

# Retrograde Autologous Priming Method Reduces Plasma Free Hemoglobin Level in Aortic Surgery

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## ABSTRACT

**Background:** Although conventional cardiopulmonary bypass (cCPB) is still the most widely used method in open heart surgery, methods such as retrograde autologous priming (RAP) are increasingly popular in terms of limiting hemodilution. Our hypothesis is that the use of the RAP method in aortic surgery may result in a limitation of hemodilution and a decrease in fHb levels. For this purpose, plasma free hemoglobin (fHb) levels were investigated in adult open aortic arch repair with axillary artery cannulation patients using cCPB and rRAP methods.

**Materials and Methods:** In this study, a total of 36 patients undergoing aortic surgery using rRAP and standard cCPB were investigated. Measurements were performed at five time points: After induction of anesthesia, 5<sup>th</sup> minute of CPB, 10<sup>th</sup> minute of antegrade cerebral perfusion, 30<sup>th</sup> minute after declamping of aorta, and at sternum closure. Besides hemodynamic variables, arterial blood gas analysis and postoperative variables, patients were assessed for fHb levels.

**Results:** The rRAP group had a significantly lower increase in fHb levels in T3, T4, and T5 time points, when compared to the cCPB group ( $p = 0.002, 0.047, 0.009$ , respectively). There was no significant difference between the rRAP and cCPB groups in other intraoperative, and postoperative variables. Also, it was observed that rRAP did not make a difference in terms of blood and blood product transfusion.

**Conclusion:** In this study, in patients undergoing aortic surgery, a reduction in the increase of fHb was observed with the rRAP method which is a simple procedure that does not require high cost or advanced technology.

**Keywords:** Aortic surgery, cardiopulmonary bypass, hemodilution, plasma free hemoglobin, restrictive fluid management, retrograde autologous priming

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## INTRODUCTION

Conventional cardiopulmonary bypass (cCPB) is currently the most widely used extracorporeal circulation method for on-pump cardiac surgery. The main components of the CPB machine include pumps, tubing, and gas (oxygenator) and heat exchange units. Exposure to non-endothelial surfaces on a CPB circuit causes a severe inflammatory responses.

This leads to activation of leukocytes and platelets, initiation of the coagulation cascade, and a decrease in the levels of circulating coagulation factors. Many mediators are released following all these complex reactions, which can contribute to capillary leakage and tissue edema.<sup>[1]</sup> During the setup of CPB circuits, approximately 1 to 2 L of fluid (balanced crystalloid solution) is used as a priming volume, results in hemodilution with temporary or persistent anemia

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and coagulopathy. Due to CPB and hemodilution, the levels of blood cells and clotting factors decrease, which may result in anemia, hemostasis disorders, end-organ dysfunction, or cognitive impairment.<sup>[2]</sup> During induction and maintenance of anesthesia, large volume fluids can be administered and this also contribute to hemodilution. Hypervolemia and hemodilution causes increased plasma fHb levels, endothelial glycocalyx (EGL) damage, and activation of inflammatory processes.<sup>[3-5]</sup> There are *in vitro* and animal model data that find increased plasma free hemoglobin (fHb) related to inflammation, infection, platelet activation, vasculopathy and thrombosis.<sup>[6]</sup> In cardiac surgery, fHb is elevated due to both hemolysis caused by extracorporeal circuits,<sup>[4]</sup> and the inflammatory response induced by oxidative stress disrupting erythrocyte membrane integrity.<sup>[5]</sup> It has been shown in studies that fHb causes end organ damage and increases mortality, these data suggest that an increase in fHb may be a biomarker for poor clinical outcomes.<sup>[7]</sup>

In recent years, methods such as the retrograde autologous priming (RAP) and mini-CPB circuits have been used to limit hemodilution. The RAP technique was described in 1998 by Rossengart *et al.*,<sup>[8]</sup> which is taking simultaneous prime fluid out of the pump when the blood is passively drawn from arterial and venous lines before the CPB starts, and was applied in the present study. In this way, CPB circuits are filled with the patient's own blood instead of prime fluid, thus minimizing hemodilution caused by prime fluids.

Studies suggesting that restrictive fluid management reduces postoperative complications, and information emphasizing the need to give the right fluid at the right time to the cardiac patient led us to develop our hypothesis for this study.<sup>[9-12]</sup> In the light of these findings, our hypothesis is that a reduction in fHb levels can be observed using a method to RAP in aortic surgery. For this purpose, we aimed to investigate intraoperative levels of fHb, by comparing restrictive RAP and conventional CPB methods in adult open aortic arch patients.

## MATERIALS AND METHODS

### Study population

This study complies with the Declaration of Helsinki and ethical approval was granted by the local institutional ethical board (no: E-18-1784, 2018). In addition, written informed consent was obtained from all the patients. This study was conducted between March - October 2018. In the restrictive RAP (rRAP) group; We applied restrictive fluid management during anesthesia and RAP during the pump.

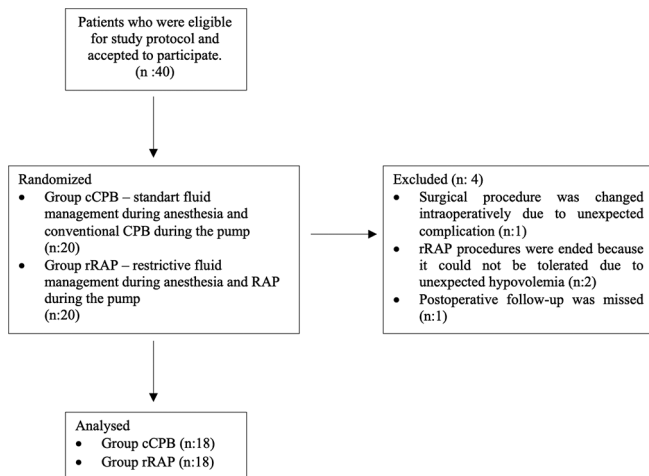
In the conventional (cCPB) group; We performed standard fluid management during anesthesia and conventional CPB during the pump. 36 adult patients who underwent elective open ascending aortic aneurysm repair using cCPB (n: 18) and rRAP (n: 18) were included in the study [Figure 1]. Exclusion criteria were off-pump surgeries, age <18 years, LVEF <40%, body weight >100 kg, emergency surgery, reoperations, preoperative renal, hepatic, or hematological disorders, preoperative medication suppressing free radicals such as corticosteroids, vitamin C, vitamin E, etc.

### Anesthesia management

Diazepam 0.15 mg kg<sup>-1</sup> was administered orally as a nighttime premedication and intramuscular 0.1 mg kg<sup>-1</sup> morphine was administered before surgery. Two venous vascular cannulations on bilateral right and left brachial veins and left radial artery cannulation were performed in the operating room. Pulse oximetry and two channel electrocardiography monitoring were performed. Invasive blood pressure monitoring was provided on the left radial artery. Anesthesia was induced with midazolam (0.15 mg kg<sup>-1</sup>), fentanyl (10 mcg kg<sup>-1</sup>), and followed by rocuronium (0.6 mg kg<sup>-1</sup>). Maintenance was achieved by sevoflurane inhalation with the help of bispectral index monitoring (BIS™, Covidien, MN, USA), remifentanyl infusion, and additional doses of rocuronium. Central venous cannulation was attained via the right internal jugular vein. Nasopharyngeal temperature monitoring was performed. During the anesthesia, the fluid management was continued in the cCPB group at 8-10 mL kg<sup>-1</sup> hr<sup>-1</sup>, while in the rRAP group 5-7 mL kg<sup>-1</sup> hr<sup>-1</sup>. Balanced isotonic solutions were preferred in fluid management. We had prepared a research protocol that we recommend that the practitioners of the study follow. In the protocol, RBC transfusion threshold is given as 7.5 gr dl<sup>-1</sup>. Indication of FFP transfusion is given as 1.5 times more INR in the presence of excessive microvascular bleeding. Compared to standard cardiac surgery, open aortic arch repair with axillary artery cannulation is more complex and has longer CPB and cross clamp times. In this study, we preferred cases of aortic aneurysm surgery to evaluate the changes that may occur more dramatically.

### CPB management

The CPB circuit (The Affinity NT Integrated Trillium CVR/Membrane Oxygenator, Medtronic, Minneapolis, MN) consisting of a venous reservoir, roller pump, oxygenator, and arterial filter, is routinely filled in our operating rooms with 1800-2000 mL of Ringer Lactate solution and 20% Mannitol (0.5 mg kg<sup>-1</sup>). The same type of CPB circuits were used in the groups. In the cCPB group, CPB was obtained by the standard method, and in



**Figure 1** : Flow diagram

the rRAP group, the patient's own blood was withdrawn from the arterial and venous cannulas before CPB started. After deairing of the CPB circuits, approximately 900-1000 mL of the priming volume (depending on the patient's hemodynamic status) were filled back into the recirculating bag and taken out of the reservoir. A recirculation bag was connected to the drain outlet of the arterial filter. When the aortic cannulation was finished, the arterial blood coming from the aorta slowly filled into the reservoir, while the prime solution was poured into the recirculation bag. On the other hand, the venous line was gently unclamped, allowing venous blood to drain from the patient into the reservoir. At this time, the arterial pump was gently rotated to maintain the proper level in the venous reservoir. The circuit was filled with patient's blood and blood and prime fluid were changed. The recirculation bag was not thrown away, it was connected to the venous reservoir for use as needed during CPB. The procedure took approximately 5-7 minutes and was performed while the patient's hemodynamics were closely monitored. During the RAP, if needed, small doses of ephedrine were administered to the patients to keep MAP between 50 and 80 mmHg. The circulation bag was then reconnected to the venous reservoir so that fluid exchange could be performed on hemodynamic requirements such as hypovolemia during CPB.

Following adequate activated clotting time ( $>480$  s), cardiopulmonary bypass was started. Cardiac arrest was initiated by antegrade crystalloid solution (Plegisol®) and maintained using 1:4 mixed blood retrograde cardioplegia at 20-min intervals. Target flow rate was  $2-2.5$  Lmin<sup>-1</sup>m<sup>-2</sup>. Mean arterial pressure (MAP) was kept between 50 and 80 mmHg, hematocrit was kept above 22%, and urinary output was kept above  $0.5$  ml kg<sup>-1</sup>. Moderate hypothermia (28°C) was applied to all patients. The electrolyte and metabolic

balance were maintained in accordance with the metabolic needs of the patient. Blood gas management during CPB was performed using the alpha-stat strategy.

### Data collection and blood sampling

Measurements were performed at five time points: After induction of anesthesia (T1), 5<sup>th</sup> minute of CPB (T2), 10<sup>th</sup> minute of antegrade cerebral perfusion (T3), 30<sup>th</sup> minute after declamping of aorta (T4), and at sternum closure (T5). Blood samples for fHb were collected in tubes without anticoagulant and centrifuged at 5000 rpm for five minutes. The separated plasma components were stored at -20°C until analysis. For the subsequent measurements of fHb levels, the Harboe method<sup>[13]</sup> was used and the concentrations were expressed as g L<sup>-1</sup>. At these five measurement periods, heart rates and blood pressures of the patients were also recorded and simultaneous arterial blood gas analysis (hemoglobin, lactate) was performed. Total amount of iv fluids, blood, and blood products, total pump and RAP fluids, preoperative and postoperative day 1 (POD<sub>1</sub>) serum creatinine values, postoperative blood and blood product requirements and postoperative complications were also recorded. An  $0.3$  mg dl<sup>-1</sup> increase in serum creatinine value was considered to be a “grade I creatinine increase”.<sup>[14]</sup>

### Statistics

Statistical analysis was performed using SPSS for Windows version 21.0 statistical software (SPSS Inc., Chicago, IL, USA). Based on previous studies on the field, a sample size of 36 patients (power = 0.80,  $\alpha$  = 0.05) would be sufficient, when 1% standard deviation difference is considered significant. Continuous variables were tested for normal distribution by the Kolmogorov-Smirnov test. Normally distributed continuous variables were expressed in mean  $\pm$  standard deviation (SD) and were compared using the independent samples t-test. Non-normally distributed variables were expressed in median (minimum-maximum) and were compared using the Mann-Whitney U test. Categorical variables were expressed in number and frequency and were compared using the Chi-square test or Fisher's exact test. A *P* value of  $<0.05$  was considered statistically significant.

### RESULTS

The preoperative and intraoperative characteristics of the patients are summarized in Table 1. There were no significant differences between the two groups concerning age, body mass index, Euroscore II, comorbidities, total surgical procedure duration, aortic cross-clamping and CPB time, blood product requirements, or urine

output ( $p > 0.05$ ). 1 unit of erythrocyte suspension was transfused intraoperatively to 6 patients in the rRAP group and 7 patients in the cCPB group. More than 1 unit of transfusion was not performed on any patient. Total volume of priming solution and total operation fluid volume were significantly higher in the cCPB group as expected ( $p < 0.001$ ), but there was no difference in transfusion rate between the groups.

Table 2 represents fHb ( $\text{g L}^{-1}$ ), lactate, heart rates (HR), mean arterial pressure (MAP), hemoglobin (Hb) levels of the two groups, at all time points. fHb values in the cCPB group were significantly higher in the T3, T4 and T5 time points than the rRAP group. (respectively  $P = 0.002, 0.025, P = 0.003$ ) [Table 2, Figure 2]. Lactate, HR, MAP, and Hb

values were not different between the groups during the time points ( $p > 0.05$ ) [Table 2].

Postoperative characteristics are given in Table 3. There were no significant differences between the groups concerning increase in serum creatinine levels, chest tube drainage, blood product transfusion, duration of mechanical ventilation, ICU stay duration or mortality ( $p > 0.05$ ).

## DISCUSSION

The main results of our study showed that; the rRAP group had a significantly lower fHb levels compared to the cCPB group at 10<sup>th</sup> minute of antegrade cerebral perfusion (T3), 30<sup>th</sup> minute after declamping of aorta (T4), and at sternum

**Table 1: Preoperative and intraoperative characteristics of study patients**

Characteristics	Group rRAP (n:18)	Group cCPB (n:18)	p value
Age (years) (Mean $\pm$ SD)	55.67 $\pm$ 10.6	52.11 $\pm$ 16.3	0.447
Gender (Female:Male)	2:16	4:14	0.371
Body Mass Index (Mean $\pm$ SD)	26.27 $\pm$ 3.03	27.97 $\pm$ 4.98	0.227
Euroscore II (Median, Min-Max)	2.06 (0.77-5.05)	2.89 (0.96-13.4)	0.359
Diabetes Mellitus (n/%)	2 (11.1)	1 (5.6)	0.546
Hypertension (n/%)	16 (88.9)	13 (72.2)	0.201
Hypercholesterolemia (n/%)	3 (16.7)	5 (27.8)	0.423
Total surgical procedure time (min) (Mean $\pm$ SD)	345 $\pm$ 71	384 $\pm$ 106	0.115
Cardiopulmonary bypass time (min) (Mean $\pm$ SD)	136 $\pm$ 33	146 $\pm$ 34	0.091
Aortic cross-clamping time (min) (Mean $\pm$ SD)	98 $\pm$ 29	103 $\pm$ 26	0.118
Total volume of priming solution (ml) (Mean $\pm$ SD)	1057 $\pm$ 157	1916 $\pm$ 222	<0.001
Total operation fluid volume (ml) (Mean $\pm$ SD)	2543 $\pm$ 482	3911 $\pm$ 513	<0.001
1 unite RBC transfusion (n/%)	6 (33.3)	7 (38.9)	0.155
Total urine output (ml) (Mean $\pm$ SD)	1300 $\pm$ 599	1533 $\pm$ 623	0.260

**Table 2: Free Hemoglobin, lactate, hemoglobin levels and hemodynamic parameters**

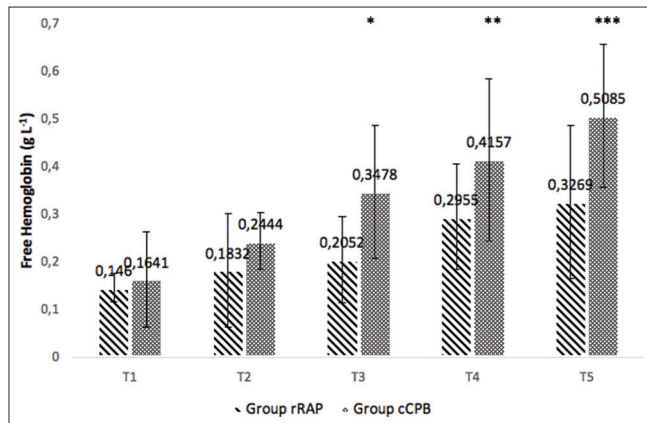
	T1 Mean $\pm$ SD	T2 Mean $\pm$ SD	T3 Mean $\pm$ SD	T4 Mean $\pm$ SD	T5 Mean $\pm$ SD
<b>fHb (<math>\text{g L}^{-1}</math>)</b>					
Group rRAP	0.1460 $\pm$ 0.03	0.1832 $\pm$ 0.12	0.2052 $\pm$ 0.09	0.2955 $\pm$ 0.11	0.3269 $\pm$ 0.16
Group cCPB	0.1641 $\pm$ 0.10	0.2444 $\pm$ 0.06	0.3478 $\pm$ 0.14	0.4157 $\pm$ 0.17	0.5085 $\pm$ 0.15
p value	0.490	0.078	0.002*	0.025*	0.003*
<b>Lactate (<math>\text{mmol L}^{-1}</math>)</b>					
Group rRAP	0.81 $\pm$ 0.4	2.40 $\pm$ 1.1	3.48 $\pm$ 1.4	4.52 $\pm$ 2.1	3.45 $\pm$ 2.0
Group cCPB	0.87 $\pm$ 0.3	2.65 $\pm$ 1.0	3.22 $\pm$ 1.7	5.08 $\pm$ 1.9	4.10 $\pm$ 1.4
p value	0.596	0.512	0.635	0.412	0.278
<b>Hb (<math>\text{g dL}^{-1}</math>)</b>					
Group rRAP	14.16 $\pm$ 1.7	9.49 $\pm$ 1.8	9.16 $\pm$ 1.4	8.70 $\pm$ 1.3	8.91 $\pm$ 1.0
Group cCPB	13.13 $\pm$ 1.5	8.91 $\pm$ 1.6	8.32 $\pm$ 1.2	8.32 $\pm$ 1.0	9.03 $\pm$ 1.2
p value	0.066	0.334	0.065	0.357	0.759
<b>MAP (mmHg)</b>					
Group rRAP	78.25 $\pm$ 9.6	56.01 $\pm$ 9.1	43.77 $\pm$ 8.9	63.83 $\pm$ 11.1	63.40 $\pm$ 9.9
Group cCPB	72.12 $\pm$ 9.3	55.18 $\pm$ 7.4	45.77 $\pm$ 9.1	57.59 $\pm$ 9.7	60.81 $\pm$ 5.2
p value	0.061	0.791	0.511	0.082	0.336
<b>HR (bpm)</b>					
Group rRAP	61.94 $\pm$ 8.2	72.85 $\pm$ 14.0	-	82.50 $\pm$ 12.8	82.66 $\pm$ 12.6
Group cCPB	63.88 $\pm$ 14.9	89.57 $\pm$ 24.8	-	75.41 $\pm$ 16.1	84.22 $\pm$ 12.3
p value	0.706	0.147	-	0.159	0.712

\* The rRAP group had a significantly lower increase in fHb levels in T3, T4 and T5 time points, when compared to the cCPB group. fHb: Plasma free hemoglobin, Hb: Hemoglobin, MAP: Mean arterial pressure, HR: Heart rate

**Table 3: Postoperative characteristic**

	Group rRAP	Group cCPB	p value
Number of patients with increase $>0.3$ mg dL <sup>-1</sup> in serum creatinine* (n/%)	3 (16.7)	4 (22.2)	0.674
Chest tube drainage ml (Median, Min-Max)	600 (600-2200)	800 (250-2800)	0.082
Number of patients with RBC-FFP transfusion n (%)	14 (51.9)	13 (48.1)	0.700
Duration of mechanical ventilation (hr) (Median, Min-Max)	9.5 (6-20)	8.5 (6-72)	0.873
Length of stay in ICU (hr) (Median, Min-Max)	21.5 (14-48)	20 (12-480)	0.812

\*Patients with 0.3 mg dL<sup>-1</sup> increase in POD1 measured creatinine compared to baseline. RBC: Red Blood Cell, FFP: Fresh Frozen Plasma, ICU: Intensive Care Unit



**Figure 2:** Serial changes of fHb at different time points during the surgery in the groups. \* $p = 0.002$ , \*\* $p = 0.025$ , \*\*\* $p = 0.003$

closure (T5) time points. The duration of postoperative mechanical ventilation, ICU stay, and chest tube drainage were similar between groups. It was observed that rRAP did not make a difference in terms of blood and blood product transfusion rates.

The CPB circuit includes a pump, oxygenator, aspiration cannules, and filters, all of which cause erythrocyte damage, leading to elevated plasma fHb levels.<sup>[15]</sup> Parameters all above and CPB duration and transfusion rate, which could increase fHb levels, were similar between groups and the same pump systems were used in all patients. Therefore, we suggest that fHb changes are related to the fluid status and the decrease in fHb increase rate shown by fluid restriction + RAP are promising.

Increasing evidence has shown that aggressive crystalloid-based fluid therapies are associated with coagulation disturbances, and immunological and inflammatory mediator dysfunctions.<sup>[16]</sup> The cellular membranes are highly permeable to fluids and can not tolerate significant gradients in hydrostatic pressure. As large volumes of fluids are administered, imbalances in intracellular and extracellular osmolarity occur. This may impair cellular regulatory mechanisms.<sup>[17]</sup> Due to impaired cellular function, cellular swelling can lead to cytosolic acidification, disruption of intracellular signaling mechanisms, disruption of numerous regulatory mechanisms of the inflammatory cascade.<sup>[16]</sup>

Both before and after surgery, fHb is considered a potential marker in organ damage.<sup>[6,18,19]</sup> Haptoglobin, an important physiological regulator of fHb levels, shows an inverse relationship with fHb for all results. Higher fHb levels and lower haptoglobin levels have been suggested to be linked to poor clinical outcomes.<sup>[6]</sup> In our study where haptoglobin values were not investigated, no difference was observed in outcome parameters in patients with a lesser fHb increase. This result may indicate that fHb is not a valuable biomarker indicating clinically significant organ dysfunction. It appears that further studies with more patients and detailed research are required to interpret changes in fHb and haptoglobin plasma levels.

In cardiac surgery, plasma fHb levels of patients who developed acute kidney injury (AKI) in the postoperative period were found to be 2-fold higher.<sup>[20,21]</sup> There was no difference in creatinine value between groups in our study. Grade I creatinine increase was observed in 3 (16.7%) of 18 patients with rRAP and 4 (22.2%) of 18 patients with cCPB. The absence of fHb and creatinine follow-up on other postoperative days was the limitation of this study in terms of detecting AKI. The development of AKI in cardiac surgery should be considered as multifactorial, such as ischemia-reperfusion injury, blood transfusion, long CPB and aortic cross-clamping times, impaired renal perfusion, and vasopressor use.<sup>[22]</sup>

In our study, postoperative chest tube drainage was slightly lower in the rRAP group, however, there was no difference in intraoperative and postoperative blood product transfusion rates. It has been shown that with RAP, excessive hemodilution is prevented and relatively higher hematocrit levels are achieved during and after CPB, thereby reducing the need for blood transfusion.<sup>[2,23,24]</sup> In another study it has been said that the RAP method reduces the need for perioperative blood transfusion, but has no effect on the clinical outcome.<sup>[25]</sup> But on the other hand, similar to ours, there are those who argue that the effect of RAP on intraoperative Hb values and the use of postoperative blood transfusion is minimal.<sup>[26,27]</sup> Another studies suggest that the RAP method caused a decrease in hospital stay, but did not affect postoperative blood

transfusion rates.<sup>[28]</sup> As has always been said, unfortunately, blood and blood product transfusions are not related to the patient, but to the doctor. Although patient blood management practices, which RAP is a part of, are frequently discussed, some more time is needed for this to be reflected in daily practice.

The risk of aortic disease increases with age due to many factors such as high oxidative stress, endothelial dysfunction and arterial wall changes.<sup>[29]</sup> In complex cardiac surgeries like aortic surgery, the duration of cardiopulmonary bypass and myocardial and cerebral protection time is prolonged. Long periods of myocardial ischemia or cardiopulmonary bypass increase the risk of morbidity.<sup>[30]</sup> Considering that we could find a more striking result, we chose this type of surgery with high oxidative stress, longer operation time, and higher risk of bleeding and morbidity in our study. Because of these features of aortic surgery, successful case histories are seen in the literature. Valleley and *et al.*<sup>[31]</sup> performed an aortic surgery on a patient with a Jehovah's Witness without transfusion, taking all blood conservative measures, including RAP. Keeling and *et al.*<sup>[32]</sup> has announced a successful case of aortic surgery with preoperative blood donation and perfusion strategies. In a study of pediatric cardiac surgery, randomized to washed versus standard red blood cells transfused, washed transfusions have been claimed to reduce some of the proinflammatory effects of transfusion possibly by reducing supernatant fHb. They found that children who had open heart surgery had an increasing risk of postoperative infection, thrombosis and mechanical ventilation, increasing peak blood lactate and decreasing mean arterial pressure and decreasing haptoglobin levels on day 1 and 2 as fHb levels increased.<sup>[7]</sup> The authors said that these results could not be fully explained by the transfusion, the storage time of the RBCs, the severity of the anatomical lesion, the duration of the CPB, the surgical complexity, and they suggested investigating why some patients had higher levels of free Hb before surgery and transfusion. Combining our results and the results of this study, it is possible that fHb is only measures of severity of comorbidity or unbalanced anatomy rather than causal physiological mediators. Hypertension, which is highly observed comorbidity in both groups in our study, is likely to have an effect on all inflammatory and oxidative markers. It seems that intraoperative anesthesia and CPB management should be balanced by avoiding excessive hemodilution and hypovolemia, and appropriate global oxygen delivery should be provided, especially in patients with complex cardiac surgery and hypertension. In our study in aortic surgery, it can be suggested that the increase in fHb levels, which can be increased due to many

preoperative and intraoperative reasons mentioned above, can be limited with the restrictive RAP method.

In conclusion, rRAP is a simple procedure that does not require high cost or advanced technology. We would like to emphasize that the increase in fHb levels were significantly low with rRAP application in aortic surgery, mechanical ventilation and ICU duration, chest tube drainage, blood and blood product transfusion rates were not changed. To our knowledge, there is no other study in the literature that has investigated fHb during rRAP procedure. Therefore, despite our limitations, we think that our findings will be instructive for other studies.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

### REFERENCES

1. Barry AE, Chaney MA, London MJ. Anesthetic management during cardiopulmonary bypass: A systematic review. *Anesth Analg* 2015;120:749-69.
2. Hofmann B, Kaufmann C, Stiller M, Neitzel T, Wienke A, Silber RE, *et al.* Positive impact of retrograde autologous priming in adult patients undergoing cardiac surgery: A randomized clinical trial. *J Cardiothorac Surg* 2018;13:1-8.
3. Myers GJ, Wegner J. Endothelial glycocalyx and cardiopulmonary bypass. *J Extra Corpor Technol* 2017;49:174-81.
4. Vercaemst L. Hemolysis in cardiac surgery patients undergoing cardiopulmonary bypass: A review in search of a treatment algorithm. *J Extra Corpor Technol* 2008;40:257-67.
5. Ulugol H, Aksu U, Kocyigit M, Kilercik M, Karduz G, Okten M, *et al.* Comparative effects of blood and crystalloid cardioplegia on cellular injury and oxidative stress in cardiovascular surgery. *Ann Thorac Cardiovasc Surg* 2019;25:10-7.
6. Cholette JM, Pietropaoli AP, Henrichs KF, Alfieri, Powers KS, Gensini F, *et al.* Elevated free hemoglobin and decreased haptoglobin levels are associated with adverse clinical outcomes, unfavorable physiologic measures, and altered inflammatory markers in pediatric cardiac surgery patients. *Transfusion* 2018;58:1631-9.
7. Cholette JM, Henrichs KF, Alfieri GM, Powers KS, Phipps R, Spinelli SL, *et al.* Washing red blood cells and platelets transfused in cardiac surgery reduces post-operative inflammation and number of transfusions: Results of a prospective, randomized, controlled clinical trial. *Pediatr Crit Care Med* 2012;13:290-9.
8. Rosengart TK, DeBois W, O'Hara M, Helm R, Gomez M, Lang SJ, *et al.* Retrograde autologous priming for cardiopulmonary bypass:

- A safe and effective means of decreasing hemodilution and transfusion requirements. *J Thorac Cardiovasc Surg* 1998;115:426–39.
9. Pearse RM, Harrison DA, MacDonald N, Gillies MA, Blunt M, Ackland G, *et al.* Effect of a perioperative, cardiac output-guided hemodynamic therapy algorithm on outcomes following major gastrointestinal surgery: A randomized clinical trial and systematic review. *JAMA* 2014;311:2181–90.
  10. Asklid D, Segelman J, Gedda C, Hjern F, Pekkari K, Gustafsson UO. The impact of perioperative fluid therapy on short-term outcomes and 5-year survival among patients undergoing colorectal cancer surgery- A prospective cohort study within an ERAS protocol. *Eur J Surg Oncol* 2017;43:1433–9.
  11. Neal JM, Wilcox RT, Allen HW, Low DE. Near-total esophagectomy: The influence of standardized multimodal management and intraoperative fluid restriction. *Reg Anesth Pain Med* 2003;28:328–34.
  12. Rosenfeldt F, Wilson M, Lee G, Kure C, Ou R, Braun L, *et al.* Oxidative stress in surgery. In: Laher I, editor. *Systems Biology of Free Radicals and Antioxidants*. Berlin Germany: Springer; 2014. p. 3929–46.
  13. Harboe M. A method for determination of hemoglobin in plasma by near-ultraviolet spectrophotometry. *Scand J Clin Lab Invest* 1959;11:66–70.
  14. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, *et al.* Acute kidney injury network: Report of an initiative to improve outcomes in acute kidney injury. *Crit Care* 2007;11:R31.
  15. Billings FT, Yu C, Byrne JG, Petracek MR, Pretorius M. Heme oxygenase-1 and acute kidney injury following cardiac surgery. *Cardiorenal Med* 2014;4:12–21.
  16. Cotton BA, Guy JS, Morris JA, Abumrad NN. The cellular, metabolic, and systemic consequences of aggressive fluid resuscitation strategies. *Shock* 2006;26:115–21.
  17. Lang F, Busch GL, Ritter M, Völkl H, Waldegger S, Gulbins E, *et al.* Functional significance of cell volume regulatory mechanisms. *Physiol Rev* 1998;78:248–73.
  18. Gladwin MT, Kaniyas T, Kim-Shapiro DB. Hemolysis and cell-free hemoglobin drive an intrinsic mechanism for human disease. *J Clin Invest* 2012;122:1205–8.
  19. Rapido F, Brittenham GM, Bandyopadhyay S, La Carpia F, L'Acqua C, McMahan DJ, *et al.* Prolonged red cell storage before transfusion increases extravascular hemolysis. *J Clin Invest* 2017;127:375–82.
  20. Billings IV FT, Ball SK, Roberts II LJ, Pretorius M. Postoperative acute kidney injury is associated with hemoglobinemia and an enhanced oxidative stress response. *Free Radic Biol Med* 2011;50:1480–7.
  21. Windsant ICV, Snoeijs MG, Hanssen SJ, Altıntaş S, Heijmans JH, Koepfel TA, *et al.* Hemolysis is associated with acute kidney injury during major aortic surgery. *Kidney Int* 2010;77:913–20.
  22. O'Neal JB, Shaw AD, Billings FT. Acute kidney injury following cardiac surgery: Current understanding and future directions. *Crit Care* 2016;20:1–9.
  23. Hwang J, Huh J, Kim J, Park S, Hwang J, Nahm FS, *et al.* The effect of retrograde autologous priming of the cardiopulmonary bypass circuit on cerebral oxygenation. *J Cardiothorac Vasc Anesth* 2011;25:995–9.
  24. Trapp C, Schiller W, Mellert F, Halbe M, Lorenzen H, Welz A, *et al.* Retrograde autologous priming as a safe and easy method to reduce hemodilution and transfusion requirements during cardiac surgery. *Thorac Cardiovasc Surg* 2015;63:628–34.
  25. Sun P, Ji B, Sun Y, Zhu X, Liu J, Long C, *et al.* Effects of retrograde autologous priming on blood transfusion and clinical outcomes in adults: A meta-analysis. *Perfusion* 2013;28:238–43.
  26. Murphy GS, Szokol JW, Nitsun M, Alspach DA, Avram MJ, Vender JS, *et al.* The failure of retrograde autologous priming of the cardiopulmonary bypass circuit to reduce blood use after cardiac surgical procedures. *Anesth Analg* 2004;98:1201–7.
  27. Nanjappa A, Gill J, Sadat U, Colah S, Abu-Omar Y, Nair S. The effect of retrograde autologous priming on intraoperative blood product transfusion in coronary artery bypass grafting. *Perfusion* 2013;28:530–5.
  28. Kearsey C, Thekkudan J, Robbins S, Ng A, Lakshmanan S, Luckraz H. Assessing the effectiveness of retrograde autologous priming of the cardiopulmonary bypass machine in isolated coronary artery bypass grafts. *Ann R Coll Surg Engl* 2013;95:207–10.
  29. Dai X, Hummel SL, Salazar JB, Taffet GE, Zieman S, Schwartz JB. Cardiovascular physiology in the older adults. *J Geriatr Cardiol* 2015;12:196–201.
  30. Apaydin AZ, Islamoglu F, Posacioglu H, Yagdi T, Atay Y, Calkavur T, *et al.* Clinical outcomes in “complex” thoracic aortic surgery. *Tex Heart Inst J* 2007;34:301–4.
  31. Valleley MS, Glogowski KR, Duncan KF, Dutoit A, Hagedorn C. Bloodless repair of aortic arch with dual aortic cannulation in a Jehovah's witness patient. *J Extra Corpor Technol* 2017;49:206–9.
  32. Keeling WB, Kerendi F, Chen EP. Total aortic arch replacement for the treatment of Kommerell's diverticulum in a Jehovah's Witness. *J Card Surg* 2010;25:333–5.