# Intraoperative Blood Collection Without Fluid Replacement for Cardiac Surgery – A Retrospective Analysis

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# ABSTRACT

Background: Transfusion rates in cardiac surgery are high.

Aim: To determine if intraoperative autologous blood removal without volume replacement is associated with fewer homologous blood transfusions without increasing acute kidney injury.

Setting and Design: Retrospective, comparative study.

**Materials and Methods:** Adult patients undergoing cardiac surgery, excluding those who underwent ventricular assist device surgery, heart transplants, or cardiac surgery without cardiopulmonary bypass were excluded, who had 1–3 units of intraoperative autologous blood removal were compared to patients without blood removal for determination of volume replacement, vasopressor support, acute kidney injury, and transfusions.

**Results:** Autologous blood removal was associated with fewer patients receiving homologous transfusions: intraoperative red cell transfusions fell from 75% (Control) to 48% (1 unit removed), 40% (2 units), and 30% (3 units), P < 0.001. Total intraoperative and postoperative homologous RBC units transfused were lower in the blood removal groups: median (interquartile range) 3 (1, 6) in Control patients and 0 (0, 2), 0 (0, 2) and 0 (0, 1) in the 1, 2, and 3 units removed groups, P < 0.001. Similarly, plasma, platelet, and cryoprecipitate transfusions decreased. After adjustment for confounders, increased amounts of autologous blood removal were associated with increased intravenous fluids, only when 2 units were removed, and trivially increased vasopressor use. However, it was not associated with acidosis or acute kidney injury.

**Conclusions:** Intraoperative autologous blood removal without volume replacement of 1–3 units for later autologous transfusion is associated with decreased homologous transfusions without acidosis or acute kidney injury.

Keywords: Acute kidney injury, autologous blood removal, cardiac surgery, transfusion

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# INTRODUCTION

Blood transfusion with cardiac surgery accounts for 20% of transfusions in the United States.<sup>[1]</sup> While restrictive transfusion thresholds have been shown to produce equivalent outcomes as liberal thresholds, the overall transfusion rate remains high.<sup>[2]</sup> Transfusions are not benign. They are associated with increased morbidity and

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mortality.<sup>[3,4]</sup> The hemodilution resulting from crystalloid priming of the cardiopulmonary bypass (CPB) circuit represents a major risk factor for blood transfusions. While several techniques are available to limit hemodilution, such as retrograde autologous priming and high-volume ultrafiltration, these may be insufficient to prevent transfusions. Additionally, the abnormal conditions

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of blood subjected to the various components of the CPB circuit can lead to platelet dysfunction and destruction.<sup>[5]</sup> The resulting thrombocytopenia or functional thrombocytopenia contributes to postoperative coagulopathy and hemorrhage, with frequent need for erythrocyte (RBC) and platelet transfusions. To minimize the need for transfusions and their associated risk of infection, acute lung injury, and immunomodulation, some physicians use intraoperative blood collection.<sup>[6-13]</sup> After induction of general anesthesia, blood is sterilely removed from the patient and stored in bags containing CPDA as a preservative and anticoagulant.<sup>[8,9,12]</sup>

When RBC are removed for intraoperative blood collection, platelets and clotting factors are also captured for reinfusion after discontinuation of CPB. Putatively, this technique conserves blood by decreasing postoperative coagulopathy and the need for transfusions by providing a sufficient quantity of fresh platelets and clotting factors to replace the ones activated or consumed during CPB.<sup>[14]</sup> However, platelet function was adversely affected by storage in CPDA<sup>[15]</sup> and did not improve thromboelastography values after CPB.<sup>[16]</sup> Studies of autologous blood removal primarily used crystalloid or colloids to replace the blood volume [acute normovolemic hemodilution (ANH)].<sup>[9,15,17]</sup> This can lead to hemodilution of platelets, clotting factors, and RBC and increase the risk of homologous RBC transfusion to prevent or treat low oxygen delivery or hemodynamic instability. Instead of crystalloid or colloid infusions to maintain intravascular volume and hemodynamics, hemodynamics can also be maintained with vasopressors. The use of vasopressors and minimizing volume administration [autologous blood removal without fluid replacement (AWOF)] is designed to limit hemodilution and the need to transfuse homologous RBC.

We hypothesized that AWOF would be associated with decreased blood transfusion requirements in a dose-dependent manner. We further hypothesized, as secondary outcomes, that AWOF would be associated with increased vasopressor requirements, no differences in metabolic (acid–base) parameters, no difference in rate of acute kidney injury (AKI), and higher hematocrit and platelet levels on arrival in the intensive care unit.

## **METHODS**

## Ethics

This study was approved by the institutional review board, which waived informed consent as it was a retrospective analysis and it was conducted in accordance with the ethical standards of the Helsinki Declaration of 1975 as revised in 2000. STROBE guidelines were used. All adult patients (age  $\geq$ 18 years) undergoing cardiac surgery between Jan 31, 2007 and Nov 6, 2013 were included in the study. Patients undergoing ventricular assist device surgery, heart transplants, or cardiac surgery without cardiopulmonary bypass were excluded.

# Patient management

Fluids (including infusions and cardioplegia, but excluding piggyback and push medicines), blood products, and vasopressors administered by the anesthesiologist or the perfusionist are recorded in the shared electronic anesthetic record (Centricity, GE Healthcare, Chicago, IL) and were abstracted from it. Laboratory values were extracted from the institutional data warehouse. AKI was defined using Kidney Disease: Improving Global Outcomes (KDIGO) stages: creatinine increase >0.3 mg/dL over 48 hours or to 150% of baseline by day 7 was stage 1; creatinine to  $\geq 200\%$  of baseline was stage 2, and  $\geq 300\%$  of baseline was stage 3. Urine output was not included in our outcome definition. Hematocrit levels were determined preoperatively, postinduction before blood was removed, postblood removal but prebypass, and 30 minutes after arrival in the ICU. The lowest intraoperative arterial pH and bicarbonate and highest lactic acid level were used as measures of worst metabolic derangement.

Patients routinely received general anesthesia with midazolam, fentanyl, propofol, and a neuromuscular blocker for induction. Etomidate was rarely used. In addition to routine EKG and pulse oximetry, patients had an arterial line and either a central venous catheter or pulmonary artery catheter. Mechanical ventilation with  $V_{T} = 6-8$  mL/kg of predicted body weight, with rate adjusted to achieve normocarbia was used. PreCBP, intravenous fluids, usually lactated ringer's solution, were minimized. Hetastarch was not used. Vasopressors were used as necessary to maintain mean arterial pressure >65 mmHg. Bolus ephedrine and phenylephrine and phenylephrine and norepinephrine infusions were used to support hemodynamics. As needed, vasopressin or epinephrine was used. After establishment of central venous access, an antifibrinolytic infusion was started and continued until shortly before leaving the operating room. Initially, aprotinin (2,000,000 KIU load, followed by infusion at 500,000 KIU/hour for the duration of the operation and a pump prime of 2,000,000 KIU) was used. After its removal from the market, we used aminocaproic acid (70 mg/kg load followed by infusion at 30 mg/kg/hr for the duration of the operation). Tranexamic acid was used when aminocaproic acid was in shortage (8 mg/kg load followed by infusion at 4 mg/kg/hr for the duration of the operation. If creatinine was 1.6-3.3 mg/dL, the tranexamic acid infusion was 3 mg/kg/hour. If creatinine was 3.4-6.6 mg/dL, the infusion was 2 mg/kg/hr. For creatinine >6.6. mg/dL or receipt of dialysis, the infusion was 1 mg/kg/hr. Additionally, 0.6 mg/kg load was added to the bypass circuit.) The decision for removal and amount of autologous blood removal was decided jointly by the surgeon and anesthesiologist. After preparation with chlorhexidine or povidone-iodine, autologous blood was aseptically removed via the central venous access and stored in bags prefilled with CPDA anticoagulant. Bags were not routinely weighed but filled based on visual inspection. Blood was stored at room temperature and gently agitated before being transfused. Prior to cardiopulmonary bypass, heparin 300 U/kg was administered intravenously. The CPB circuit was primed with 900 - 1100 mL of fluid, usually PlasmaLyte. If autologous priming was not used, an additional 300 - 500 mL of fluid was added to the bypass circuit. These volumes were recorded on the anesthetic record and included in the fluid analyses. Mild (32-35°C) or moderate (28-31°C) hypothermia was employed on bypass, with sweeps adjusted to maintain  $PaCO_2 = 40 \text{ mmHg}$ .<sup>[18]</sup> Deep ( $\leq 25^{\circ}$ C) hypothermia was used with circulatory arrest.<sup>[18]</sup> Additional heparin doses were given to keep the activated clotting time >400 sec. After separation from CPB, heparin was reversed with protamine (1-1.3 mg per 100 units of initial heparin dose) and confirmed by ACT returning to baseline values. Additional doses of protamine could be given if the ACT was elevated. Heparin concentration assays were not used. After reversal of heparin, the autologous blood was transfused. Physical measures of thrombosis, such as thromboelastography, were not employed. RBC transfusions were based on hematocrit levels (over the study period, the transfusion trigger for RBC decreased from 22-24% to ~18%) and clinical judgment, which included hemodynamics. Plasma, platelet, and cryoprecipitate transfusions were based on clinical judgment, inspection of the surgical field, and, when available, laboratory tests.

### Power analysis

Based on current practice, we assumed that 20% of patients have no autologous blood removed and that intraoperative transfusion rate is 20%, then to find a 3% change, an amount for which we would consider changing our practice, in the transfusion rate to 17 or 23% in patients who have any autologous blood removed, with alpha = 0.05 and power = 0.8, would require 4000 subjects.

## Statistical analysis

Baseline characteristics were described with means (standard deviations), medians (interquartile range),

frequency, and percentages. Differences in categories were tested using one-way ANOVA, the Kruskal-Wallis test, or the Chi-square test. To determine the independent associations of autologous blood removal with outcomes, we used Akaike Information Criteria based linear and logistic regressions. We further analyzed the data using propensity matching. Here, nonparsimonious binary logistic regression using sex, age, ASA class, emergency status, surgery type, year of surgery, type of antifibrinolytic used, height, weight, body mass index, body surface area, platelet count, INR, creatinine, and postinduction hematocrit value was used to calculate a propensity to be in the AWOF group. AWOF patients were matched to Control patients by similar propensity scores using a nearest neighbor greedy algorithm. The match was considered successful if all variables had standardized differences <10%. All analyses were performed with R version 2.14.2 (R Foundation for Computing, Vienna, Austria). Linear regression results are presented as estimate B (95% confidence interval) and logistic regressions as adjusted odds ratio (aOR) (95% confidence interval). As the dose-response (outcome associated with the number of autologous blood units removed) might be nonlinear or have a threshold, we analyzed number of autologous units as a categorical variable in all regressions.

# Sensitivity analysis

The main analyses were done adjusting for albumin volume in a 3:1 ratio for 5% and 15:1 ratio for 25% as is traditionally considered.<sup>[19]</sup> As more recent research has suggested that equal volumes of albumin and crystalloid produce equal expansions of blood volume,<sup>[20]</sup> we did sensitivity analyses of all regressions using unadjusted volumes.

## RESULTS

We studied 2809 patients,  $61 \pm 15$  years old, 1874 (67%) male, with body mass index 29.5  $\pm$  6.3 kg/m<sup>2</sup>. The preoperative hematocrit was 39.0  $\pm$  5.4%. Five hundred ninety-six patients (21%) had no blood removed (Control group), whereas 482 (17%), 1257 (45%), and 474 (17%) AWOF patients had 1, 2, or 3 units of blood removed, respectively. AWOF patients had higher preoperative hematocrits, but lower creatinine levels and platelet counts [Table 1]. After anesthesia induction and before blood removal, AWOF patients had higher hematocrits than the Control group, but the postinduction hematocrit did not differ within the AWOF group by number of units removed [Table 1].

# Processes of care

Intravenous fluid administration was less in AWOF group with one unit removed compared to Control

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Table 1: Baseline and operative characteristics. Intravenous fluids adjusted and CPB volume adjusted has the administered volume
adjusted for the volume of albumin given (3:1 for 5% and 15:1 for 25% albumin)

Female	n	its <i>n</i> =596	1 un	·+ 100					
emale				it <i>n</i> =482	2 uni	ts <i>n</i> =1257	3 uni	ts <i>n=</i> 474	Р
emale		%	n	%	n	%	n	%	
	231	39	204	42	420 <sup>a, B</sup>	33	80 <sup>A, B, C</sup>	17	< 0.001
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Р
Age (year)	60	16	64 <sup>A</sup>	15	61 <sup>B</sup>	15	59 <sup>B, C</sup>	14	0.101
Height (cm)	171	11	169ª	11	172 <sup>A, B</sup>	10	176 <sup>A, B, C</sup>	10	<.001
Weight (kg)	84	21	82	19	88 <sup>A, B</sup>	20	96 <sup>A, B, C</sup>	21	<.001
Preoperative hematocrit (%)	35.6	6.6	38.2	5.0	40 <sup>A, B</sup>	4	41.1 <sup>A, B, C</sup>	4.1	<.001
Preoperative creatinine (mg/dL)	1.4	1.1	1.2ª	1.0	1.1 <sup>A, B</sup>	0.6	1.0 <sup>A, B</sup>	0.4	<.001
Preoperative platelets $(1000/\mu L)$	223	79	224	68	214 <sup>a, B</sup>	64	204 <sup>A, B, C</sup>	59	<.001
Operative Characteristics									
Type of surgery									
CABG	153	26	138	29	172 <sup>a, b</sup>	14	14 <sup>a, b, c</sup>	3	< 0.001
Valve	145	24	132	27	385ª	31	94 <sup>b, c</sup>	20	< 0.001
Aortic	80	13	55	11	273 <sup>a, b</sup>	22	269 <sup>a, b, c</sup>	57	< 0.001
Other	72	12	57	12	160	13	11 <sup>a, b, c</sup>	2	< 0.001
Combined	146	24	100	21	267	21	86	18	0.088
Use of hypothermic circulatory arrest		5	30	6	139 <sup>a, b</sup>	11	167 <sup>a, b, c</sup>	35	< 0.001
Antifibrinolytic used		Ũ	00	Ũ	107		107	00	-0.001
Aminocaproic acid	470	79	407ª	84	993 <sup>⊾</sup>	79	394	83	0.021
Tranexamic acid	36	6	64ª	13	158ª	13	75ª	16	< 0.001
Aprotinin	88	15	9ª	2	104 <sup>a, b</sup>	8	2 <sup>a, c</sup>	0.4	< 0.001
Cell saver used	115	19	ý2	19	219	17	26	5	< 0.001
Antifibrinolytic doses	110	17	12	17	217	17	20	0	\$0.001
Aminocaproic acid (g)	18	10	17ª	8	19 <sup>в</sup>	10	23 <sup>A, B, C</sup>	10	< 0.001
Tranexamic acid (g)	2.4	2.4	2.0	1.4	2.1	1.2	3.2 <sup>B, C</sup>	1.1	< 0.001
Aprotinin (10,000KIU)	450	127	486	220	494	141	678	78	0.029
Postinduction hematocrit (%)	30.8	5.9	400 32.5 <sup>∧</sup>	5.3	33.8 <sup>A</sup>	5.5	35.14	5.5	<.001
Nadir hematocrit (%)	22.4	4.2	22.0	4.2	23.0 <sup>a, b</sup>	4.1	22.8 <sup>B</sup>	3.9	< 0.001
Cardiopulmonary bypass time (min)	141	72	134 <sup>A</sup>	62	152 <sup>A, b</sup>	72	195 <sup>a, b, c</sup>	68	< 0.001
Circulatory arrest time* (min)	33	14	33	15	33	14	30 <sup>c</sup>	10	0.212
()	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Р
Case Duration (min)	438	(365, 557)	423ª	(360, 506)	442 <sup>a, b</sup>	(363, 556)	524 <sup>a, b, c</sup>	(450, 617)	< 0.001
Cell saver volume (mL)	400 0	(0, 0)		(0, 0)	0 <sup>a, b</sup>	(0, 0)	0 <sup>a, b, c</sup>	(0, 0)	< 0.001
Cell saver volume* (mL)	500	(350, 750)	256ª	(244, 488)	265 <sup>a, b</sup>	(250, 464)	354 <sup>a, b, c</sup>	(0, 0)	<0.001
ntravenous fluids (mL)	1000	(1000, 1500)	1000 <sup>A</sup>	(900, 1400)	1000 <sup>B</sup>	(900, 1600)	1212 <sup>a, B, C</sup>	(1000, 1750)	0.011
ntravenous fluids adjusted (mL)	1000	(1000, 1300)	1000	(900, 1400)	1100 <sup>B</sup>	(1000, 2000)	1500 <sup>A, B, C</sup>	(1000, 1730)	<.001
CPB volume (mL)	1600	(1000, 2000)	1600	(900, 1550)	1950 <sup>b</sup>	(1000, 2000) (1000, 3300)	3000 <sup>A, B, C</sup>	(1000, 2244)	<.001
CPB volume adjusted (mL)	1775	(900, 3002) (900, 3500)	1600	(1000, 3100)	2000 <sup>B</sup>	(1000, 3500)	3000 <sup>-4, B, C</sup>	(1700, 5050)	<.001

A<0.01, a<0.05 compared to Control Group, B<0.01, b<0.05 compared to autologous blood removal without fluid replacement group with 1 unit removed, C<.01, c<.05 compared to autologous blood removal without fluid replacement group with 2 units removed. CPB – cardiopulmonary bypass. SD – standard deviation. IQR – interquartile range \*only for patients who received circulatory arrest or cell saver, otherwise for all patients

patients. Only when three units were removed, was intravenous fluid administration greater [Table 1]. The number of boluses of vasopressor doses was statistically, but not clinically, significantly higher in the AWOF groups (median 9 interquartile range (4, 14) for control group, 10.5 (5,17), 10 (5,16), and 13 (8,19) for AWOF = 1, 2, and 3, respectively, P < 0.001). Total phenylephrine dose was greater, but epinephrine and norepinephrine doses were less in the AWOF groups [Table 2]. While there were slight differences in nadir intraoperative pH and bicarbonate among the four groups, overall, there was no trend between pH, bicarbonate, and groups (P = .744 and. 128, respectively). Similarly, while lactic acid levels were lower in AWOF patients with one (2.6  $\pm$  1.4 mmol/L) and two (3.0  $\pm$  1.8 mmol/L) units removed compared to Control ( $3.6 \pm 2.6 \text{ mmol/L}$ ), P < .001 and .005, respectively, there was no overall trend in lactic acid levels with the number of blood units removed (P = .410) [Table 3].

By multivariable linear regression, AWOF patients had similar or slightly better nadir pH, nadir bicarbonate, and peak lactic acid levels then Control patients [Table 4]. Using multiple linear regression to adjust for other demographics, preoperative laboratory values, types of surgery, and antifibrinolytics, AWOF was associated with slightly greater amounts of ephedrine and phenylephrine but lesser amounts of epinephrine, norepinephrine, or vasopressin [Table 4]. There was no difference in the amounts of intravenous or CPB fluids [Table 4].

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#### **Table 2: Vasoactive medications**

	C	ontrol		Numl	per of unit	s of blood rem	noved		Р
	0 uni	ts <i>n</i> =596	1 un	it <i>n</i> =482	2 unit	s <i>n</i> =1257	3 uni	ts <i>n</i> =474	
	n	%	n	%	n	%	n	%	
Vasopressor boli									
Ephedrine	104	17	112ª	23	341 <sup>A</sup>	27	128 <sup>A</sup>	27	< 0.001
Epinephrine	96	16	45ª	9	117ª	9	38ª	8	< 0.001
Norepinephrine	1	0.2	0	0	3	0.2	0	0	0.530
Phenylephrine	552	93	453	94	1194	95	464 <sup>a, b, C</sup>	98	0.001
Vasopressin	88	15	75	16	147 <sup>в</sup>	12	70	15	0.082
Vasopressor infusion									
Epinephrine	70	12	35 <sup>A</sup>	7	67ª	5	9 <sup>a, b, c</sup>	2	< 0.001
Norepinephrine	380	64	332	69	808	64	310	65	0.273
Phenylephrine	476	80	432ª	90	1116ª	89	451 <sup>a, b, c</sup>	95	< 0.001
Vasopressin	102	17	61 <sup>A</sup>	13	146ª	12	51ª	11	0.004
Any vasopressor infusion	560	94	465	96	1211ª	96	461ª	97	0.007
	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Р
Vasopressor boluses (number)	9	(4, 14)	10.5 <sup>A</sup>	(5, 17)	10 <sup>A</sup>	(5, 16)	13 <sup>A, B, C</sup>	(8, 19)	<0.001
Vasopressor boluses total dose		,				( · · )		<b>,</b> , ,	
Ephedrine (mg)	0	(0, 0)	0 <sup>a</sup>	(0, 0)	0 <sup>A, B</sup>	(0, 5)	0 <sup>A, b</sup>	(0, 5)	< 0.001
Epinephrine (mcg)	0	(0, 0)	0 <sup>a</sup>	(0, 0)	0 <sup>a, b</sup>	(0, 0)	0 <sup>a, b, c</sup>	(0, 0)	< 0.001
Norepinephrine (mcg)	0	(0, 0)	0ª	(0, 0)	0 <sup>a, b</sup>	(0, 0)	0 <sup>a, b, c</sup>	(0, 0)	0.530
Phenylephrine (mcg)	900	(388, 1700)	1100ª	(500, 2100)	1190 <sup>a, b</sup>	(550, 2000)	1500 <sup>a, b, c</sup>	(900, 2300)	< 0.001
Vasopressin (units)	0	(0, 0)	0ª	(0, 0)	0 <sup>a, b</sup>	(0, 0)	0 <sup>a, b, c</sup>	(0, 0)	0.094
Vasopressor infusion dose									
Epinephrine (mcg)	32	(10, 120)	20ª	(10, 40)	20 <sup>a, b</sup>	(10, 50)	18 <sup>a, b, c</sup>	(10, 24)	0.011
Norepinephrine (mcg)	196	(0, 694)	163ª	(0, 448)	117 <sup>a, b</sup>	(0, 431)	118 <sup>a, b, c</sup>	(0, 416)	0.003
Phenylephrine (mg)	3.3	(0.6, 7.5)	4.3ª	(1.7, 7.7)	4.3 <sup>a, b</sup>	(1.6, 7.7)	5.0 <sup>a, b, c</sup>	(2.4, 8.9)	< 0.001
Vasopressin (units)	0	(0, 0)	0ª	(0, 0)	0 <sup>a, b</sup>	(0, 0)	0 <sup>a, b, c</sup>	(0, 0)	0.001

A < 0.01, a < 0.05 compared to Control Group, B < 0.01, b < 0.05 compared to autologous blood removal without fluid replacement group with 1 unit removed, C < .01, c < .05 compared to autologous blood removal without fluid replacement group with 2 units removed. IQR – interquartile range

# Transfusions

Overall, 1322 (47%) of patients were transfused RBC intraoperatively and 1425 (51%) at any time. We found that there was a decrease in the proportion of patients given intraoperative RBC transfusions as the number of autologous units increased: 75% (0 units) to 48% (1 unit), 40% (2 units), and 30% ( $\geq 3$  units), P < 0.001. We also found similar decreases in plasma and platelet transfusions from 53% to 19%, P < .001and from 57% to 23%, P < .001, respectively, but not in cryoprecipitate [Table 3]. After we adjusted for other factors associated with RBC transfusion, patients with AWOF were less likely to be given RBC, plasma, and platelets and AWOF was associated with fewer units of RBC, plasma, and platelets transfused [Table 5]. However, the number of cryoprecipitate units transfused was decreased only for patients with three units removed. Any (intraoperative + postoperative) homologous transfusions were similarly decreased by AWOF [Tables 3 and 5].

Postoperatively, first ICU hematocrits were slightly lower in Control Group and AWOF = 1 compared to AWOF Groups 2 and 3: (Control) 27.5  $\pm$  4.4% versus (Group 1) 27.1  $\pm$  4.3%, versus (Group 2) 28.1  $\pm$  4.0%, versus (Group 3) 28.3  $\pm$  3.9%, respectively, P < .001. After adjusting for other factors, AWOF was associated with slightly lower or similar hematocrit levels on ICU arrival [B = -0.9 (-1.4,-0.4), P < .001; B = -0.3 (-0.8,0.1), P = 0.120; and B = -0.2 (-0.8,0.4) P = 0.480. Platelet counts at ICU arrival were lower in the AWOF groups [Table 2] but after adjustment, only AWOF of three units was associated with lower counts (B = -20 (-27,-13), P < 0.001 [Table 4].

## Other outcomes

AWOF patients with two or three units removed had slightly lower rates of KDIGO stage 1 or 3 AKI [Table 3]. However, after using logistic regression, AWOF was not associated with AKI [Table 5]. Reexploration for hemorrhage did not differ among groups [Table 3].

# Sensitivity analyses

When we repeated the regressions using actual intravenous and cardiopulmonary fluids instead of adjusting for the putative greater volume expansion attributed to albumin, we had similar results [Supplementary Tables 1 and 2]. In particular, AWOF was still associated with lower odds of transfusion and fewer units when transfused. Compared to Control Group, AWOF of 1, 2, or 3 units was associated with 2 (1,3), 3 (2, 3), or 5 (3,6) fewer RBC units transfused, respectively; all P < 0.001.

# Propensity score matching

When we used propensity scores to match patients with AWOF to Control patients, we had 488 well-matched

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#### **Table 3: Transfusions and other outcomes**

	Con	trol		Num	ber of units o	of blood re	moved		Р
	0 units	n=596	1 unit	n=482	2 units <i>i</i>	n=1257	3 units	n=474	
	n	%	n	%	n	%	n	%	
Intraoperative transfusion									
Red cells	449	75	229 <sup>A</sup>	48	504 <sup>а, в</sup>	40	140 <sup>A, B, C</sup>	30	<.001
Plasma	313	53	1324	27	3714	30	89 <sup>A, B, C</sup>	19	<.001
Platelet	341	57	143	30	426 <sup>A</sup>	34	108 <sup>A, b, C</sup>	23	<.001
Cryoprecipitate	82	14	27	6	155	12	37	8	0.122
Postoperative transfusions				-				-	
Red cells	139	23	68ª	14	110 <sup>a, b</sup>	9	33 <sup>a, b</sup>	7	< 0.00
Plasma	30	5	8ª	2	26ª	2	5ª	1	< 0.00
Platelets	39	7	14ª	3	33ª	3	<b>9</b> ª	2	< 0.00
Cryoprecipitate	2	0.3	0	0	2	0.2	0	0	0.399
Any transfusions	2	0.0	0	0	2	0.2	0	0	0.077
Red cells	471	79	258ª	54	542 <sup>a, b</sup>	43	154 <sup>a, b, c</sup>	32	< 0.00
Plasma	316	53	133°	28	375°	43 30	90 <sup>a, b, c</sup>	19	<0.00
		58		20 30	375- 434ª	30	90 <sup>a, a, a</sup>	24	<0.00
Platelets Cryoprecipitate	346 346	58 14	145ª 27ª	30 6	434- 156 <sup>b</sup>	35 12	37 <sup>a, c</sup>	24 8	<0.00
Cryoprecipitate	Median	IQR	Median	IQR	Median	IQR	Median	IQR	<0.00 P
	Median	IUR	Median	IUR	weulan	IUR	Median	IUR	P
Intraoperative transfusions	0	(1 ()	01	(0, 0)	01	(0, 0)	0 <sup>A, B, C</sup>	(0, 1)	
Red cells (units)	3	(1, 6)	0 <sup>A</sup>	(0, 2)	0 <sup>A</sup>	(0, 2)	-	(0, 1)	< 0.00
Plasma (units)	1	(0, 4)	0 <sup>A</sup>	(0, 1)	0 <sup>A, b</sup>	(0, 2)	0 <sup>A, C</sup>	(0, 0)	< 0.00
Platelets (units)	1	(0, 4)	0^	(0, 1)	0 <sup>A, b</sup>	(0, 2)	0 <sup>A, C</sup>	(0, 0)	< 0.00
Cryoprecipitate (units)	0	(0, 0)	0 <sup>A</sup>	(0, 0)	0 <sup>B</sup>	(0, 0)	0 <sup>A, C</sup>	(0, 0)	0.009
Postoperative transfusions									
Red cells (units)	0	(0, 0)	0ª	(0, 0)	0 <sup>a, b</sup>	(0, 0)	0 <sup>a, b, c</sup>	(0, 0)	< 0.00
Plasma (units)	0	(0, 0)	0ª	(0, 0)	0 <sup>a, b</sup>	(0, 0)	0 <sup>a, b, c</sup>	(0, 0)	< 0.00
Platelets (units)	0	(0, 0)	0 <sup>a</sup>	(0, 0)	0 <sup>a, b</sup>	(0, 0)	0 <sup>a, b, c</sup>	(0, 0)	< 0.00
Cryoprecipitate (units)	0	(0, 0)	0ª	(0, 0)	0 <sup>a, b</sup>	(0, 0)	0 <sup>a, b, c</sup>	(0, 0)	0.400
Any transfusions									
Red cells (units)	3	(1,6)	0ª	(0, 2)	0 <sup>a, b</sup>	(0, 2)	0 <sup>a, b, c</sup>	(0, 1)	< 0.00
Plasma (units)	1	(0, 4)	0ª	(0, 1)	0 <sup>a, b</sup>	(0, 2)	0 <sup>A, b, c</sup>	(0, 0)	< 0.00
Platelets (units)	1	(0, 4)	0ª	(0, 1)	O <sup>a, b</sup>	(0, 2)	0 <sup>b, c</sup>	(0, 0)	< 0.00
Cryoprecipitate (units)	0	(0, 0)	0ª	(0, 0)	0 <sup>a, b</sup>	(0, 0)	0 <sup>a, b, c</sup>	(0, 0)	< 0.00
Other Outcomes								,	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Р
Minimum arterial pH	7.32	0.09	7.34 <sup>A</sup>	0.06	7.33 <sup>a, b</sup>	0.06	7.32 <sup>B, C</sup>	0.05	0.744
Maximum lactic acid (mmol/L)	3.6	2.6	2.6 <sup>A</sup>	1.4	3.0 <sup>A, B</sup>	1.8	3.6 <sup>B, C</sup>	1.7	0.410
Minimum bicarbonate (mEq/L)	22.0	2.8	22.3	2.3	22.4 <sup>A</sup>	2.3	22.1°	2.1	0.128
First ICU hematocrit (%)	27.5	4.4	27.0	4.3	28.1 <sup>a, B</sup>	4.0	28.3 <sup>A, B</sup>	4.0	< 0.00
First ICU platelet count $(1000/\mu)$	156	58	145 <sup>A</sup>	52	144 <sup>A</sup>	50	127 <sup>A, B, C</sup>	39	< 0.00
Reexploration	23	4	14	3	32	3	12	3	0.432
KDIGO stage 1	165	28	141	29	301ª	24	107ª	23	0.402
KDIGO stage 2	23	4	15	3	43	3	18	4	0.917
KDIGO stage 2 KDIGO stage 3	39	7	16	3	43 25 <sup>A</sup>	2	8 <sup>A, B</sup>	2	<.001

A < 0.01, a < 0.05 compared to Control Group, B < 0.01, b < 0.05 compared to autologous blood removal without fluid replacement group with 1 unit removed, C < .01, c < .05 compared to autologous blood removal without fluid replacement group with 2 units removed. Any transfusion is intraoperative+postoperative transfusion. KDIGO – Kidney Disease: Improving Global Outcomes. SD – standard deviation. IQR – interquartile range

pairs (all standardized differences <10%). In particular, the postinduction hematocrit was 31.7  $\pm$  5.8% in the Control group versus 31.6  $\pm$  5.7% in the AWOF group, P = .883, standardized difference = 1.8%. Of the 488 AWOF patients, 135 had one, 295 had two, and 58 had three units removed. Similar to the traditional analysis, AWOF patients were more likely to receive vasopressor boluses, more phenylephrine but less norepinephrine, and slightly more fluid adjusted for albumin dose [Supplementary Table 3]. In these paired patients, AWOF patients were less likely to receive intraoperative homologous blood transfusions (75 vs. 53%, P < .001 for RBC; 53 vs. 34%, P < .001 for plasma; 57 vs. 39%, P < .001 for platelets), but had similar rates of

cryoprecipitate [Supplementary Table 3]. These differences persisted through the postoperative period. Despite this higher transfusion amount, Control patients did not have higher postoperative hematocrits [Supplementary Table 3].

## DISCUSSION

We found that we were successful at removing 1 - 3 units of blood for later transfusion with minimal, if any, increase in intravenous fluids and only small increases in vasopressor requirements. This amount of intraoperative blood collection was associated with fewer transfusions and was well tolerated with no increase in lactic acid,

Table 4: Linear regression showing the association among processes of care, intermediate outcomes, and the number of autologous blood units removed and patients with no autologous blood removed (Control group). Regressions used the adjusted intravenous fluids and cardiopulmonary bypass volume adjusted for the volume of albumin given (3:1 for 5% and 15:1 for 25% albumin). Any transfusion is sum of intraoperative and postoperative

				Number	of units of bloc	d remove	d		
		1 unit			2 units			3 units	
	В	95% CI	Р	В	95% CI	Р	В	95% CI	Р
Factor									
Vasopressor boluses (#)	2	(1, 3)	0.001	2	(1, 3)	< 0.001	4	(3, 6)	< 0.001
Ephedrine dose (mg)	1	(0, 2)	0.118	2	(1, 3)	< 0.001	2	(1, 4)	< 0.001
Phenylephrine boli dose (mcg)	97	(-117, 311)	0.373	62	(-109, 233)	0.480	425	(212, 639)	< 0.001
Phenylephrine total dose (mcg)	340	(-680, 1360)	0.513	383	(-432, 1199)	0.357	1844	(812, 2876)	< 0.001
Epinephrine total dose (mcg)	-116	(-181, -52)	< 0.001	-125	(-176, -73)	< 0.001	-154	(-219, -89)	< 0.001
Norepinephrine total dose (mcg)	-145	(-261, -28)	0.015	-238	(-331, -145)	< 0.001	-254	(-372, -136)	< 0.001
Vasopressin total dose (units)	-0.2	-1.1, 0.7)	0.652	-0.7	(-1.4, 0.1)	0.073	-1.4	(-2.4, -0.4)	0.005
CPB fluids adjusted (mL)	3	(-71,77)	0.937	104	(45, 164)	< 0.001	182	(106, 257)	< 0.001
Intravenous fluids adjusted (mL)	-38	(-139, 64)	0.470	89	(8, 170)	0.032	101	(-4, 205)	0.059
Minimal arterial pH	0.01	(0.01, 0.2)	0.022	0.01	(0.00, 0.02)	0.005	0.01	(0.00, 0.02)	0.058
Maximum lactate (mmol/L)	-0.6	(-0.8, -0.4)	< 0.001	-0.3	(-0.5, -0.1)	< 0.001	-0.5	(-0.7, -0.3)	< 0.001
Minimum bicarbonate (mEq/L)	0.2	(-0.1, 0.5)	0.298	0.5	(0.2, 0.7)	< 0.001	0.6	(0.3, 0.9)	< 0.001
Intraoperative transfusions					( , , ,			( , , ,	
Red cell (units)	-2	(-3, -1)	< 0.001	-2	(-3, -2)	< 0.001	-4	(-5, -3)	< 0.001
Plasma (units)	-1	(-2, -1)	< 0.001	-1	(-2, -1)	< 0.001	-3	(-3, -2)	< 0.001
Platelets (units)	-1	(-1, -0.3)	0.002	-1	(-1, -0.4)	< 0.001	-2	(-3, -2)	< 0.001
Cryoprecipitate (units)	-0.1	(-0.3, 0)	0.163	-0.1	(-0.2, 0)	0.202	-0.5	(-0.7, -0.3)	< 0.001
First postoperative hematocrit (%)	-0.9	(-1.4, 0.4)	< 0.001	-0.3	(-0.8, 0.1)	0.120	-0.2	(-0.8, 0.4)	0.480
First ICU platelet count $(1000/\mu L)$	-4	(-10, 1)	0.139	-4	(-9, 1)	0.141	-20	(-26, -13)	< 0.001
Any transfusions					( ) )			( ) )	
Red cell (units)	-3	(-4, -3)	< 0.001	-3	(-4, -3)	< 0.001	-5	(-6, -4)	< 0.001
Plasma (units)	-2	(-3, -1)	< 0.001	-2	(-2, -1)	< 0.001	-4	(-4, -3)	< 0.001
Platelets (units)	-1	(-2, -1)	< 0.001	-1	(-2, -1)	< 0.001	-3	(-3, -2)	< 0.001
Cryoprecipitate (units)	-0.3	(-0.4, 0.1)	0.004	-0.1	(-0.3, 0)	0.117	-0.3	(-0.5, -0.1)	0.001

CPB - cardiopulmonary bypass. B - linear regression coefficient. Compared to no autologous blood removed, B is the change in the amount of the factor when autologous blood was removed and then transfused. 95% CI - 95% confidence interval

decrease in bicarbonate concentrations or pH, or increase in AKI.

Importantly, we found that AWOF was not associated with AKI, which is similar to one study of ANH, but different than another ANH study, which found lower (28.2% v 24.1%, P < .001) rate of AKI in patients with autologous blood transfusions.<sup>[6,7]</sup> While transfusion in cardiac surgery has been associated with AKI,<sup>[21]</sup> unlike Goldberg *et al.*'s study,<sup>[7]</sup> we did not find autologous blood to be associated with a lower AKI rate. Our study differs by removing blood without replacing the lost volume, which may contribute to a fall in cardiac output and renal blood flow. However, compared to ANH, it maintains hematocrit and thus may produce similar oxygen delivery.

We also found that despite fewer RBC transfusions, the change in hematocrit from postinduction to ICU was similar in the propensity matched groups. Our findings of fewer RBC, plasma, and platelet transfusions are similar to studies that used ANH.<sup>[6,8-11]</sup> Given the small numbers of patients who received cryoprecipitate, we may have been underpowered to find a benefit. Platelet count on ICU arrival was lower in the third unit AWOF group [Table 3]; but this was not associated with increased rate of reexploration for hemorrhage [Table 3].

AWOF was associated with a 33-36% lower odds ratio of receiving homologous blood transfusions per unit of blood removed [Table 5]. Our findings of decreased autologous transfusions in AWOF is similar to both prospective randomized and retrospective observational studies and one meta-analysis that found that ANH reduces transfusions.<sup>[6,8-11]</sup> Its similarity is obvious that larger amounts of autologous transfusions were associated with lesser transfusion rates. Our results differ from two studies that found no benefit from ANH.<sup>[12,13]</sup> While the volume of autologous blood removed in one study was relatively smaller (1 unit),<sup>[13]</sup> the volume in the other study was larger  $[1,099 \pm 333 \text{ ml} (range, 430-1900 \text{ ml})]$ .<sup>[12]</sup> It is possible that large volume removal with fluid replacement leads to excessive hemodilution such that subsequent transfusion is necessary. Other studies of autologous transfusion did not provide information on vasopressors, making comparisons difficult.[22-24]

AWOF attempts to balance the benefits of autologous blood transfusion with the risks of hypovolemia. Larger volumes of autologous blood result in a higher Table 5: Adjusted odds ratio in patients with 1, 2, or 3 units of autologous blood removed compared to patients who had no autologous blood removed (Control group). Regressions used the adjusted intravenous fluids and cardiopulmonary bypass volume adjusted for the volume of albumin given (3:1 for 5% and 15:1 for 25% albumin). Any transfusion is sum of intraoperative and postoperative

Number of units of blood			Autologo	ous blood	removal withou	t fluid repla	acement		
removed		1 unit			2 units			3 units	
	Odds	ratio 95% Cl	Р	Odds	ratio 95% Cl	Р	Odds	ratio 95% Cl	Р
Factor									
Calcium administration	2.34	(0.60, 9.16)	0.224	2.73	(0.94, 7.96)	0.066	undef	(0,)	0.990
Any vasopressor infusion	1.70	(0.87, 3.30)	0.118	2.23	(1.32, 3.77)	0.003	3.52	(1.61, 7.69)	0.002
Ephedrine administration	1.08	(0.76, 1.55)	0.663	1.54	(1.14, 2.07)	0.004	1.51	(1.02, 2.24)	0.039
Intraoperative transfusion									
Red cell	0.36	(0.25, 0.52)	< 0.001	0.25	(0.18, 0.34)	< 0.001	0.09	(0.06, 0.14)	< 0.001
Plasma	0.49	(0.35, 0.68)	< 0.001	0.36	(0.27, 0.48)	< 0.001	0.08	(0.05, 0.12)	< 0.001
Platelet	0.46	(0.33, 0.63)	0.001	0.39	(0.30, 0.52)	< 0.001	0.10	(0.07, 0.16)	< 0.001
Cryoprecipitate	0.52	(0.29, 0.91)	0.023	0.73	(0.49, 1.08)	0.118	0.16	(0.09, 0.29)	< 0.001
Any transfusions									
Red cells (units)	0.41	(0.28, 0.60)	< 0.001	0.24	(0.17, 0.33)	< 0.001	0.09	(0.05, 0.14)	< 0.001
Plasma (units)	0.48	(0.34, 0.68)	< 0.001	0.35	(0.26, 0.48)	< 0.001	0.08	(0.05, 0.12)	< 0.001
Platelets (units)	0.43	(0.31, 0.61)	< 0.001	0.38	(0.28, 0.51)	< 0.001	0.11	(0.07, 0.16)	< 0.001
Cryoprecipitate (units)	0.52	(0.28, 0.95)	0.033	0.83	(0.55, 1.27)	0.388	0.19	(0.10, 0.37)	< 0.001
KDIGO stage 1 or worse	1.14	(0.84, 1.55)	0.398	0.99	(0.76, 1.29)	0.970	0.96	(0.66, 1.37)	0.810
KDIGO stage 2 or worse	0.64	(0.34, 1.25)	0.197	0.85	(0.51, 1.41)	0.528	0.72	(0.35, 1.51)	0.386

KDIGO – Kidney disease improving global outcome, within the first three postoperative days. Undef – undefined

hematocrit and may proportionally decrease platelet and plasma transfusions by providing fresh platelets and clotting factors postbypass when they are needed. However, larger volumes of autologous blood removal increase the risk of hypovolemia, need for vasopressors, and organ hypoperfusion and injury. Administration of intravenous fluids to maintain normovolemia (ANH) leads to hemodilution, anemia, and the potential for organ dysfunction. In particular, anemia on CBP is associated with AKI and mortality – probably from the decreased oxygen carrying capacity of the resultant anemic blood.<sup>[21,25]</sup> AWOF by minimizing hemodilution should lead to a higher oxygen carrying capacity, but its effects on oxygen delivery need further study.

Our study extends those findings to the use of AWOF and shows that AWOF is achievable and has no evidence of perfusion deficits as measured by acid–base balance or AKI. Future studies should compare AWOF to ANH, as AWOF should produce less hemodilution and may lead to fewer transfusions. Additionally, the lesser blood volume may contribute to decreased hemorrhage.<sup>[26]</sup>

There are several limitations to this study. First, this is a single center study and individual transfusion practices may not be generalizable to other institutions. Multi-center study is needed to confirm our finding. Second, as this was not a blinded study and there was no transfusion protocol, decisions to order homologous blood may have been based, at least in part, on the lack of autologous blood. This bias would create an apparent benefit to transfusion rates in AWOF group. We are also limited in that fluid intake did not include piggyback and push medicines. While typically similar across cases, their absence from fluid intake may have created a small unknown bias. Furthermore, we did not have information on preoperative anticoagulant and antiplatelet use or on use of retrograde autologous priming of the bypass circuit. If use was unbalanced across groups, it may have introduced bias. Both the total population and the propensity matched groups may have unknown confounders that influenced the decision to remove or not remove blood, and this might bias our results. Prospective randomized studies are suggested to overcome these limitations. Finally, while our study had fewer patients than desired by the power analysis, we were able to find a clinically and statistically significant decrease in transfusions in patients who had blood removed without fluid replacement, due to a larger-than-expected effect size. We also had a higher transfusion rate than estimated for the power calculation, however our intra- and post-operative transfusion rates (32% for three units removed to 79% for none) is similar to or better than a recent trial comparing restrictive (52.3%) versus liberal (72.6%) transfusion criteria.<sup>[2]</sup> The main strengths of this study are that we included patients undergoing a variety of cardiac procedures, not just coronary artery bypass grafts, and that we found similar results with both traditional logistic regression and propensity matching analysis.

In conclusion, we found that AWOF of 1-3 units for later autologous transfusion is associated with decreased homologous transfusions without acidosis or AKI.

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## **Conflicts of interest**

There are no conflicts of interest.

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linear regression coefficient. Compared to no autologous blood removed, B is the change in the amount of the factor when autologous blood was removed and then transfused. 95% cl – 95% confidence interval.	npared 5% Cl –	to no autologou 95% confidence	s blood remov interval.	/ed, B is th	e change in the	amount of the	factor wh	en autologous l	olood was
			Number of u	inits of blo	Number of units of blood removed				
	1 unit			2 units			3 units		
Factor	В	95% CI	p-value	В		p-value	В	95% CI	p-value
Vasopressor boluses (#)	1	(0, 2)	0.017	2	(1, 3)	<0.001	4	(3, 6)	<0.001
Ephedrine dose (mg)	0	(-1, 2)	0.492	2	(1, 3)	<0.001	2	(0, 3)	0.036
Phenylephrine boli dose (mcg)	97	(-117, 311)	0.373	62	(-109, 233)	0.480	425	(212, 639)	<0.001
Phenylephrine total dose (mcg)	590	(-422, 1602)	0.253	408	(-447, 1262)	0.350	1453	(274, 2632)	0.016
Epinephrine total dose (mcg)	-97	(-163, -33)	0.003	-132	(-187, -78)	<0.001	-194	(-270, -119)	<0.001
Norepinephrine total dose (mcg)	-71	(-186, 44)	0.229	-184	(-281, -87)	0.546	-230	(-364, -96)	<0.001
Vasopressin total dose (units)	-0.2	(-1.1, 0.6)	0.595	-0.7	(-1.4, 0.1)	0.077	-1.4	(-2.4, -0.4)	0.006
CPB fluids (mL)	-75	(-337, 187)	0.575	-59	(-280, 163)	0.603	216	(-89, 521)	0.116
CPB fluids adjusted (mL)	-124	(-402, 154)	0.382	06-	(-325, 145)	0.454	147	(177, 471)	0.374
Intravenous fluids (mL)	-211	(-492, 70)	0.141	-117	(-354, 121)	0.336	69	(-258, 397)	0.678
Intravenous fluids adjusted (mL)	-274	(-593, 45)	0.093	-42	(-312, 228)	0.759	171	(-201, 543)	0.369
Minimal arterial pH	0.01	(0.01, 0.2)	0.002	0.01	(0.00, 0.01)	0.084	0.01	(0.00, 0.02)	0.038
Maximum lactate (mmol/L)	-0.7	(-0.9, -0.4)	<0.001	-0.4	(-0.6, -0.2)	<0.001	-0.7	(-0.9, -0.4)	<0.001
Minimum bicarbonate (mEq/L)	0.2	(-0.1, 0.5)	0.266	0.4	(0.1, 0.6)	0.004	0.5	(0.1, 0.9)	0.011
Intraoperative transfusions									
Red cell (units)	-2	(-3, -1)	<0.001	-2	(-3, -2)	<0.001	-4	(-5, -3)	<0.001
Plasma (units)	Ļ	(-2, -1)	<0.001	-1	(-2, -1)	<0.001	'n	(-3, -2)	<0.001
Platelets (units)	-1	(-1, -0.3)	0.002	-1	(-1, -0.4)	<0.001	-2	(-3, -2)	<0.001
Cryoprecipitate (units)	-0.1	(-0.3, 0)	0.163	-0.1	(-0.2, 0)	0.202	-0.5	(-0.7, -0.3)	<0.001
First ICU hematocrit (%)	-0.7	(-1.3, -0.2)	0.005	-0.4	(-0.8, 0.1)	0.100	-0.2	(-0.8, 0.4)	0.217
First ICU platelet count (1000/ $\mu$ L) -5	) -5	(-10, 1)	0.115	-4	(-9, 1)	0.106	-20	(-27, -13)	<0.001
Any transfusions									
Red cell (units)	-2	(-3, -1)	<0.001	'n	(-3, -2)	<0.001	ч	(-6, -3)	<0.001
Plasma (units)	<u>-</u>	(-2, -1)	<0.001	<u>-</u>	(-2, -1)	<0.001	'n	(-4, -3)	<0.001
Platelets (units)	Ļ	(-1, -0.3)	0.001	4	(-1, -0.5)	<0.001	'n	(-3, -2)	<0.001
Cryoprecipitate (units)	-0.1	(-0.3, 0)	0.108	-0.1	(-0.2, 0)	0.070	-0.6	(-0.8, -0.4)	<0.001

linear regression coefficient. Compared to no autologous blood removed B is the change in the amount of the factor when autologous blood was autologous blood units removed to patients with no autologous blood removed (Control group). Regressions used the unadjusted intravenous fluids and cardiopulmonary bypass volume. Any transfusion is sum of intraoperative and postoperative. CPB – cardiopulmonary bypass. B – Supplementary Table 1. Linear regression showing the association between processes of care, intermediate outcomes and the number of

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Supplementary Table 2. Adjusted odds ratio in patients with 1, 2, or 3 units of autologous blood removed compared to patients who had no autologous blood removed (control group). Regressions used the unadjusted intravenous fluids and cardiopulmonary bypass volume. Any transfusion is sum of intraoperative and postoperative. KDIGO – Kidney disease improving global outcome, within the first 3 postoperative days. Undef – undefined.	ed odds r ntrol grou ative and	atio in patients Jp). Regression: postoperative.	with 1, 2, or 3 s used the unao KDIGO – Kidne	units of au djusted in V disease	utologous blooc travenous fluid; improving glob	l removed com s and cardiopuli al outcome, wit	pared to pa monary byl .hin the firs	atients who ha bass volume. <i>I</i> t 3 postoperat	d no Iny ive days.
			Number of u	nits of blo	Number of units of blood removed				
	1 unit			2 units	10		3 units		
Factor	Odds r	Odds ratio 95% Cl	p-value	Odds	Odds ratio 95% Cl	p-value	Odds r	Odds ratio 95% Cl	p-value
Calcium administration	2.26	(0.61, 8.41)	0.223	2.28	(0.88, 5.95)	0.091	undef	undef $(0, \infty)$	0.986
Any vasopressor infusion	1.69	(0.90, 3.15)	0.101	1.62	(1.01, 2.59)	0.044	1.87	(0.97, 3.61)	0.061
Ephedrine administration	1.14	(0.81, 1.60)	0.461	1.73	(1.32, 2.26)	<0.001	1.90	(1.37, 2.64)	<0.001
Intraoperative transfusion									
Red cell	0.35	(0.25, 0.50)	<0.001	0.24	(0.17, 0.32)	<0.001	0.09	(0.06, 0.13)	<0.001
Plasma	0.50	(0.36, 0.70)	<0.001	0.37	(0.28, 0.48)	<0.001	0.09	(0.06, 0.13)	<0.001
Platelet	0.48	(0.35, 0.66)	0.001	0.39	(0.29, 0.51)	<0.001	0.10	(0.07, 0.16)	<0.001
Cryoprecipitate	0.58	(0.34, 1.01)	0.053	0.81	(0.56, 1.16)	0.248	0.22	(0.13, 0.37)	<0.001
Any transfusions									
Red cells (units)	0.41	(0.28, 0.60)	<0.001	0.25	(0.18, 0.34)	<0.001	0.09	(0.06, 0.15)	<0.001
Plasma (units)	0.48	(0.34, 0.67)	<0.001	0.36	(0.26, 0.48)	<0.001	0.08	(0.05, 0.12)	<0.001
Platelets (units)	0.43	(0.31, 0.60)	<0.001	0.39	(0.29, 0.52)	<0.001	0.11	(0.07, 0.17)	<0.001
Cryoprecipitate (units)	0.47	(0.26, 0.88)	0.017	0.81	(0.53, 1.23)	0.315	0.18	(0.09, 0.33)	<0.001
KDIGO stage 1 or worse	1.15	(0.85, 1.55)	0.378	0.98	(0.76, 1.27)	0.888	0.91	(0.64, 1.28)	0.572
KDIGO stage 2 or worse	0.64	(0.33, 1.23)	0.181	0.85	(0.51, 1.41)	0.516	0.71	(0.34, 1.48)	0.361

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and outcomes. Any transfusion is intraoperative + postoperative transfusion. KDIGO – Kidney disease improving global outcome.	berative	transfusion. KDIGO – Kidney disease in	nproving	global outcome. CPB –	
cardiopulmonary bypass.					
Factor	No Auto	No Autologous	Yes Aı	Yes Autologous	p-value
	N = 488		N = 488	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
	۲	%	С	%	
Received vasopressor infusion	455	93	476	98	0.023
Received ephedrine	86	18	128	26	0.002
Intraoperative transfusion					
Red cells	364	75	260	53	<0.001
Plasma	259	53	166	34	<0.001
Platelets	280	57	189	39	<0.001
Cryoprecipitate	99	14	61	12	0.704
Postoperative transfusion					
Red cells	105	22	68	14	0.003
Plasma	23	5	14	3	0.180
Platelets	30	6	11	2	0.004
Cryoprecipitate	2	0.4	1	0.2	0.999
Any transfusion					
Red cells	379	78	283	58	<0.001
Plasma	261	53	167	34	<0.001
Platelets	283	58	190	39	<0.001
Cryoprecipitate	68	14	61	12	0.571
KDIGO stage 1	131	27	138	28	0.635
KDIGO stage 2	18	4	13	3	0.711
KDIGO stage 3	27	9	18	4	0.217
Reexploration for hemorrhage	19	4	17	3	0.865
	Mean	SD	Mean	SD	
Postinduction hematocrit (%)	31.7	5.8	31.6	5.7	0.883
Vasopressor boluses (#)		(4, 14)	11		<0.001
Ephedrine (mg)		(0, 0)	0	(0, 5)	<0.001
Phenylephrine (mcg) Epinephrine (mcg)	4284 0	(1600, 8843) (0, 0)	5634 0	(2732, 9184) (0, 0)	<0.001 0.008
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Supplementary Table 3. Propensity score matched no autologous blood removed with autologous blood removed patients with processes of care

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Munimum bicarbonate (mL) (multicavenous fluids (mL) (multicavenous fluids adjusted (mL) (multicavenous fluids adjusted (mL) (multicavenous fluids adjusted (mL) (multicavenous fluids (mL) (multicavenous fluids (mL) (multicavenous fluids (multi	<ul> <li>(2, 2)</li> <li>(1000 (1000, 1500)</li> <li>(1000 (2000)</li> <li>(1000, 2000)</li> <li>(1000, 3500)</li> <li>(1000, 3500)&lt;</li></ul>	1000 1300 2000		
	(1000, 2000) (988, 3100) (1000, 3500) 0.09 2.5 2.8 4.2 4.5 57 interquartile range	1300 2000	(TUUU, T/UU)	0.099
	(988, 3100) (1000, 3500) 0.09 2.5 2.8 4.2 4.5 57 interquartile range	2000	(1000, 2000)	0.003
	(1000, 3500) 0.09 2.5 2.8 4.2 4.5 57 interquartile range		(1000, 3463)	0.033
	0.09 2.5 2.8 4.2 57 interquartile range	2100	(1000, 3525)	0.046
	2.5 2.8 4.2 4.5 57 interquartile range	7.33	0.06	0.096
	2.8 4.2 4.5 57 interquartile range	2.9	1.8	<0.001
	4.2 4.5 57 interquartile range	22.0	2.3	0.780
	4.5 57 interquartile range	22.0	4.0	0.002
	57 interquartile range	29.9	4.0	0.739
First ICU platelet count (1000/μL) 154	interquartile range	144	51	0.004
Median		Media	Median interquartile range	
ß	(0, 6)	1	(0, 3)	<0.001
1	(0, 4)	0	(0, 2)	<0.001
1	(0, 4)	0	(0, 2)	<0.001
Cryoprecipitate (units) 0	(0, 0)	0	(0, 0)	0.551
0	(0, 0)	0	(0, 0)	0.002
0	(0, 0)	0	(0, 0)	0.139
0	(0, 0)	0	(0, 0)	0.003
Cryoprecipitate (units) 0	(0, 0)	0	(0, 0)	0.566
3	(1, 6)	1	(0, 4)	<.001
1	(0, 4)	0	(0, 2)	<.001
1	(0, 4)	0	(0, 2)	<.001
Cryoprecipitate (units) 0	(0, 0)	0	(0, 0)	0.452