Online July 24, 2019
doi: 10.5761/atcs.oa.19-00106

Original Article

Effect of Autotransfusion Using Intraoperative Predonated Autologous Blood on Coagulopathy during Thoracic Aortic Surgery: A Randomized Controlled Trial

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Background: Intraoperative predonated autologous blood transfusion is thought to replenish platelets and coagulation factors and ameliorate coagulopathy. This study aimed to evaluate whether intraoperative predonated autotransfusion improves coagulopathy during thoracic aortic surgery.
Methods: Patients who underwent thoracic aortic surgery were randomized into two groups as follows: those who received intraoperative predonated blood (group A: n = 31) and those who did not receive (group N: n = 22). In group A, autologous blood was retransfused immediately after cessation of cardiopulmonary bypass (c-CPB).
Results: The mean intraoperative allogenic blood or blood product transfusion requirements were significantly lesser in group A than in group N (packed red blood cells [RBCs]: 6.3 ± 5.1 vs. 9.1 ± 4.3 units, p = 0.04; fresh frozen plasma [FFP]: 3.0 ± 4.1 vs. 6.1 ± 5.7 units, p = 0.03). After c-CPB, hemoglobin (Hb) level, platelet count, and coagulopathy became significantly worse than those at the start of surgery in both the groups. However, the values significantly improved 30 min after c-CPB only in group A. Renal function was significantly worse in group N.
Conclusions: Intraoperative predonated autotransfusion significantly improved coagulopathy, with reduced allogeneic blood transfusion volume during thoracic aortic surgery. Furthermore, reduction of allogeneic blood transfusion may reduce the adverse effects on renal function.

Keywords: autotransfusion, intraoperative predonation, coagulopathy, thoracic aortic surgery

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Received: April 15, 2019; Accepted: June 2, 2019
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Introduction

Cardiopulmonary bypass (CPB) is associated with coagulopathy and platelet count reduction.[1)] In patients undergoing thoracic aortic surgery in particular, prolonged CPB and circulatory arrest with hypothermia result in more pronounced alterations of the coagulation systems.[2)] Bleeding induced by coagulopathy requires transfusion of allogeneic blood or blood products. Fresh frozen plasma (FFP) and platelets include coagulation factors and thus ameliorate coagulopathy. However, from the point of view of the side effects associated with autologous transfusions, allogeneic blood transfusions, rather than autologous transfusion, have many adverse effects, including anaphylactic shock and transfusion-related acute lung injury. In addition, transfusion-transmitted viral infections such as hepatitis and human immunodeficiency virus (HIV) or graft-versus-host disease may occur in case of allogenic blood transfusion. Therefore, autotransfusion is considered safer than allogeneic blood transfusion. Furthermore, the amount of blood transfusion is associated with long-term adverse events.[3]

Concerning intraoperative predonated autotransfusion, autologous blood is collected before CPB and retransfused intraoperatively after CPB. This technique reduces the amount of allogeneic blood transfusion. Furthermore, it ameliorates coagulopathy because predonated autologous blood replenishes platelets and coagulation factors.[4–7] This technique has been established for coronary artery bypass grafting (CABG), in which the storage time of autologous blood is very short. However, the efficacy of autotransfusion using the intraoperative predonation technique for thoracic aortic surgery, in which the procedure is much longer for CPB than for CABG, has not been fully estimated yet.

The aim of this study was to evaluate whether autotransfusion using an intraoperative predonation technique improves coagulopathy during thoracic aortic surgery with moderate hypothermic circulatory arrest (MHCA).

Patients and Methods

Study design

This randomized study was implemented with the approval of the institutional review board of Yamaguchi University Hospital. Informed consent was obtained from all the patients; the study was registered at the University Hospital Medical Information Network Center (UMIN000009986; https://upload.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000011512). In all, 53 adult patients who underwent total or hemi-aortic arch replacement with MHCA were randomized into two groups to either receive or not receive intraoperative predonated autotransfusion between March 2012 and February 2014 (for 2 years). The subjects included 62 patients during this period; however, nine patients were excluded because we could not obtain their consent. We divided the 53 patients into two groups: group A and group N. In group A, 31 patients received intraoperative predonated autotransfusion and allogeneic transfusion, and in group N, 22 patients did not receive intraoperative predonated autotransfusion. The patients were followed up until December 2016.

The analysis was based on the results of the reduction of the prothrombin time international normalized ratio (PT-INR) from 2.74 to 1.65 (standard deviation [SD], 0.6) in patients who received intraoperative predonated autotransfusion in the previous study. The required sample size was calculated to be at least 12 patients in both the groups, with a statistical power of 80%. In all, 20 sealed envelopes were prepared (1:1 ratio, no stratification). When the patient was accepted for enrollment in the study, a person without any involvement in the study opened the envelope. In total, 20 additional envelopes were prepared during the study period. The investigators were not blinded.

Exclusion criteria

We excluded patients who met the following criteria: (1) severe hypotension; (2) *Treponema pallidum* hemagglutination assay (TPHA), hepatitis B surface antigen, hepatitis C virus or HIV infection positive; (3) fever (body temperature of >38°C); (4) tooth extraction within 72 hours before the operation; (5) bacillemia; and (6) judged as unsuitable.

Anesthetic management

All the patients were placed in the supine position and monitored with five-lead electrocardiography. In addition, an arterial line and a pulmonary artery catheter were used for monitoring hemodynamic parameters. Brain oxygenation was monitored using near-infrared spectroscopy. Transcranial Doppler ultrasonography was used to measure the cerebral parameters, and esophageal, bladder, and rectal temperatures were monitored during operation.

Surgical technique

In all cases, the chest was opened via a median sternotomy under general anesthesia. The bilateral axillary arteries were exposed for arterial cannulation. CPB was established with bilateral axillary arterial cannulation and bicaval drainage. The patient's body temperature was cooled down to 25°C and measured rectally, followed by implementation of lower body circulatory arrest with moderate hypothermia. Antegrade selective cerebral perfusion was established by axillary perfusion with clamped brachiocephalic and left subclavian arteries and by direct cannulation of the left common carotid artery. Antegrade cold blood cardioplegia was administered to achieve and maintain cardiac arrest. Open distal anastomosis was first performed. The arch vessels were reconstructed individually, and finally, proximal anastomosis was completed.

Table 1 Preoperative characteristics

	Group A (n = 31)	Group N (n = 22)	p value
Age (year)	69.2 ± 9.7	70.1 ± 7.7	0.71
Male:female (n)	18:13	12:10	>0.99
Weight (kg)	59.4 ± 13.5	60.2 ± 11.8	0.84
Hb (g/dL)	12.1 ± 1.9	11.7 ± 1.9	0.40
Platelet (10^4µL)	18.5 ± 7.4	18.5 ± 8.6	0.98
GFR (mL/min/1.73 m^2)	68.9 ± 4.8	58.7 ± 28.6	0.19
Hypertension (n, %)	26 (83.9%)	19 (86.4%)	>0.99
Dyslipidemia (n, %)	10 (32.3%)	8 (36.4%)	0.78
Diabetes mellitus (n, %)	4 (12.9%)	5 (22.7%)	0.469
Current smoker (n, %)	4 (12.9%)	6 (27.3%)	0.29
Chronic lung disease (n, %)	4 (12.9%)	2 (9.1%)	>0.99
Reoperation (n, %)	1 (3.2%)	0 (0%)	>0.99
Emergency (n, %)	12 (38.7%)	8 (36.4%)	>0.99
Aortic pathology			0.69
Acute aortic dissection (n, %)	12 (38.7%)	8 (36.4%)	
Chronic aortic dissection (n, %)	5 (16.1%)	2 (9.1%)	
Aneurysm (n, %)	14 (45.2%)	12 (54.5%)	
JapanSCORE (%)			
30-day operative mortality	6.9 ± 4.4	9.1 ± 8.2	0.22
EuroSCORE II (%)	5.2 ± 3.2	7.3 ± 7.6	0.18

eGFR: estimated glomerular filtration rate; Hb: hemoglobin

Table 2 Operative data

	Group A (n = 31)	Group N (n = 22)	p value
Operation mode			0.63
Total arch replacement (n, %)	28 (90.3%)	21 (95.5%)	
Hemi-arch replacement (n, %)	3 (9.7%)	1 (4.5%)	
Operation time (min)	593 ± 102	608 ± 111	0.63
CPB time (min)	330 ± 65	336 ± 52	0.72
Aortic clamp time (min)	251 ± 61	245 ± 47	0.70
SCP time (min)	157 ± 64	180 ± 48	0.15
LBCA time (min)	101 ± 31	108 ± 30	0.39
Lowest rectal temperature (°C)	23.4 ± 1.2	23.5 ± 1.1	0.70

CPB: cardiopulmonary bypass; LBCA: lower body circulatory arrest; SCP: selective cerebral perfusion

Intraoperative predonation harvest technique and transfusion practice

In group A, autologous blood was collected from the femoral arterial line before CPB. Approximately 15–20 mL/kg whole blood was collected prior to the systemic administration of heparin. The collected blood was stored in citrate phosphate dextrose in an adenine bag and retransfused after cessation of CPB (c-CPB). In all patients, a cell-saving device was used before CPB and after c-CPB. The blood transfusion requirement was determined by the anesthesiologist, perfusionist, and surgeon. The lowest hematocrit was maintained at ≥20%, and when necessary, only allogeneic red blood cell (RBC) transfusion was given during CPB in both the groups. In group N, no allogeneic blood transfusion during 30 minutes after c-CPB was administered to compare the differences in the blood components and parameters of coagulopathy between the groups.

Blood sampling

Blood samples were obtained to evaluate the blood components and coagulation profile at the start of surgery, during c-CPB, 30 minutes after c-CPB, and at the end of surgery. We compared the amount of intraoperative transfusion requirements and early and mid-term clinical outcomes.

Statistical analyses

Quantitative data are expressed as mean ± SD. Statistical comparisons between the two groups were performed

Table 3 Intraoperative blood loss and transfusion

	Group A (n = 31)	Group N (n = 22)	p value
Autologous predonation volume (g)	1099 ± 308	-	-
Blood loss (g)	654 ± 429	784 ± 449	0.29
Blood transfusion			
RBC (unit)	6.3 ± 5.1	9.1 ± 4.3	0.04
FFP (unit)	3.0 ± 4.1	6.1 ± 5.7	0.03
Platelets (unit)	22.3 ± 6.2	21.4 ± 4.7	0.57
Non-RBC usage (n, %)	5 (16.1%)	0 (0%)	0.04
Non-FFP usage (n, %)	17 (54.8%)	6 (27.3%)	0.04

FFP: fresh frozen plasma; RBC: red blood cell

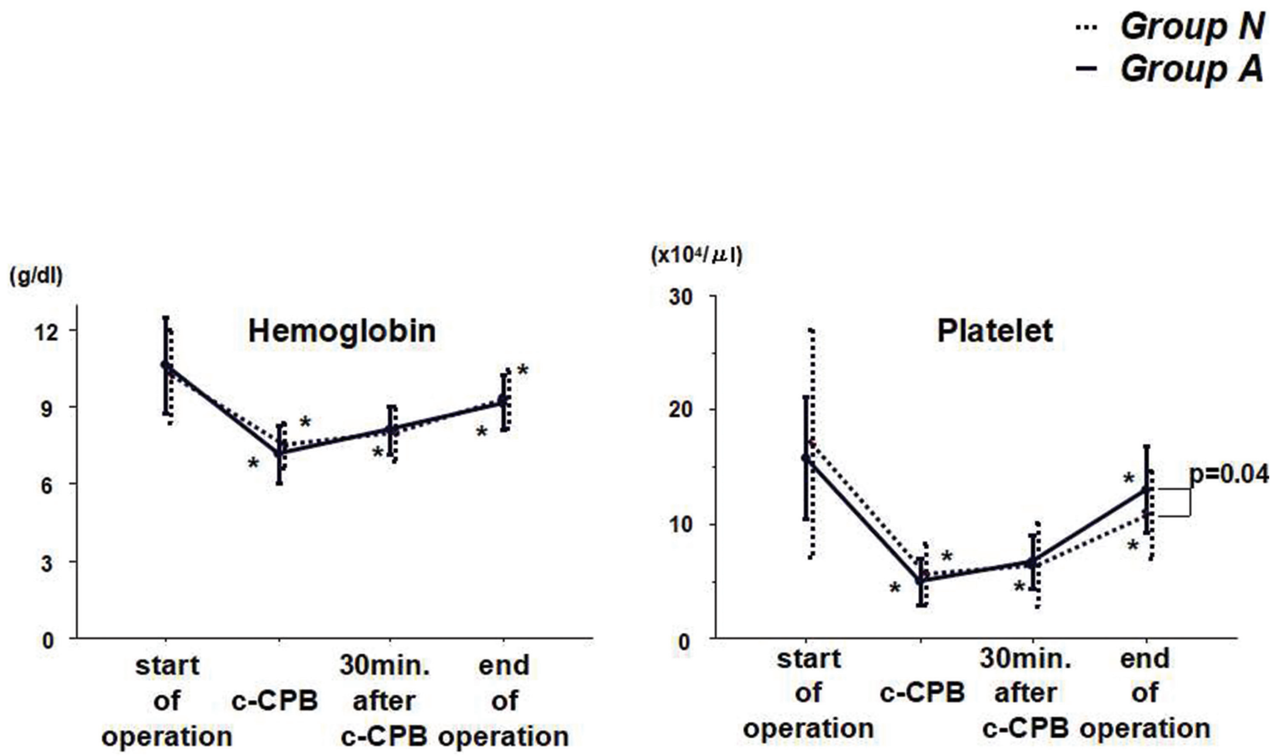

Fig. 1 Hb level and platelet count. The serial changes in Hb and platelet counts. A transient worsening of Hb level and platelet count was observed during c-CPB in both groups. However, in group A, Hb level and platelet count recovered 30 minutes after the c-CPB. In group N, the levels did not recover (*p <0.01, vs. the previous value). c-CPB: cessation of cardiopulmonary bypass; Hb: hemoglobin

using an unpaired Student's *t*-test or the Fisher's exact test and a log-rank test using the StatView 5.0 software (SAS Institute Inc., Cary, NC, USA). P values of <0.05 were considered statistically significant.

Results

Preoperative characteristics such as age, sex, weight, preoperative hemoglobin (Hb) level, preoperative estimated glomerular filtration rate (eGFR), and emergency rate were similar between the two groups (**Table 1**). The surgical data of the patients were not significantly different between the two groups (**Table 2**).

The volume of intraoperative blood loss and required amount of allogenic blood transfusion are shown in **Table 3**. The mean blood loss was 654 ± 429 g in group A and 784 ± 449 g in group N, but did not reach a statistically significantly difference. However, the mean required amount of intraoperative allogenic blood transfusion was significantly lesser in group A than in group N (mean amount of RBCs: 6.3 vs. 9.1 units, p = 0.04; mean amount of FFP: 3.0 vs. 6.1 units, p = 0.03).

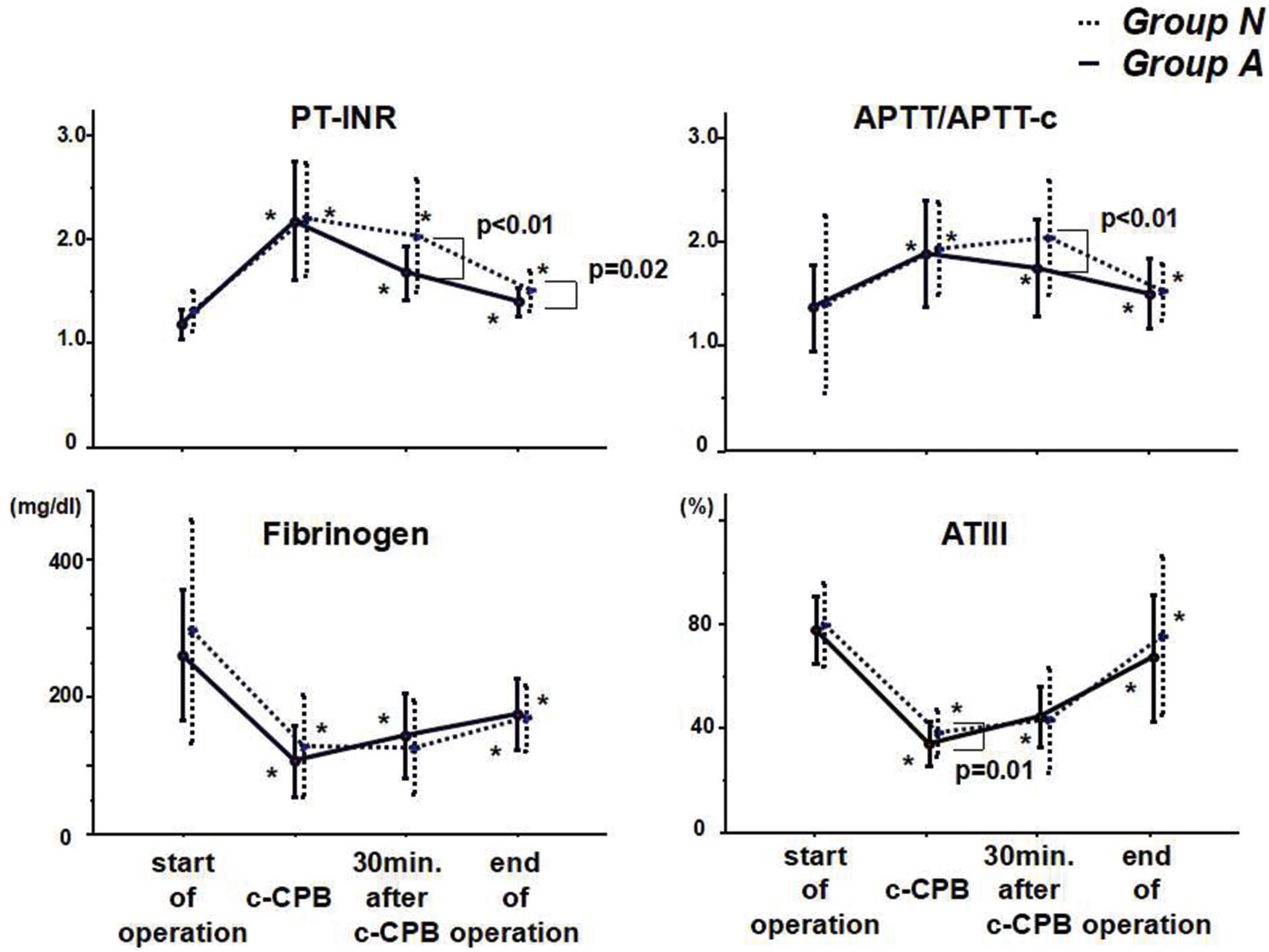

Fig. 2 Serial changes of coagulation factors. A transient worsening in coagulation factors was observed during c-CPB in both groups. However, the coagulation factors recovered 30 minutes after c-CPB in group A but not in group N, except for PT-INR. In group A, PT-INR and APTT recovered 30 minutes after the start of c-CPB more than those in group N (*p < 0.01, vs. the previous value). APTT: activated partial thromboplastin time; c-CPB: cessation of cardiopulmonary bypass; PT-INR: international normalized ratio of prothrombin time

Similarly, cases without RBC (non-transfusion with allogenic RBCs) and transfusions (non-transfusion with an allogenic FFP) were significantly more frequent in group A than in group N (non-RBC use rate: 16.1% vs. 0%, p = 0.04; non-FFP use rate: 54.8% vs. 27.3%, p = 0.04; **Table 3**).

We assessed the serial changes in Hb level, platelet count (**Fig. 1**), and coagulation factors (**Fig. 2**). A transient exacerbation of Hb level, platelet count, and coagulation factors were observed during c-CPB in both groups. However, in group A, the Hb level, platelet count, and coagulation factors recovered after autologous blood retransfusion. Most notably, PT-INR and activated partial thromboplastin time (APTT) recovered 30 minutes after c-CPB in group A but not in group N. In both the groups, coagulation factor levels also recovered at the end of surgery.

No hospital deaths occurred in either group, and no significant differences in postoperative data were found between the two groups, including reoperation for bleeding, except for the lowest eGFR values (**Table 4**). Reoperation for bleeding was required in one case in group A and two cases in group N. However, these were not due to coagulopathy. Although preoperative eGFR was similar in both groups, the lowest value during postoperative hospitalization was significantly higher in group A than in group N (lowest eGFR: 59.7 ± 26.0 vs. 43.9 ± 21.3 mL/[min·1.73 m^2], p = 0.02).

The postoperative survival rates of the patients are shown in **Fig. 3**. The 4-year survival rate was 84.6% in group A and 85.0% in group N. The postoperative survival rate was not significantly different between the two groups (p = 0.19).

Table 4 Postoperative data

	Group A (n = 31)	Group N (n = 22)	p value
Drainage (mL/8 h)	305.3 ± 220.1	500.9 ± 538.6	0.20
Lowest eGFR (mL/min/1.73 m^2)	59.7 ± 26.0	43.9 ± 21.3	0.02
Hospital mortality (n, %)	0 (0%)	0 (0%)	>0.99
Major complications (n, %)	6 (19.3%)	4 (18.2%)	>0.99
Reoperation for bleeding (n, %)	1 (3.2%)	2 (9.1%)	0.56
Newly dialysis (n, %)	0 (0%)	1 (4.5%)	0.42
Deep sternum infection (n, %)	1 (3.2%)	1 (4.5%)	>0.99
Stroke (n, %)	2 (6.5%)	0 (0%)	0.51
Prolonged ventilation (>24 h) (n, %)	4 (12.9%)	3 (13.6%)	0.56

eGFR: estimated glomerular filtration rate

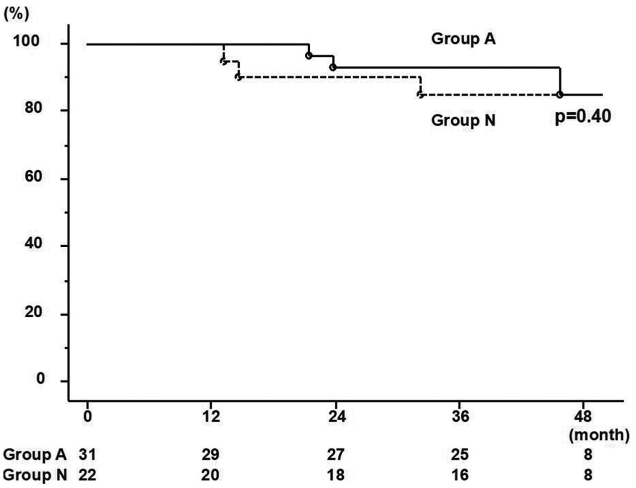

Fig. 3 Postoperative survival curve. Survival estimation according to the Kaplan–Meier method. The 4-year survival rate was 84.6% in group A and 85.0% in group N.

Comment

Our study indicated that autotransfusion using intraoperative predonation not only reduced the required amount of allogenic blood transfusion but also improved coagulopathy. Coagulopathy due to CPB gradually improved after the c-CPB, but autotransfusion using intraoperative predonation improved earlier and more clearly. To our knowledge, this is the first study to report the application of autotransfusion using intraoperative predonation in thoracic aortic surgery.

Autotransfusion using intraoperative predonation was first described by Dodrill.[8] Autotransfusion protocols were previously established using preoperative or intraoperative autologous blood predonation, the cell-saver technique, and the platelet-rich plasma apheresis technique. Autotransfusion using preoperative predonation must be prepared such that platelet or coagulation factors are consumed during storage, and the cell-saver technique is likely to cause the breakdown of RBCs. On the other hand, autotransfusion using intraoperative predonation may replenish platelet and coagulation factors and ameliorate coagulopathy because of its short storage time.[5,6] Furthermore, intraoperative predonation reduces Hb levels by supplementing extracellular fluid instead of whole blood and decreases the Hb level per milliliter of bleeding.[7] Autotransfusion using intraoperative predonation is thought to be useful; however, a few studies revealed the normalization of platelet and coagulation factors using the technique only during CABG.[5,6] One of the reasons is thought to be storage time. Platelet adhesiveness has been shown to be preserved during storage.[9] Flom-Halvorsen et al. demonstrated no indication of the presence of coagulation factors in pooled blood after approximately 1 hour.[10] As far as the storage time is concerned for coagulation factors, the shorter the storage time, the better. The storage time was approximately >5 hours in our study; however, platelet count and coagulation factors recovered after autologous blood retransfusion.

Early and mid-term outcomes were not significantly different between the two groups. Although the patients in the intraoperative predonation group experienced a milder exacerbation of renal function, no significant differences in the other postoperative factors were found, even in the amount of blood loss. Recent studies have shown improved surgical outcomes[11–13]; for this reason, no significant difference in mortality was observed in this study. As many previous studies reported, if the frequency of allogeneic blood transfusion could be reduced, the morbidity and acute kidney injury rates would decrease.[14–16] In addition, a reduction in allogeneic blood transfusion rate could occur, although the mean blood loss did not reach a statistically significant difference in this study.

The reason for this is that when proper blood transfusion is performed, blood loss can be controlled. Recently, Zhou et al.[17] reported the efficacy of autologous platelet-rich plasma for ascending aortic arch repair. It is beneficial because it reduces the risk of transfusion-transmitted diseases and anaphylactic shock caused by allogeneic blood transfusion. This technique improved coagulopathy and reduced allogeneic blood transfusions; however, it is slightly complicated. As autotransfusion using intraoperative predonation does not require the use of auxiliary tools, the process is simple and cost-effective.

In conclusion, autotransfusion using intraoperative predonation significantly improved coagulopathy, demonstrating a reduction in allogeneic blood transfusion rate during thoracic aortic repair with hypothermic circulatory arrest. This method has been suggested as a useful transfusion therapy during thoracic aortic surgery.

Limitations

We could not confirm by the subgroup analysis the emergency cases with preoperative coagulopathy such as acute aortic dissection. We do not have a large enough sample size for subgroup analysis, and coagulopathy is difficult to define on the basis of the preoperative values of the coagulation factors. We could not prove the possibility that this method is useful for patients with preoperative coagulopathy. After accumulating more cases, we would like to examine whether this technique improves coagulopathy in patients preoperatively.

Disclosure Statement

No conflict of interest is declared for this study.

References

1) Harker LA. Bleeding after cardiopulmonary bypass. N Engl J Med 1986; **314**: 1446-8.
2) Boldt J, Knothe C, Welters I, et al. Normothermic versus hypothermic cardiopulmonary bypass: do changes in coagulation differ? Ann Thorac Surg 1996; **62**: 130-5.
3) Koch CG, Li L, Duncan AI, et al. Transfusion in coronary artery bypass grafting is associated with reduced long-term survival. Ann Thorac Surg 2006; **81**: 1650-7.
4) Kochamba GS, Pfeffer TA, Sintek CF, et al. Intraoperative autotransfusion reduces blood loss after cardiopulmonary bypass. Ann Thorac Surg 1996; **61**: 900-3.
5) Whitten CW, Allison PM, Latson TW, et al. Evaluation of laboratory coagulation and lytic parameters resulting from autologous whole blood transfusion during primary aortocoronary artery bypass grafting. J Clin Anesth 1996; **8**: 229-35.
6) Flom-Halvorsen HI, Øvrum E, Øystese R, et al. Quality of intraoperative autologous blood withdrawal used for retransfusion after cardiopulmonary bypass. Ann Thorac Surg 2003; **76**: 744-8; discussion 748.
7) Schönberger JP, Bredée JJ, Tjian D, et al. Intraoperative predonation contributes to blood saving. Ann Thorac Surg 1993; **56**: 893-8.
8) Derbyshire AJ, Dodrill FD, Hughes CH, et al. The use of the heart-lung apparatus in human cardiac surgery. J Thorac Surg 1957; **33**: 60-74.
9) Hardesty RL, Bayer WL, Bahnson HT. A technique for the use of autologous fresh blood during open-heart surgery. J Thorac Cardiovasc Surg 1968; **56**: 683-8.
10) Vamvakas EC, Carven JH. Transfusion and postoperative pneumonia in coronary artery bypass graft surgery: effect of the length of storage of transfused red cells. Transfusion 1999; **39**: 701-10.
11) Tanaka Y, Mikamo A, Suzuki R, et al. Mortality and morbidity after total aortic arch replacement. Ann Thorac Surg 2014; **97**: 1569-75.
12) Okita Y, Okada K, Omura A, et al. Total arch replacement using antegrade cerebral perfusion. J Thorac Cardiovasc Surg 2013; **145**: S63-71.
13) Committee for Scientific Affairs, The Japanese Association for Thoracic Surgery, Masuda M, Okumura M, Doki Y, Endo S, et al. Thoracic and cardiovascular surgery in Japan during 2014: annual report by the Japanese Association for Thoracic Surgery. Gen Thorac Cardiovasc Surg 2016; **64**: 665-97.
14) Dietrich W, Thuermel K, Heyde S, et al. Autologous blood donation in cardiac surgery: reduction of allogeneic blood transfusion and cost-effectiveness. J Cardiothorac Vasc Anesth 2005; **19**: 589-96.
15) Kuduvalli M, Oo AY, Newall N, et al. Effect of peri-operative red blood cell transfusion on 30-day and 1-year mortality following coronary artery bypass surgery. Eur J Cardiothorac Surg 2005; **27**: 592-8.
16) Dzik WH, Fleisher AG, Ciavarella D, et al. Safety and efficacy of autologous blood donation before elective aortic valve operation. Ann Thorac Surg 1992; **54**: 1177-80; discussion 1180-1.
17) Zhou SF, Estrera AL, Loubser P, et al. Autologous platelet-rich plasma reduces transfusions during ascending aortic arch repair: a prospective, randomized, controlled trial. Ann Thorac Surg 2015; **99**: 1282-90.