Transfusion Use and Hemoglobin Levels by Blood Conservation Method After Cardiopulmonary Bypass

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Background. **Guidelines recommend modified ultrafiltration (MUF) and cell washing for blood conservation after cardiopulmonary bypass (CPB), although information on outcomes is lacking. This research compared online MUF (ultrafiltration of the patient's entire circulating volume) with off-line MUF (ultrafiltration of the residual CPB volume) and centrifugation (cell washing of the residual CPB volume).**

Methods. **This prospective cohort study enrolled 99 consecutive patients, grouped by method (group I, online MUF, n = 35; group II, off-line MUF, n = 30; group III, centrifugation, n = 34). Primary outcome was transfusion by 18 hours. Secondary outcomes were 18-hour hemoglobin levels, fluid balance (weight change), and biomarker levels indicating coagulation and organ function.**

Results. **By 18 hours, 22.9%, 6.7%, and 14.7% of group I, II, and III patients, respectively, had undergone transfusion ($P = .19$). Percentage weight gain differed by group (group I, 5.7%; group II, 1.3%; group III, 4.5%; $P < .0001$). Baseline to 18-hour hemoglobin change also differed by group, with the group I increase significantly exceeding that of group II ($P = .002$) but not differing from group III ($P = .36$). After adjustment for European System for Cardiac Operative Risk Evaluation II (EuroSCORE), weight gain, and transfusion, only the group II to III difference remained significant ($P = .002$).**

Conclusions. **Online MUF does not appear to offer a reduction in blood transfusion over other methods. Although patients undergoing online MUF had greater improvement in baseline to 18-hour hemoglobin compared with patients undergoing off-line MUF, this benefit appeared attributable to fluid shifting. Off-line MUF was associated with the least frequent transfusions. Although online MUF does not appear to reduce blood transfusion, larger prospective randomized controlled studies are required for confirmation.**

(Ann Thorac Surg 2020;110:1520-6)

Although cardiac surgery frequently involves blood transfusions, blood conservation techniques exist to reduce transfusion use. By applying online modified ultrafiltration (MUF), the patient remains connected to the circuit after cardiopulmonary bypass (CPB) while the entire blood volume circulates through a hemofilter, removing excess plasma water.[1] In off-line MUF, the patient is removed from the CPB circuit, and only the residual pump-volume is hemofiltered and reinfused.[1,2] When using a third method, our current practice, the residual circuit volume is salvaged using a centrifugation (CF) system, where red blood cells (RBCs) are separated from plasma, washed, and reinfused while other blood components are discarded.[1] The 2011 update to the Blood Conservation Guideline Task Force did not comment on variations of MUF.[3] The rationale for this study was to evaluate the potential clinical outcomes associated with these 3 blood conservation techniques, specifically in a prospective observational (nonrandomized) clinical study for postoperative transfusion (primary outcome), hemoglobin (Hgb) concentrations, fluid requirements, and other biochemical and clinical outcomes. We hypothesized fewer patients undergoing transfusion would lead to greater Hgb improvements and enhanced clinical and biochemical variables among online MUF-treated patients 18 hours postoperatively.

Accepted for publication Mar 11, 2020.

Presented at the American Society of Extracorporeal Technology conference, Nashville, TN, Mar 8-10, 2019.

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The Supplemental Tables can be viewed in the online version of this article [https://doi.org/10.1016/j.athoracsur.2020.03.029] on http://www.annalsthoracicsurgery.org.

Published by Elsevier Inc.

0003-4975/$36.00
https://doi.org/10.1016/j.athoracsur.2020.03.029

Abbreviations and Acronyms

ACT = activated clotting time
aPTT = activated partial thromboplastin time
ATS = autotransfusion system
CF = centrifugation
CPB = cardiopulmonary bypass
GGT = γ-glutamyl transferase
Hgb = hemoglobin
ICU = intensive care unit
IL-6 = interleukin-6
MUF = modified ultrafiltration
RBC = red blood cell

Patients and Methods

After approval by the University of Saskatchewan (Saskatoon, SK, Canada) ethics committee, the study recruited consecutive patients who gave written consent, who were 40 to 80 years of age , and who were scheduled for elective or urgent cardiac surgery (ie, primary or redo cases of either coronary artery bypass graft with and without valve procedures or valve procedures). Emergency cases or patients with kidney dysfunction, Hgb lower than 100 g/L, stroke, or coagulopathies were excluded. Approached as a feasibility study, we selected a convenience sample, with 30 patients minimum per group, between October 28, 2014 and July 28, 2016.

Patients underwent 1 of 3 treatment methods (group I, online MUF; group II, off-line MUF; or group III, CF) at surgeon preference. Although operating room and intensive care unit (ICU) personnel were blinded to assignment, the perfusionist and anesthesiologist were not, thus addressing group II's requirement for additional protamine. Anesthesia followed standard cardiac surgical protocol. Heparin dosing was determined by a hemostasis management system (HMS, Medtronic, Minneapolis, MN). CPB was initiated after attaining an activated clotting time (ACT) longer than 480 seconds.

A Sorin heart-lung machine (Sorin, Munich, Germany) was primed with 2 L of Plasma-Lyte A, 50 mEq of sodium bicarbonate, 100 mL of 25% albumin, 2.5 mL/kg of mannitol, and 10 KU of heparin. After cannulation, the prime was reduced with retrograde autologous priming,[4] thereby allowing replacement of circuit crystalloid with the patient's blood. Specifically, the arterial and venous lines were drained into the venous reservoir, and the crystalloid was pumped into a recirculation bag. ACTs and heparin concentrations were 480 seconds or longer and 300 U/kg, respectively. After decannulation, heparin was reversed by an HMS-determined protamine dose, and ACTs returned to baseline. Patients were transported to the ICU on calibrated weight-measuring beds.

Online Modified Ultrafiltration (Group I)

After CPB termination, online MUF was performed with the patient remaining cannulated and connected to the CPB circuit. Blood withdrawn from the arterial-line was pumped through a Sorin DHF-6 hemofilter (Sorin Group Italia-Livanova, Milan, Italy) for continuous excess crystalloid removal. The outlet-line of the hemofilter was connected to the venous-line, thus allowing blood to be continuously reinfused through the venous cannula. Pump flows ranged between 250 and 350 mL/min for approximately 10 minutes. Target patient Hgb ranged between 100 and 120 g/L.

Off-line MUF (Group II)

Residual CPB volume salvage used multiple-pass hemofiltration (Hemobag, Global Blood Resources LLC., Somers, CT), a Sorin Modified UHF Hemofilter, and a roller-head pump from the heart-lung machine. After CPB termination and aortic decannulation, the arterial line was connected to the Hemobag, and the residual CPB circuit was flushed into it in an antegrade manner. Pump flows of 250 to 300 mL/min circulated the volume through the recovery loop with continuous removal of excess crystalloid, which was discontinued when the desired pressure (350 mm Hg) and Hgb concentration (150 to 180 g/L) were achieved. Processed blood (similar to whole blood) containing RBCs, platelets, clotting factors, plasma proteins, and plasma was reinfused into the patient, followed by an additional 50 mg of protamine to reverse residual heparin. We have reported that hemofilters inadequately remove heparin.[1] Because protamine, with its brief 5-minute half-life, had been administered after decannulation, additional protamine was required when the heparin-containing hemofiltered blood was transfused approximately 10 minutes later.

Centrifugation (Group III)

The CF method (cell washing) used the Medtronic Autolog Autotransfusion System (ATS) (Medtronic Inc, Minneapolis, MN). After CPB termination and aortic decannulation, the sterile end of the vent line was connected to the arterial cannula's Luer port while the opposite end was connected to the cardiotomy reservoir of the ATS. The residual CPB circuit was flushed in antegrade method with crystalloid into the ATS reservoir. After CF, only packed RBCs remained, and they were saline washed, bagged, and reinfused into the patient whereas all other blood components (electrolytes, plasma proteins, platelets, clotting factors, plasma, and heparin) were discarded.

Blood Samples

Blood was drawn at baseline (after CPB but before intervention), on ICU arrival (~1.5 hours after intervention), and at both 8 and 18 hours after intervention. The 18-hour end point represents the typical time of patient transfer to the ward. Serum Hgb (index of oxygen transport), albumin (index of colloid osmotic pressure), activated partial thromboplastin time (aPTT) and platelet count (indices of clotting), creatinine (index of renal function), high-sensitivity C-reactive protein (hs-CRP) (index of inflammation[1]), γ-glutamyl transferase (GGT; biliary marker associated with cardiovascular disease mortality[5,6]), and lactate (predictor of complication

Table 1. Demographic and Clinical Patient Characteristics Before Intervention

Variable[a]	Group I Online MUF (n = 35)	Group II Off-line MUF (n = 30)	Group III Centrifugation (n = 34)	*P* Value
Time	October 2014–June 2016	November 2014–July 2016	October 2014–September 2015	…
Sex, n (%), male/female	22 (62.9)/13 (37.1)	21 (70.0)/9 (30.0)	21 (61.8)/13 (38.2)	.76
Age, y	68 (60, 75)	72 (59, 77)	70 (63, 74)	.59
Height, cm	165 (160, 172)	169 (164.9, 175)	169.3 (160, 174)	.39
Weight, kg	74.3 (66.9, 80.0)	77.8 (69.0, 82.6)	75.5 (68.4, 79.6)	.43
Body mass index, kg/m^2	26.8 (24.2, 28.9)	26.1 (24.4, 28.2)	26.0 (23.9, 29.9)	.80
EuroSCORE	2.7 (1.9, 4.4)	1.9 (1.3, 4.0)	1.9 (1.4, 2.7)	.02[b]
Procedure, n (%)				
CABG	21 (60.0)	24 (80.0)	25 (73.5)	.34
CABG with valve repair or replacement	7 (20.0)	2 (6.9)	3 (8.8)	….
Valve repair or replacement only	7 (20.0)	3 (10.3)[c]	6 (17.6)	…
Surgeon, n (%)				
A	3 (8.6)	1 (3.3)	21 (61.8)	<.001
B	3 (8.6)	2 (6.7)	9 (26.5)	…
C	29 (82.9)	27 (90.0)	4 (11.8)	…
Prime volume, mL	885 (810, 1068)	764 (680, 925)	790 (721, 940)	.02
Cross-clamp time, min	97 (77, 113)	86.5 (73, 105)	95 (85, 115)	.25
Cardiopulmonary bypass time, min	113 (98, 144)	110 (94, 120)	118.5 (103, 138)	.19
Ejection fraction, %	56 (46, 64)	57 (50, 64)	60 (50, 65)	.45
Creatinine, μmol/L	78 (70, 94)	69.5 (62, 79)	70.5 (62, 86)	.16
Creatinine clearance, mL/m^2	81.1 (69.1, 98.3)	89.1 (71.3, 108.1)	81 (72.5, 102)	.69
Hemoglobin, g/L	93 (86, 99)	95.5 (89, 100)	94 (90, 102)	.58
Platelets, × 10^9	137 (114, 164)	140 (127, 189)	144 (130, 186)	.69

[a]Continuous variables expressed as median (interquartile range); pairwise comparisons; [b]I vs II, *P* = .021; II vs III, *P* = .97; I vs III, *P* = .015; [c]Includes 1 redo procedure.

CABG, coronary artery bypass graft; EuroSCORE, European System for Cardiac Operative Risk Evaluation; MUF, modified ultrafiltration.

post-CPB[7]) levels were measured by the hospital laboratory. Interleukin-6 (IL-6; inflammatory injury marker[8]) was measured by enzyme-linked immunosorbent assay (R & D Systems, Oakville, Canada).

Statistical Analysis

Because Shapiro-Wilk testing assessed many continuous variables as non-Gaussian, and medians were evaluated, with overall group comparisons made with Kruskal-Wallis testing; where significant, pairwise Wilcoxon rank-sum testing followed. Categorical comparisons used the χ^2 test, or the Fisher exact test if more than 20% of cells had expected values lower than 5. Alpha was set at 0.05, with Bonferroni correction for pairwise comparisons (0.05/3 = 0.017). Because serum Hgb baseline to 18-hour differences did not depart from normal values when tested, linear regression modeling was used to examine the relationship between group and Hgb change, thus adjusting for potentially influential group differences. SAS software version 9.4 (SAS Institute Inc, Cary, NC) was used for analysis.

Results

Patient demographic and clinical characteristics are shown in Table 1. Patients were similar among the groups other than group I's higher European System for Cardiac Operative Risk Evaluation II (EuroSCORE II), higher prime volumes, and surgeon differences. One surgeon performed the majority of group I and group II procedures, whereas another primarily undertook procedures in group III. Group procedure types were similar.

A total of 23% percent of group I patients, 15% of group III, and 7% of group II (*P* = .19) (Table 2) had RBC transfusion in the ICU (Supplemental Table 1). Median serum Hgb levels are shown in Figure 1; baseline values were similar across groups (*P* = .58). On ICU arrival, group I's value was highest, but by 18 hours, group III's value exceeded the others (Table 3).

Postoperative fluid balance values were not significantly different among groups (Table 4). Median postoperative weight changes, both absolute and relative (ie, percentage), did differ, with groups I and III increasing significantly more than group II. Median group chest tube drainage, ventilation time, and length of ICU stay showed no significant differences (Table 4).

Biochemical parameters were compared among groups at baseline (Supplemental Table 2), on ICU arrival, at 8 hours, and at 18 hours (Table 3). At baseline, group II had lower levels of GGT, but differences were not clinically significant. Group I had higher median IL-6 levels at baseline, but after the intervention, these levels differed only at 18 hours, higher for group III compared with groups I and II. On ICU arrival, group II had a higher

Table 2. Group Blood Product Administration

Variable: Blood Product Transfused	Group I Online MUF (n = 35)	Group II Off-line MUF (n = 30)	Group III Centrifugation (n = 34)	*P* Value
RBCs				
No	27 (77.1)	28 (93.3)	29 (85.3)	.19
Yes	8 (22.9)	2 (6.7)	5 (14.7)	…
Platelets				
No	29 (82.9)	27 (90.0)	29 (85.3)	.72
Yes	6 (17.1)	3 (10.0)	5 (14.7)	…
Frozen plasma				
No	27 (77.1)	28 (93.3)	32 (94.1)	.07
Yes	8 (22.9)	2 (6.7)	2 (5.9)	…

MUF, modified ultrafiltration; RBCs,= red blood cells.

median albumin level and a lower median lactate level than group III, but these differences did not persist. Increased aPTT, present on arrival for group I vs group II, remained elevated at 8 hours.

Regarding linear regression (Supplemental Table 3), statistically significant variation in baseline to 18-hour Hgb change was seen between groups I and II ($P = .002$) and between groups II and III ($P < .001$) in the univariate model (model 1). Compared with the 11.4% increase in Hgb values in group I patients (intercept), the Hgb increase in group II patients was 9.5 percentage points less ($P = .002$), at 1.9%. The 14.1% increase in group III patients was not significantly different vs group I, at only 2.7 percentage points higher ($P = .36$). However, in the model adjusting for percentage of weight change, transfusion, and EuroSCORE, the difference between groups I and II became nonsignificant (model 5). Evaluating covariates separately (models 2 to 4), this loss of significance occurred with the addition of percentage of weight change. However, the difference between groups II and III remained when controlling for the foregoing factors ($P = .002$; model 6). Prime volume differences did not result in different baseline Hgb levels before the intervention.

Comment

Outcomes of blood conservation techniques after cardiac surgery vary.[9,10] Ultrafiltration preserves plasma protein and cellular components despite prolonged operating-room time (online MUF) and inadequate heparin removal (off-line MUF). CF offers quick recovery of RBCs from the surgical field and processing of the residual CPB volume, thereby increasing hematocrit values, although major components of blood are lost.[11] Hemoconcentration by online MUF initially rendered the highest ICU arrival Hgb (Figure 1) because the entire patient circulating volume was concentrated. Correspondingly, patients who only had the residual pump volume hemofiltered and reinfused (off-line MUF) achieved the lowest median value. Patients receiving volume from the centrifuged technique, concentrated RBCs only, were intermediate. Supplemental Table 4 provides a summary of technique differences.

At our center, Hgb concentrations lower than 70 g/L, whether on CPB or in the ICU, trigger RBC transfusion.

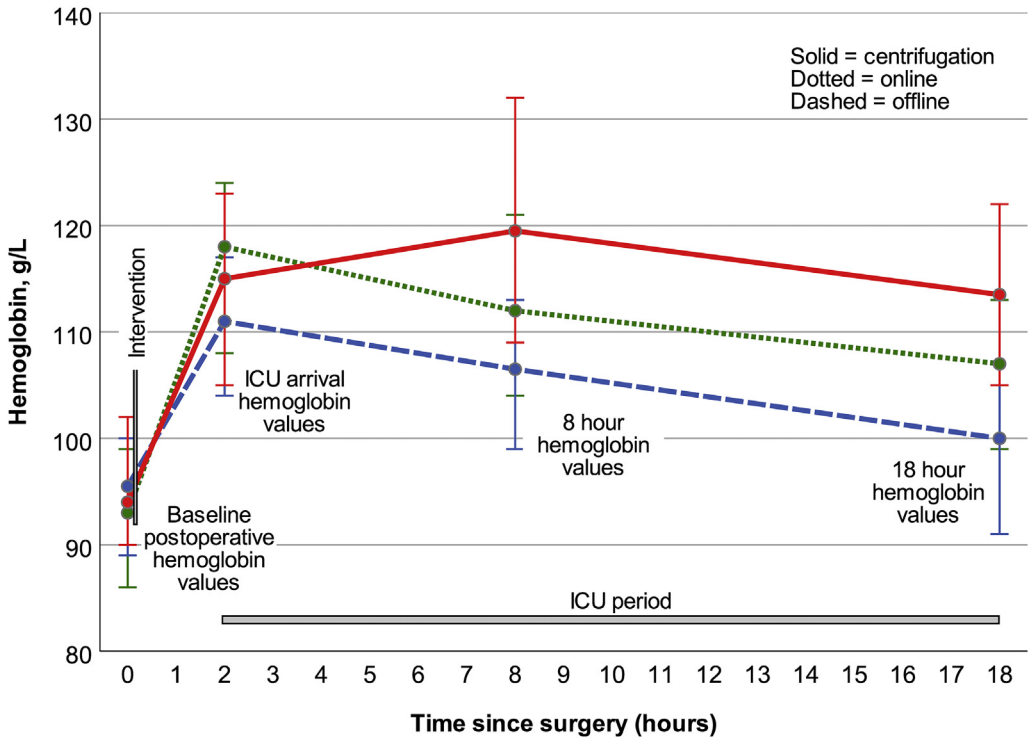

Figure 1. Median group hemoglobin concentrations with interquartile ranges at baseline after termination of cardiopulmonary bypass, on intensive care unit (ICU) arrival, and at 8 and 18 hours postoperatively. (Solid line, centrifugation; dotted line, online; dashed line, off-line.)

Table 3. Group Biochemical Outcome Parameters, Medians (Interquartile Range)

Variable	Time	Group I Online MUF (n = 35)	Group II Off-line MUF (n = 30)	Group III CF (n = 34)	*P* Value[a]			
					Overall	I vs II	II vs III	I vs III
Hemoglobin, g/L	Arrival	118 (108, 124)	111 (104, 117)	115 (105, 123)	.02	.007	.14	.19
	8 h	112 (104, 121)	106.5 (99, 113)	119.5 (109, 132)	.003	.05	.001	.05
	18 h	107 (99, 113)	100 (91, 105)	113.5 (105, 122)	.001	.011	<.001	.024
Albumin, mmol/L	Arrival	30 (28, 31)	32 (29, 33)	29.5 (27, 31)	.019	.03	.008	.52
	8 h	30 (28, 32)	31 (28, 33)	31 (30, 32)	.22			
	18 h	30 (26, 31)	29 (27, 31)	29 (28, 30)	.97			
Creatinine clearance, mL/min	Arrival	84.9 (69.3, 101.3)	86.9 (71.8, 109.4)	80.9 (73.3, 93.7)	.72	…	…	…
	8 h	77.8 (62.7, 94.7)	74 (64.5, 105.3)	81.8 (67.3, 95.2)	.78			
	18 h	75.2 (63, 90.8)	77.5(64.6, 105.3)	82 (64, 100.9)	.67			
γ-Glutamyl transferase, U/L	Arrival	17.5 (11, 42)	13 (9, 26)	19 (10, 31)	.07			
	8 h	20 (13, 47)	15 (11, 26)	24 (13, 31)	.17			
	18 h	19 (14, 41)	14.5 (10, 25)	12 (12, 30)	.15			
Lactate, mmol/L	Arrival	1.6 (1.2, 2.5)	1.6 (1.2, 1.9)	2.3 (1.4, 3.6)	.02	.45	.007	.04
	8 h	1.5 (1.2, 2.4)	1.6 (1.1, 1.8)	1.7 (1.4, 2.4)	.20			
	18 h	1.9 (1.2, 2.3)	1.8 (1.1, 2.1)	1.7 (1.5, 2.2)	.69			
Creatinine, μmol/L	Arrival	72 (61, 82)	67.5 (62, 81)	72 (61, 82)	.55	…	…	…
	8 h	75 (64, 93)	74.5 (65, 87)	75 (64, 93)	.52			
	18 h	77 (61, 96)	73 (63, 83)	77 (61, 96)	.34			
aPTT, s	Arrival	33 (32, 35)	31 (30, 33)	31 (29, 33)	.01	0.017	.78	.009
	8 h	31 (29, 35)	29 (27, 31)	30 (29, 35)	.01	0.04	.07	.26
	18 h	NA	NA	NA				
High sensitivity-C-reactive protein, mg/L	Arrival	1.5 (0.9, 3.4)	1 (0.5, 3.1)	1.1 (0.3, 3.3)	.37	…	…	…
	8 h	12 (8.4, 17)	8.1 (6.1, 19.3)	9.7 (6.4, 12.6)	.17			
	18 h	88.5 (65.7, 114.1)	92.2 (75.6, 111.4)	91.3 (58.3, 105.5)	.94			
Interleukin-6, pg/mL	Arrival	35.2 (14.2, 56)	44.2 (37.5, 59.5)	43.1 (30.4, 156.4)	.06	…	…	…
	8 h	65.8 (42.2, 104)	68.5 (55.5, 110.6)	64.6 (49.9, 116)	.73			
	18 h	35.8 (16.1, 59.6)	24.2 (15.8, 36.4)	58.5 (49.6, 87.1)	<.001	.15	<.001	<.001

[a]Pairwise comparisons only when overall test significant.

aPTT, activated partial thromboplastin time; CF, centrifugation; MUF, modified ultrafiltration; 8 h, 8 hours postoperatively; 18 h, 18 hours postoperatively.

Although more patients in the online MUF group underwent transfusion, their mean increase in Hgb level from ICU arrival to 18 hours was only greater than that of patients in the off-line MUF group, the group with the fewest transfusions. Although not statistically significant, patients receiving CF blood were more likely to undergo transfusion than off-line MUF group patients, an observation consistent with observations by Malhotra and colleagues,[10] who reported a lower number of transfusions in patients undergoing ultrafiltration compared with CF in off-pump coronary artery bypass grafts. Notably, transfusion does not drive the associations between group and Hgb change; adding transfusion as a covariate when group indicator was used as the lone predictor did not substantially change its estimates. The off-line MUF group had the lowest Hgb at 18 hours (100 g/L) compared with the other 2 groups (107 and 114 g/L), but generally fewer off-line MUF group patients received RBCs (6.7% vs 14.7% and 22.9%), platelets (10.0% vs 14.7% and 17.1%), and fresh frozen plasma (FFP) (6.7% vs. 22.9% and 5.9%) than the other 2 groups.

Perioperative net fluid balance can be assessed by measuring fluid input and losses, although some losses are difficult to measure.[12] Weighing patients is a method of measuring net fluid retention,[13] and 18-hour weight changes suggest that group I retained considerably more fluid. Although ICU staff were blinded to assignment, many online MUF group patients were reported to be dehydrated and hypotensive, requiring fluid infusion. This observation agrees with a report of ultrafiltration chiefly affecting the vascular compartment and subsequent hypotension.[14] Hypovolemia may occur because online MUF attempts to return patients to normal hematocrit values by water removal, perhaps excessively contracting the vascular volume to a "dry" state. In a proportion of individuals, compensatory fluid administration is suspected to have resulted in RBC dilution, which triggered transfusion.

Online MUF may result in dehydration and fluid shifts. When controlling for weight change (fluid administration) in the regression model, the estimated baseline to 18-hour Hgb change decreased, rather than increased, as

Table 4. Group Clinical Outcome Parameters, Medians (Interquartile Range)

Variable	Group I Online MUF (n = 35)	Group II Off-line MUF (n = 30)	Group III Centrifugation (n = 34)	*P* Value[a]			
				Overall	I vs II	II vs III	I vs III
Ultrafiltrate volume, mL	1075 (1000, 1300)	750 (550, 1000)	NA	<.001	…	…	…
ICU balance, mL	1465 (500, 3481)	997 (344, 1499)	875 (182, 2244)	.15	…	…	…
Weight change, kg	4.0 (3.4, 4.9)	1.0 (0.6, 1.8)	3.4 (2.9, 4.2)	<.001	<.001	<.001	.021
Weight change, %	5.4 (4.2, 6.4)	1.3 (0.8, 2.1)	4.8 (4.0, 5.6)	<.001	<.001	<.001	.06
Chest tube loss, mL	790 (630, 920)	735 (590, 930)	830 (600, 960)	.70	…	…	…
Ventilation time, h	6 (4.3, 10)	6.9 (5, 8.3)	7 (6, 10)	.41	…	…	…
ICU length of stay, h	23.8 (22, 28.3)	23.5 (21.5, 25.8)	23.5 (21.5, 26.0)	.81	…	…	…

[a]Pairwise comparisons only performed when overall test significant.

ICU, intensive care unit; IQR, interquartile range; MUF, modified ultrafiltration; NA, not applicable because filtration is not part of the centrifugation method; comparison by Wilcoxon rank-sum test.

would be expected without fluid administration. Conversely, positive fluid balances suggest an ongoing vascular fluid demand, secondary to fluid shifting into tissues. Thus, suspected fluid extravasation appears responsible for the greater Hgb improvement seen in patients undergoing online MUF vs off-line MUF because this difference became nonsignificant when weight change was controlled.

Supporting the foregoing, fluid shifting, a recognized perioperative phenomenon, peaks 5 hours postoperatively and persists up to 72 hours.[12] The endothelial glycocalyx, an integral circulation compartment, regulates permeability, maintains equilibrium, prevents edema,[15,16] and sequesters plasma.[17,18] Glycocalyx damage, a possible result of prolonged exposure to artificial CPB surfaces or ischemia/reperfusion-related injury, could influence postoperative balances.[17,18]

Serum albumin maintains 80% of the colloid osmotic pressure,[19,20] and it appears integral to glycocalyx functioning.[18] On ICU arrival, the median level was significantly higher in group II vs III, a finding supporting previous reports demonstrating higher protein levels after off-line MUF vs cell-saving device.[9,10,21] Considering that group I's median albumin concentration at arrival was, in a presumed state of contracted fluid volume, similar to that of group III, albumin levels may have been reduced after online MUF, thereby contributing to fluid shifting. Group I's higher proportion of fresh frozen plasma recipients could also be attributed to glycocalyx dysfunction.[22]

Regarding organ dysfunction, there were no significant group differences in median creatinine clearance values at any time point to suggest group-specific acute kidney injury. However, serum lactate was higher in group III vs group II and group I on ICU arrival, similar to a report of higher lactate levels in control subjects compared with online MUF group patients during the same time period.[23] However, at 18 hours, no significant differences remained, contrasting other work identifying persistent 24-hour elevations.[24] Although some baseline differences in GGT and IL-6 were observed among groups, these were not clinically concerning. Only IL-6 levels were notably different in our sample by 18 hours, with levels in CF patients having significantly higher concentrations compared with both MUF methods. This finding contrasts with those of other studies detecting early elevations with both MUF[25] and CF.[24,26] Although aPTT values showed significant differences, these also lacked clinical impact because chest tube drainage and coagulation products transfused were not remarkably different. This was interesting given plasma protein and clotting factor losses after CF.

Among this study's limitations is the lack of randomization, which would have provided additional residual confounding control; although initially proposed, randomization was unachievable as a result of surgeons' intervention preferences. Because "Surgeon C" performed nearly all the group I and II procedures, these group comparisons have minimal risk of confounding by surgeon. However, because "Surgeon A" performed many group III cases, this strong association between surgeon and group prevents separation of intervention and physician influences when comparing with group III. We are unaware of influential surgeon differences; all are well experienced, and the case mix within the groups does not suggest different practice profiles. Additionally, given that the sample was small and limited to nonemergency cases, findings may not apply to cases of greater acuity. Patients requiring transfusion were relatively few, thus prohibiting more extensive modeling of this outcome or the effect of method on number of RBC units received.

Overall, our study failed to support the expected benefit of transfusion reduction for online MUF. Its increases in Hgb concentration after surgery to 18 hours were not found to exceed that of CF, and improvement when compared with off-line MUF appears secondary to fluid shifts. Although Hgb improvement may be more favorable with CF than with off-line MUF, the off-line MUF group had the lowest blood transfusion proportion, least fluid administration, and lowest weight gain. Overall, the many measured laboratory values showed relatively few statistical or clinically concerning differences across the techniques. This finding suggests that

costs in time or money can also inform method choice. On the basis of our findings and because of its limitations, our study provides justification for and indicates the need for larger prospective randomized controlled studies comparing these 3 blood conservation methods.

Funding was received from the Department of Surgery, College of Medicine, University of Saskatchewan. Hemobag was provided by Global Blood Resources. The authors wish to thank Drs Thomson, Dalshaug, and Mycyk, and Sharon Wandzura, for their assistance, and Jennifer Bezaire, Marnie Olson, Victor Uppal, Mark Rosin and Jo-Anne Marcoux for their support with this study.

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