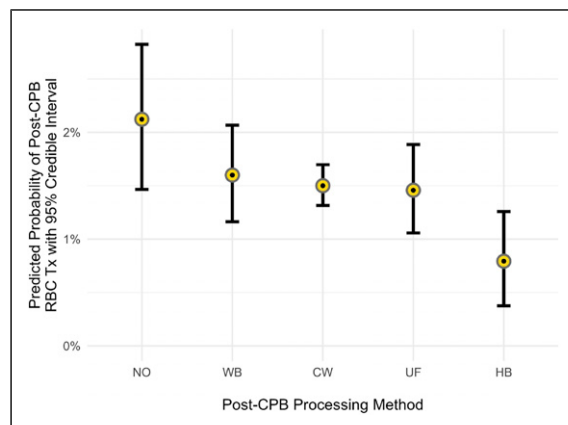


Figure 2. Model predicted probability of post-cardiopulmonary bypass red blood cell transfusion by post-cardiopulmonary bypass blood processing technique. Abbreviations: CPB: cardiopulmonary bypass; CW: cell washing; HB: hemobag; NO: no processing; RBC: red blood cells; UF: ultrafiltration; WB: whole blood.

based solutions are also administered as resuscitative fluids and as a means of maintaining colloid osmotic pressure. Post-CPB processing of this residual circuit volume is usually pursued to minimize the degree of hemodilution by removing plasma water to increase HCT as well as to improve platelet and coagulation factor levels.^{8,9} The remaining volume is then reinfused to the patient to both maintain hemodynamics and reestablish hemostatic processes that had been interrupted by the use of anticoagulants. This hemoconcentration has been shown to increase the patient HCT, increase platelet levels, and improve circulating protein values.¹⁰

While the most common form of post-CPB residual blood processing is centrifugation with CW, as has also been shown in the present study, other modalities exist to serve similar purposes.^{8,10,11} Each of these techniques possess unique methodologies which affect end-product characteristics of the returned volume. In this study, we compared the techniques of CW, UF and HB in improving post-CPB HCT and the likelihood of receiving an intraoperative post-CPB RBC transfusion. We also evaluated the effect of two additional techniques of reinfusing unprocessed residual CPB-blood (WB) and no reinfusion at all (NO). In a small study of the WB technique, other investigators have shown an increase in hemoglobin, fibrinogen, and platelet counts, with no degradation in coagulation assessment.¹⁷ Discarding of post-CPB blood only represented 1.9% of the studied population. While we did not assess why the NO technique was used, it is not inconceivable to posit that some believe that pro-inflammatory substances generated by extracorporeal circulation remain in processed

Table 3. Bayesian mixed-effects logistic regression model results.

Variable and contrast	Model-estimated change in odds of post-CPB RBC transfusion with 95% credible interval	Statistical reliability of model-estimated change in odds
Post-pump method: HB vs CW	0.5 [0.28, 0.89]	0.991
Post-pump method: NO vs CW	1.41 [1.03, 1.93]	0.982
Post-pump method: UF vs CW	0.96 [0.72, 1.28]	0.602
Post-pump method: WB vs CW	1.06 [0.8, 1.39]	0.661
Age (years): 73 vs 59	1.2 [1.15, 1.25]	>.999
Sex: Female vs Male	1.09 [1.01, 1.18]	0.986
Body mass index (kg/m ²): 33 vs 26	0.85 [0.81, 0.89]	>.999
First HCT during CPB (%): 40 vs 33	0.73 [0.68, 0.79]	>.999
Lowest HCT during CPB (%): 29 vs 23	0.2 [0.17, 0.22]	>.999
Total asanguineous volume in (mL): 3230 vs 1995	1.74 [1.6, 1.88]	>.999
Total asanguineous volume out (mL): 5200 vs 2993	1.1 [1.03, 1.17]	0.998
Total time on CPB (min): 132 vs 75	1.48 [1.37, 1.6]	>.999
Units RBC added on CPB: 22 vs 0	2.11 [1.05, 4.26]	0.982
Units RBC added to CPB circuit prime: 10 vs 0	4.25 [1.49, 11.19]	0.997
Procedure type: Valve vs CABG	0.93 [0.84, 1.03]	0.915
Procedure type: CABG and valve vs CABG	1.12 [1, 1.26]	0.972

Abbreviations: CABG: coronary artery bypass graft; CPB: cardiopulmonary bypass; CW: cell washing; HB: hemobag; HCT: hematocrit; NO: no processing; RBC: red blood cells; UF: ultrafiltration; WB: whole blood.

blood and negatively influence patient outcome.¹⁸ We have previously shown that the use of CW is associated with a significant increase in postoperative HCT, with more than a two-fold increase observed when processed CPB salvaged blood with an ICS device was given.¹⁹ Although RBC mass is conserved with this technique, all other elements of blood, including platelets, plasma and coagulation factors, are discarded through the washing process, and could impose a dilutional coagulopathy,²⁰ as well as an increased risk for inflammation and infection.^{18,21} Because of this limitation, other techniques that either employ ultrafiltration or direct re-infusion of unprocessed salvaged blood, or avoid processing and transfusing post-CPB residual blood altogether, have been advocated.^{11,22}

All cases utilized ICS throughout the operative procedure, so collected blood would have been collected and processed regardless of the post-CPB salvaged blood technique. Unsurprisingly, the CW technique had the largest volume of autotransfusate available for return, which was more than double that seen in all other techniques except with WB. To assess whether or not there was sufficient autotransfusate available for return, a minimum return volume of 250 mL was used, which is the approximate volume found in a unit of RBC. Both the CW and UF techniques resulted in 100% availability

of that target volume, while the NO method had only 31% of cases reaching that level. This emphasizes the contribution of ICS in processing and returning higher volumes of shed blood throughout a cardiac surgical procedure, which is supported by the highest level of evidence used to establish clinical practice guidelines.⁷

Use of ultrafiltration concentrates all formed elements of blood and coagulation proteins, resulting in increased red cell mass and platelets. Ultrafiltration is widely used during cardiac surgery with one study reporting usage of 45.5% across the United States.²³ In the present study, the highest HCT change from last-in-OR to first-in-ICU was observed in both the UF and HB groups with only a 0.5% difference between these two groups. In a meta-analysis on the use of ultrafiltration during cardiac surgery, reduction in both allogenic blood product transfusion and bleeding was demonstrated, but the effect was greatest in those receiving MUF,²⁴ which is similar to the UF and HB techniques reported here. While not measured in this study, it is conceivable that these techniques also likely increased the concentration of platelets and coagulation proteins, which may have decreased the rate of postoperative bleeding and the need for transfusion of platelets or other plasma products. In contrast to the presented meta-analysis,²⁴ and to the results of our study, a more

recent randomized clinical trial of isolated CABG patients failed to demonstrate a benefit when comparing post-CPB ultrafiltration processed salvaged blood to unprocessed blood.²⁵ These differences may reflect the patient populations, which differed between studies, with valve and combined procedures included in the meta-analysis²⁴ and the present study but not in the more recent randomized clinical trial.²⁵ In addition to the removal of excess plasma water, ultrafiltration has been shown to lower circulating reactive pro-inflammatory cytokines in pediatric cardiac surgical patients.²⁶ Although its effect on improving post-surgical recovery is equivocal,²⁷ The use of ultrafiltration has also been shown to increase RBC fragility, which results in higher levels of plasma free hemoglobin (pFHb) than cell salvage processing, but the clinical effect of these changes remains to be determined.^{28,29} Yan and colleagues investigated whether the increase in pFHb affected postoperative renal function.³⁰ Increases in pFHb were transient, did not last beyond 3 hours post-surgery, and were not associated with resultant acute kidney injury. An additional concern with the use of ultrafiltration is the presence of residual heparin in the end-product, which may predispose the patient to an increased risk of bleeding if not properly reversed with protamine.^{31,32}

The finding that the HB group had the lowest likelihood for receiving a post-CPB transfusion might be explained by the methodology used with this technique when compared to both the CW and UF methods. In a small clinical study, other investigators compared HB to CW techniques and found that the HB group had a higher generated end-product concentration of HCT, fibrinogen, albumin, and total protein levels.³³ However, unlike the present study, they did not find any differences in RBC transfusion, where we have shown a predicted reduced likelihood for transfusion when HB is employed. Similarly, McNair and colleagues have shown that the use of HB, described as off-line MUF, was associated with the lowest rate of RBC transfusion when compared to CW, in-line MUF, and UF.¹⁰ Beckmann and colleagues also evaluated the HB technique and found more than a two-fold increase in the processed volume HCT as well as improved patient coagulation status, represented by reduced prothrombin times.³⁴ An additional benefit of the HB method is that protamine can be administered prior to processing of residual volume, which would normally delay decannulation as seen when the UF technique is used. A disadvantage of the use of the HB technique is that it requires an additional cost for the system. While the same may be true for an ultrafiltrator, its use has grown more common during CPB especially when crystalloid-based cardioplegic formulations, such as

del Nido and histidine-tryptophan-ketoglutarate solutions, are utilized.^{35,36}

It is clear that the processing and return of post-CPB salvaged blood is one component of a comprehensive blood management program for cardiac surgical patients and that a multifactorial approach to limiting blood product exposure spans the entire perioperative course.⁷ In the present study, the greatest likelihood for receiving a transfusion of RBC was present in operations where no blood processing technique was utilized. While the last HCT in the OR was lowest in the NO group, they also received the highest allogenic RBC transfusions during CPB. This implies that a lower RBC transfusion during CPB would likely have resulted in a more depressed HCT levels post-CPB. It has been shown that both the first HCT in the OR and first HCT on CPB are critically important factors influencing the risk for receiving an RBC transfusion.³⁷

Limitations

There are several limitations to this study. Although collected prospectively, the registry data utilized in this analysis are still observational and were collected in a non-randomized manner. Furthermore the retrospective study design is subject to limitations of inherent selection bias, and the reported results are limited to observed associations between the implementation of the described protocols and improved patient outcomes and do not demonstrate a direct cause-and-effect relationship. Registry data does not permit the investigation of granular factors that may have confounded the results presented. Fourth, while an attempt to standardize post-CPB blood processing techniques was made by the use of national guidelines, it cannot be confirmed that these were always followed. Algorithms for RBC transfusion were not utilized, and we have previously shown that thresholds for transfusion represent a significant factor in determining blood product administration.²⁰ The use of ICS is highly recommended as a best practice technique during cardiac surgery and was used in all cases. Therefore, it is difficult to separate its influence when used throughout the entire intraoperative period versus solely as a post-CPB process. This study was limited to the intraoperative period, so the effect of postoperative blood management cannot be accounted for in these analyses. All results are limited to short-term intraoperative outcomes, and intermediate-term or long-term follow-up data were not available. Finally, the potential for the miscoding of data exists, which despite steps for validation, must be considered in any secondary analysis of registry data. Despite the existence of benefits and detriments associated with each

of the techniques and transfusion guidelines, variations exist throughout cardiac centers and the decision is frequently led by the preferences of the surgical team. In the current study, transfusion triggers and institutional protocols are not accounted for as there is a diversity in practice. However, nadir HCT on CPB in all groups did not reflect that one group was more prone to receive blood transfusion.

Conclusions

Variation in the methods for post-CPB blood processing exist. Discarding of residual CPB blood was associated with a higher likelihood of intraoperative post-CPB RBC transfusion, while the HB technique resulted in the lowest predicted risk for receiving an intraoperative post-CPB RBC transfusion. Attentive patient blood management requires that residual CPB blood not be discarded. Further prospective studies are necessary to determine if these results are reproducible and whether these measured differences in endpoints impact the postoperative course.

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References

- Raphael J, Chae A, Feng X, et al. Red blood cell transfusion and pulmonary complications: the society of thoracic surgeons adult cardiac surgery database analysis. *Ann Thorac Surg* 2024; 117(4): 839–846. DOI: [10.1016/j.athoracsur.2023.12.012](https://doi.org/10.1016/j.athoracsur.2023.12.012).
- Mazzeffi MA, Holmes SD, Taylor B, et al. Red blood cell transfusion and postoperative infection in patients having coronary artery bypass grafting surgery: an analysis of the society of thoracic surgeons adult cardiac surgery database. *Anesth Analg* 2022; 135: 558–566.
- Tang M, Ravn HB, Andreasen JJ, et al. Fewer transfusions are still more-red blood cell transfusions affect long-term mortality in cardiac surgery. *Eur J Cardio Thorac Surg* 2023; 63: e24101.
- Huang D, Chen C, Ming Y, et al. Risk of massive blood product requirement in cardiac surgery: a large retrospective study from 2 heart centers. *Medicine (Baltim)* 2019; 98: e14219.
- Yousuf MS, Samad K, Ahmed SS, et al. Cardiac surgery and blood-saving techniques: an update. *Cureus* 2022; 14: e21222.
- Menkis AH, Martin J, Cheng DC, et al. Drug, devices, technologies, and techniques for blood management in minimally invasive and conventional cardiothoracic surgery: a consensus statement from the international society for minimally invasive cardiothoracic surgery (ISMICS) 2011. *Innovations* 2012; 7: 229–241.
- Tibi P, McClure RS, Huang J, et al. STS/SCA/AMSECT/SABM update to the clinical practice guidelines on patient blood management. *J Extra Corpor Technol* 2021; 53: 97–124.
- Sutton RG, Kratz JM, Spinale FG, et al. Comparison of three blood-processing techniques during and after cardiopulmonary bypass. *Ann Thorac Surg* 1993; 56: 938–943.
- Stammers AH, Morrow JF, Brady CP, et al. Ultrafiltration of the waste plasma effluent from cardiopulmonary bypass circuit contents processed with a cell-washing device. *J Extra Corpor Technol* 1996; 28: 134–139.
- McNair ED, McKay WP, Mondal PK, et al. Transfusion use and hemoglobin levels by blood conservation method after cardiopulmonary bypass. *Ann Thorac Surg* 2020; 110: 1520–1526.
- Eichert I, Isgro F, Kiessling AH, et al. Cell saver, ultrafiltration and direct transfusion: comparative study of three blood processing techniques. *Thorac Cardiovasc Surg* 2001; 49: 149–152.
- Global Blood Resources. <https://www.mybloodfirst.com/perfusionists/methodology-perfusionists.php> (accessed 15 July 2024). Somers, CT, USA).
- R Core Team. *R: a language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing, 2023. <https://www.R-project.org/> (accessed 12 April 2024).
- Dowle M, Srinivasan A. 'data.table': extension of 'data.frame'. *R package version 1.14.8*. <https://CRAN.R-project.org/package=data.table> (2023, accessed 12 April 2024).
- Subirana I, Sanz H, Vila J. Building bivariate tables: the 'compareGroups' package for R. *J Stat Software* 2014; 57(12): 1–16. <https://www.jstatsoft.org/v57/i12/> (accessed 12 April 2024).
- Harrell FE Jr. 'rmsb': Bayesian regression modeling strategies. *R package version 0.0.2*. <https://CRAN.R-project.org/package=rmsb> (2022, accessed 12 April 2024).
- Yolande-Iyer YL, Hayward P, McNicol L, et al. The effects on coagulation of the reinfusion of unprocessed residual blood from the cardiopulmonary bypass. *BMC Res Notes* 2016; 9: 61.

18. van Klarenbosch J, van den Heuvel ER, van Oeveren W, et al. Does intraoperative cell salvage reduce postoperative infection rates in cardiac surgery? *J Cardiothorac Vasc Anesth* 2020; 34: 1457–1463.
19. Stasko AJ, Stammers AH, Mongero LB, et al. The influence of intraoperative autotransfusion on postoperative hematocrit after cardiac surgery: a cross-sectional study. *J Extra Corpor Technol* 2017; 49: 241–248.
20. Sikorski RA, Rizkalla NA, Yang WW, et al. Autologous blood salvage in the era of patient blood management. *Vox Sang* 2017; 112: 499–510.
21. Paparella D, Whitlock R. Safety of salvaged blood and risk of coagulopathy in cardiac surgery. *Semin Thromb Hemost* 2016; 42: 166–171.
22. 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: 210–216.
23. Stammers AH, Tesdahl EA, Mongero LB, et al. Zero-balance ultrafiltration during cardiopulmonary bypass is associated with decreased urine output. *J Extra Corpor Technol* 2021; 53: 27–37.
24. Boodhwani M, Williams K, Babaev A, et al. Ultrafiltration reduces blood transfusions following cardiac surgery: a meta-analysis. *Eur J Cardio Thorac Surg* 2006; 30: 892–897.
25. Whitlock R, Mathew J, Eikelboom J, et al. Processed residual pump blood in cardiac surgery: the processed residual blood in cardiac surgery trial. *Transfusion* 2013; 53: 1487–1492.
26. Bierer J, Stanzel R, Henderson M, et al. Novel inflammatory mediator profile observed during pediatric heart surgery with cardiopulmonary bypass and continuous ultrafiltration. *J Transl Med* 2023; 21: 439.
27. Kosour C, Dragosavac D, Antunes N, et al. Effect of ultrafiltration on pulmonary function and interleukins in patients undergoing cardiopulmonary bypass. *J Cardiothorac Vasc Anesth* 2016; 30: 884–890.
28. Vonk AB, Muntajit W, Bhagirath P, et al. Residual blood processing by centrifugation, cell salvage or ultrafiltration in cardiac surgery: effects on clinical hemostatic and ex vivo rheological parameters. *Blood Coagul Fibrinolysis* 2012; 23: 622–628.
29. Harm SK, Waters JH, Lynn P, et al. Changes in mechanical fragility and free hemoglobin levels after processing salvaged cardiopulmonary bypass circuit blood with a modified ultrafiltration device. *J Extra Corpor Technol* 2012; 44: 21–25.
30. Yan S, Zhao Y, Lou S. Ultrafiltration and reinfusion of residual cardiopulmonary bypass pump blood: a prospective non-randomized controlled study. *Artif Organs* 2019; 43: 641–646.
31. Williams GD, Ramamoorthy C, Totzek FR, et al. Comparison of the effects of red cell separation and ultrafiltration on heparin concentration during pediatric cardiac surgery. *J Cardiothorac Vasc Anesth* 1997; 11: 840–844.
32. Abbas U, Loomba RS, Urbas C, et al. Effects of modified ultrafiltration on thromboelastographic profile after pediatric cardiac surgery. *J Extra Corpor Technol* 2021; 53: 50–56.
33. Colli A, Balduzzi S, Ruyra X. The Hemobag: the modern ultrafiltration system for patients undergoing cardiopulmonary bypass. *J Cardiothorac Surg* 2012; 7: 55.
34. Beckmann S, Lynn P, Miller S, et al. Evaluation of coagulation factors and platelet function from an off-line modified ultrafiltration technique for post-cardiopulmonary bypass circuit blood recovery. *Perfusion* 2012; 28: 214–222.
35. Stammers AH, Tesdahl EA, Mongero LB, et al. Does the type of cardioplegic technique influence hemodilution and transfusion requirements in adult patients undergoing cardiac surgery? *J Extra Corpor Technol* 2017; 49: 231–240.
36. Stammers AH, Tesdahl EA, Mongero LB, et al. Does the type of cardioplegia used during valve surgery influence operative nadir hematocrit and transfusion requirements? *Perfusion* 2018; 33: 638–648.
37. Stammers AH, Tesdahl EA, Mongero LB, et al. The effect of various blood management strategies on intraoperative red blood cell transfusion in first-time coronary artery bypass graft patients. *Perfusion* 2020; 35: 217–226.