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Research

Hemoadsorption and coagulation systemic rebalance in patients undergoing non-elective cardiac surgery and treated with anti-thrombotics

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Short Title: Hemoadsorption in cardiopulmonary bypass rebalances bleed & coagulation

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Abstract

Introduction: Insufficient withdrawal duration of antithrombotics leads to excessive bleeding after major surgery. We hypothesize that intraoperative hemoadsorption (HA) can reduce postoperative allogeneic transfusion requirements and excessive bleeding events (EBE), without an increase in ischemic/thromboembolic events (ITE) in patients who have taken antithrombotics and undergone nonelective cardiac surgery. **Methods:** A total of 460 patients admitted to our hospital from 2018 to 2022 were included in this study and divided into two groups: HA and non-HA. Because of the risk of bias due to differences in antithrombotic type, withdrawal duration or basic coagulation function, propensity score matching was used for analyses. **Results:** Out of 154 cases in the HA group, 144 pairs were successfully matched. No HA safety events such as hemolysis, hypotension or device failure occurred. After matching, the two groups were found to be comparable in preoperative antithrombotic type, withdrawal duration, platelets and coagulation function, and demographic and perioperative characteristics. Although the HA group did not have a reduced incidence of EBE, this group exhibited significant decreases in the transfusion rate and volume, the incidence of ITE, acute kidney injury and central nervous system injury. **Conclusions:** For patients who undergone nonelective cardiac surgery and taken antithrombotics, HA can simply and safely rebalance of postoperative coagulation system, have associations with reduced transfusion and postoperative ITE.

Introduction

Insufficient withdrawal time of antithrombotics is one of the risk factors for excessive bleeding, which impairs the outcome of open heart surgery[1–3]. Aspirin is a cyclooxygenase inhibitor, while clopidogrel is a P_2Y_{12} receptor inhibitor, both of which are platelet aggregation inhibitors that prevent thromboembolism in coronary artery disease. Anticoagulants designed to prevent venous thrombosis, such as warfarin, are the routine choice for patients with atrial fibrillation, atrial thrombus, stroke, deep vein thrombosis, and artificial valve implantation. All antithrombotics should be ceased 1-2 weeks before elective surgery; emergency or limit-term surgery may affect the function of platelets and coagulation factors due to insufficient antithrombotic withdrawal time, resulting in excessive bleeding, transfusion, and prolonged ICU and hospital stays [4].

Previous studies have suggested that when ticagrelor (a similar drug of clopidogrel) withdrawal duration is shorter than 24 hours before surgery, surgical related bleeding morbidities will increase significantly[5]. However, nonelective surgery makes no sufficient time to withdrawal, and the bleeding risk cannot be properly solved by preoperative platelet transfusion[6], because the circulative residual antithrombotics can continue to inhibit new platelets. In addition, the protein binding rate of clopidogrel is as high as 98%, and that of aspirin is more than 70%. The high protein binding characteristics make concentration decrease difficult through ultrafiltration or dialysis during surgery. Therefore, some researchers have started using cytokine adsorption devices in vitro to remove antithrombotics [7,8]. They found that within one hour of in vitro recirculation, 91% of the antithrombotics were removed from the blood. In a report evaluating the clearance effect of adsorption devices on antibiotics in a pig model, they found that 16/17 of their clearance rate can be improved[9]. A successful case was reported regarding the removal of apixaban (a kind of factor Xa inhibitor) by an adsorption device in a high-risk patient with a EuroScore of 54% in emergency mitral valve replacement[10].

According to the above, we hypothesize that high-risk bleeding patients who take long-term antithrombotics undergo nonelective open cardiac surgery, using a Hemoadsorption (HA) device during cardiopulmonary bypass (CPB), which can significantly reduce allogeneic transfusion perioperatively and postoperative cardiac surgery related excessive bleeding events (EBE), without increasing postoperative systemic infection, cardiac surgery related ischemic/thromboembolic events (ITE), or vital organ morbidities.

Methods

We performed a single center, ambispective observational study in Xiangya Hospital from January 1, 2018 to December 31, 2022. Retrospective or prospective depends on whether it is before September 2020 or after, because since then, HA was approved for cardiac surgery by the medical committee of our hospital to absorb harmful substances such as inflammatory factors, pathogenic factors, drugs, or toxins. The use of HA was determined by the surgeon or perfusionist based on the patient's condition. All nonelective CPB cardiac surgery patients with a history of long-term antithrombotics (withdrawal duration within seven days) were included. Meanwhile, the inclusion criteria included no medical or anesthetic contraindication for surgery, the absence of resin or plastic allergy, and acceptance of informed consent. They were divided into the HA group and the non-HA group according to whether the HA device (HA380, Jafron, China) was applied intraoperatively. Because bias exists in different types of antithrombotics, withdrawal durations or basic coagulation functions, the ethics review committee approved using the propensity score matching method in this study (202209620). We obtained informed consent to use patients' clinical data for medical research. The patients were excluded from the analysis for age<14 or >80 years old, pregnancy state, previous bleeding or coagulation disorders, vitamin K1 to reverse anticoagulation, allogenic transfusion, fever or systemic infection before surgery, heparin allergy, intraoperative unexpected blood loss ≥ 500 ml that cannot be saved, abnormal interruption or use of multiple HAs intraoperatively, expected CPB duration less than 60 minutes, participation in other blood related clinical studies, incomplete records after surgery, Jehovah Witness, or IABP/ECMO support before and after surgery. No additional blood samples were collected in this study, and the excluded patients and the study flow chart are shown in Fig. 1.

For the HA group, the HA device was integrated in the CPB circuits with a partial flow of 300 ml/min through a rolling pump (Fig. 2. A), while routine CPB surgery was performed for the non-HA group (Figure. 2. B). Intraoperative blood dilution, hypothermia, and anticoagulation were maintained according to surgical requirements.

All patients were cared for by the same team of anesthesiologists, surgeons, perfusionists and intensivists. All patients received regular blood conservation therapy [9,10], including collecting and washing of all the lost blood in the cell saver intraoperatively, washing and reinfusing residual blood in the CPB circuits, reduction of priming volume, administration of 375 IU/kg of body weight of unfractionated heparin maintaining an activated clotting time >480 s during the CPB period, and the use of a biocompatible oxygenator, ultrafiltration and antifibrinolytic agents. The details of anesthesia, surgical procedures and CPB have been reported previously [11]. Postoperatively, all patients were transported to the intensive care unit (ICU), intubated and ventilated. The duration of postoperative mechanical ventilation (MV), length of ICU stay and posthospital stay and short-term outcomes (postoperative EBE, ITE, transfusion rate and volume, transfusion products, postoperative inotropic administration, blood loss, morbidity, and mortality) were recorded.

Postoperative cardiac surgery–related EBE, as defined by the occurrence of one or more of the following five components during the procedure through hospital discharge: fatal bleeding; perioperative intracranial bleeding within 48 hours; surgical reexploration for the purpose of controlling bleeding; 12-hour chest tube output of more than 1 L, or packed red blood cell (RBC) transfusion of more than 6 units. Postoperative cardiac surgery–related ITE, as defined by the occurrence of one or more of the following six components during the procedure through hospital discharge: myocardial infarction (MI), ischemic stroke, ischemic spinal cord injury, deep vein thrombosis (DVT), pulmonary embolism (PE), and local arterial embolism. The RBC transfusion rate was defined as the overall blood transfusion rate of package RBCs from the surgical day to discharge. Allogeneic transfusions were performed according to the "Granducato algorithm" [12].

Inotropic administration was defined as the use of dopamine, dobutamine, noradrenaline or adrenaline (μg/kg/min) for at least 1 h during the first 24 h postoperatively. Postoperative morbidity included multiple organ dysfunction syndrome (MODS), low cardiac output[13], central nervous system (CNS) injury[14], acute kidney injury [15], acute hepatic injury [16], systemic infection, pleural effusion/pneumothorax requiring closed-chest drainage, delayed incision healing, and 30-day mortality (including patients who died 30 days postoperatively but were not discharged).

The primary outcome was RBC transfusion rate, and the secondary outcomes were the incidence of EBE, ITE, the volume of allogeneic transfusion (including RBC, platelets, plasma, and cryoprecipitates), MV duration, ICU stay, posthospital stay, and 30-day mortality.

Statistical analysis

Categorical variables are summarized as frequencies and percentages, while continuous variables are expressed as the mean±SD when the data were normally distributed and as the interquartile range (IQR) [P50(P25, P75)] when the data were nonnormally distributed. To generate two evenly matched cohorts of patients who received HA or not, we propensity score matched patients by using the following pre- and intraoperative variables according to univariate logistic regression and the guidance of statistical experts: sex, age, BMI, preoperative antithrombotics (anticoagulation, anti-platelet, or both) and withdrawal time (<1 day;≥1 day and <5 days;≥5 days and <7 days), other preoperative high bleeding risk factors (including anemia, thrombocytopenia, chronic renal or hepatic disease, prior cardiac surgery, stroke, malignant tumor, spontaneous bleeding, oral NSAIDs or steroids, infective endocarditis, poor EF<30%), surgical procedures, and CPB duration. Of the 154 patients who received HA, we matched 144 pairs (93.5% were matched successfully) during the same period. The matching tolerance was 0.1, and the propensity scores ranged from 0.036 to 0.809. Multivariate analysis of variance was used to determine whether the effects of the HA group after matching were influenced by the CPB duration or surgical procedures. A *P* value <0.05 was considered significant. Missing data within 10% were filled with multiple imputations. Data analysis was performed using IBM SPSS 23.0 (SPSS Software, IBM Corp., Armonk, NY, USA).

Results

From 2018 to 2022, a total of 6927 cardiac surgical procedures were performed, 6.6% (460/6927) of which were nonelective surgeries and had antithrombotics histories before surgery. After 24 cases were excluded according to the exclusion criteria, 436 patients were included, of which 154 patients were in the HA group. Three different types of antithrombotics, anticoagulation (mainly referred to warfarin, or the combination of other traditional Chinese medicines containing ginseng), antiplatelet (referred to one or more of aspirin, clopidogrel, ticagrelor, and rivaroxaban), or antithrombotics (referring to the combination of anticoagulation and antiplatelet), were assigned to 48.6% (212/436), 48.4% (211/436), and 3% (13/436), respectively, based on their mechanisms. Nonelective surgery referred to emergency, urgent, and limited-term surgery (the duration from drug withdrawal to surgery was less than a week), of which 12.6% (55/436) were <1 day; 69.5% (303/436) were ≥1 day and <5 days; and 17.9% (78/436) had a duration of ≥5 days and <7 days. After matching, the differences between the two groups were smaller as shown in Fig. 3 and Table 1.

The patients in the HA group were more female, older, body smaller, had a higher proportion of previous cardiac surgery and infective endocarditis, a lower proportion of aortic and combined procedures, and a shorter duration of CPB (see Table 1). All the above, except for the shorter CPB duration and different procedures, indicated that the HA group seemed to require more allogeneic transfusions. Before matching, the HA group had a significant RBC transfusion rate reduction, platelet transfusion rate reduction, allogenic transfusion volume reduction, fewer ITE, organ morbidities, and a shorter posthospital stay (see Table 2). Because of poorer preoperative and simpler intraoperative conditions in the HA group than in the non-HA group, it was hard to say that all the outcome benefits came from the HA.

After matching, the demographic and perioperative characteristics were better adjusted and comparable (see Table 1). Compared with the non-HA group, the HA group had a significantly reduced RBC transfusion rate and volume, a shortened posthospital stay, a lower incidence of ITE, low cardiac output, acute kidney injury, and CNS injury (see Table 2).

To further determine whether the advantages of the HA group after matching were influenced by the CPB duration or surgical procedures, we conducted a multivariate analysis of variance. If an interaction was found, a simple effect analysis was performed again. We did not find any interaction between the group and the CPB duration in any outcomes. We found that there was a significant interaction between the group and the procedures that may affect the incidence of low cardiac output. The HA group had a higher incidence of low cardiac output in combined procedures, while the non-HA group had a higher incidence of low cardiac output in valve surgery(see Fig. 4. A). We also found that there was a significant interaction between the group and the procedures that may affect posthospital stay. The posthospital stay for aortic and combined procedures in the non-HA group was prolonged (see Fig. 4. B). After removing these outcomes, we found that HA could reduce the RBC transfusion rate and volume, and reduce the incidence of ITE, acute kidney injury and CNS injury.

After matching, the preoperative INR and PT were similar and comparable in the two groups. We found that the PT on postoperative Day 1 , the PT on postoperative Day 3, and the INR on postoperative Day 3 in the HA group were lower than those in the non-HA group (see Figure 5).

Discussion

Our study where HA was applied during CPB for patients where antithrombotics were stopped less than a week before surgery found no reduction in the incidence of postoperative EBE. However, this intervention did reduce the incidence of perioperative allogeneic blood transfusion, postoperative ITE, acute kidney and CNS injury.

Antithrombotics withdrawal before cardiac surgery to reduce perioperative bleeding is a routine treatment in clinical practice. The latest blood conservation guidelines stipulate that any anticoagulant or antiplatelet therapy should be discontinued for at least 3-7 days for high bleeding risk patients, and it is best to discontinue the medication for 2 weeks for those who received combination therapy[17,18]. The contradiction often lies in clinical practice: the more types and doses of antithrombotics there are, the higher the risk of embolism in patients. Once such patients need cardiac surgery, they immediately become at high bleeding risk, leading to a dilemma for the management of bleeding and embolism.

This is currently the largest clinical study that aimed determine whether intraoperative HA technology can rebalance bleeding and embolism in cardiac surgery. Compared with the non-HA group, the HA group had advantages regarding reduced RBC transfusion rate and incidence of postoperative ITE (see Table 2). These results were consistent with Hassan's research[4,19], which showed that intraoperative HA can reduce bleeding and hemostatic dose in high bleeding risk cardiac emergency surgery patients who were given rivaroxaban, apixaban, and ticagrelor preoperatively. However, there is limited published data reporting use of HA during cardiac surgery and the incidence of postoperative ITE. Compared with previous studies, our study expanded the inclusion (patients with preoperative antithrombotics underwent both emergency and limited-term surgery) criteria and observation fields (not only bleeding but also thromboembolism). Some studies have noted that patients with high levels of allogeneic transfusion are more susceptible to thrombotic events[20,21], the mechanisms of which may be related to the activation of inflammatory pathways, promotion of thrombin activation, and venous thrombosis. Our study also found that the HA group had a lower incidence of postoperative ITE, but whether this is a direct effect of the adsorption of inflammatory factors by HA or the beneficial HA-mediated reduction in allogeneic transfusion requirements (or both) is unknown. This is also one of the limitations of this article, as it is not a randomized controlled trial, so it can only prove the correlation between HA and reducing the incidence of postoperative ITE, rather than a causal connection.

There were previous reports of HA potentially causing myocardial injury[22,23], which was inconsistent with our findings. Our results suggest that the incidence of postoperative low cardiac output is lower in the HA group after matching, which seems to be a myocardial protective effect of HA. However, the matching factors only included poor EF<30% but not a comprehensive evaluation of preoperative cardiac condition. Therefore, the cardiac advantage of significance may not be of clinical difference in this cohort.

The main limitation of this study is the ambispective observational design rather than randomized controlled design, so the condition of antithrombotics withdrawal in the two groups may not be fully comparable. In addition, single Chinese race patients in a single center, and different routine treatments in different centers may limit the external validity of our findings. Third, the treatment duration of HA is limited by the CPB duration, and hemostatic or anticoagulant measures cannot be matched after surgery, both of which may lead to differences in efficacy. Fourth, the HA group still had significantly shorter CPB durations after matching, a factor well recognized to be associated with coagulation disturbances in cardiac surgery. However, the data of this study were extracted from an electronic data system, and the propensity score matching method reduced bias that affects bleeding, transfusion, and coagulation function before and during surgery, which can reduce the differences between the two groups to some extent. Appropriately, we conducted a multivariate analysis of variance, and found that the advantages of the HA group were not influenced by the shorter CPB duration. Additionally, data were collected in a consistent manner using consistent definitions and practices.

Conclusions

For nonelective cardiac surgery patients who have received antithrombotics therapy before surgery, prophylactic application of HA during CPB can simply and safely rebalance the postoperative coagulation system, and is associated with reductions in transfusion requirements and postoperative ITE.

Statement

Statement of Ethics

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Xiangya Hospital (approval number 202209620). Written informed consent was obtained for each recruited patient in this study.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Q.Y.L.: data collection and writing. L.D.: design, analyzed the data, writing and edited the final version of the manuscript. E.W.: supervision. C.L.Z: figures and data collection. ZHX: data collection. F.Z: data collection. T.Y.O: data collection. F.Y.L.: supervision. Y.Y.D.: analyzed the data.

Data Availability Statement

The data that support the findings of this study are not publicly available due to privacy reasons but are available from the corresponding author upon reasonable request. Further enquiries can be directed to the corresponding author.

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Figure Legends

Fig. 1. Flow chart of this study

Fig. 2. Illustration of Hemoadsorption (HA) integrated in cardiopulmonary bypass (CPB) circuits
A： HA group (the hemoadsorption device was integrated in CPB circuits, with a flow of 300ml/min); The arrow indicates the direction of blood flow, the blue represents venous blood, and the red represents arterial blood;
B：non-HA group (traditional CPB circuit, no hemoadsorption device).

Fig. 3. Preoperative antithrombotics and withdrawal duration between the HA group and the non-HA group
A, The proportion of antithrombotics type before and after matching between the two groups；B, The proportion of withdrawal duration before and after matching between the two groups
HA, hemoadsorption；non-HA, non-hemoadsorption；AC, anticoagulation；AP, anti-platelet；AT, antithrombotics（anticoagulation + anti-platelet）

Fig. 4. The groups interacted with procedures, affecting the incidence of postoperative low cardiac output and posthospital stay
HA, hemoadsorption；CABG, coronary artery bypass graft.
A (1) and A (2): The interaction between groups and procedures affected the incidence of postoperative low cardiac output. In the non-HA group, the incidence of postoperative low cardiac output was higher in valve procedures. While in the HA group, the incidence of postoperative low cardiac output was higher in combined procedures.
B (1) and B (2): The interaction between groups and procedures affected posthospital stay. In the non-HA group, the posthospital stay were longer for aortic procedures and combined procedures.
* a higher Estimated Marginal Mean value (P<0.05)

Fig. 5. The perioperative INR and PT between the two groups after matching
INR, international normalized ratio; PT, prothrombin time; HA, hemoadsorption；pre, pre-operatively; pod, postoperative day
* a significant difference between the groups (P<0.05)

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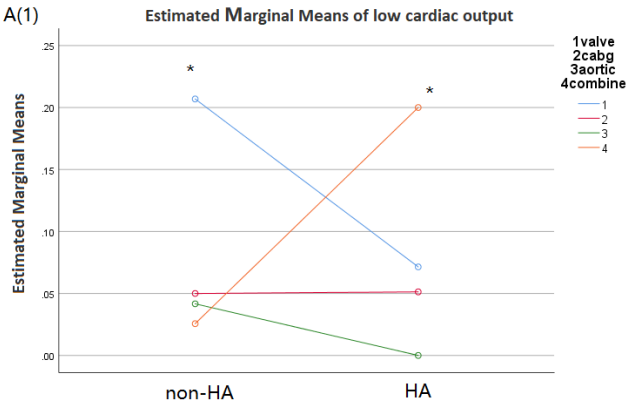

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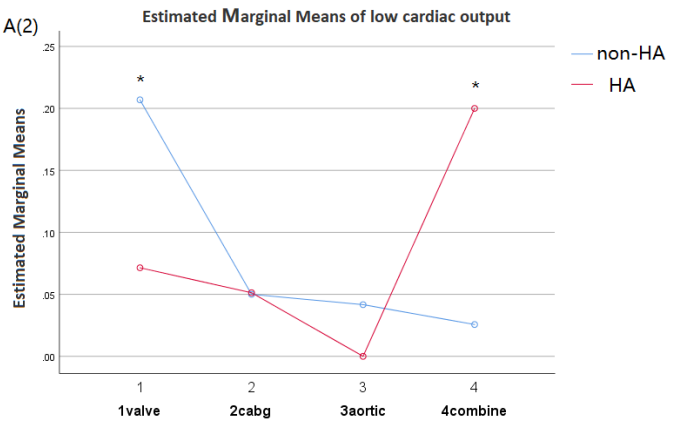

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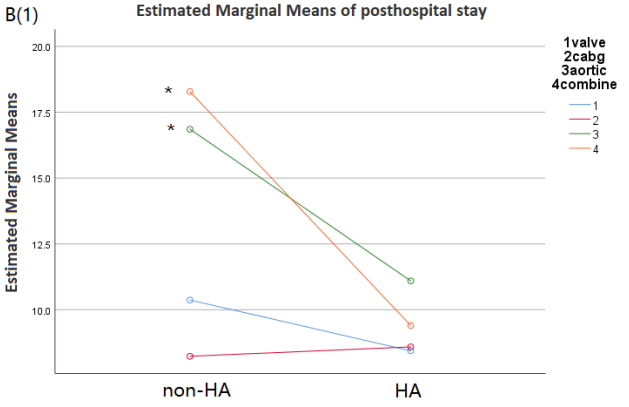

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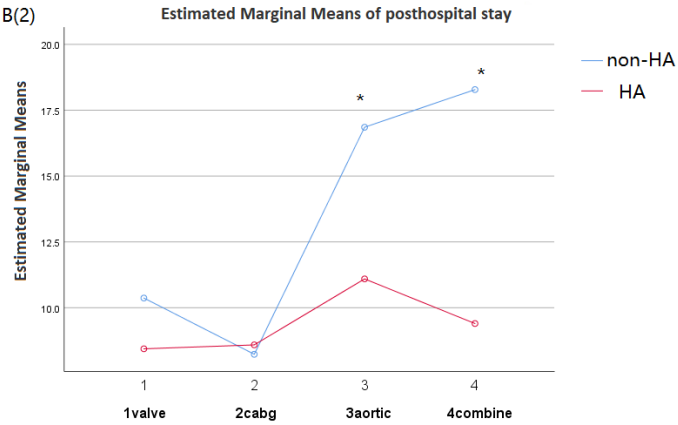

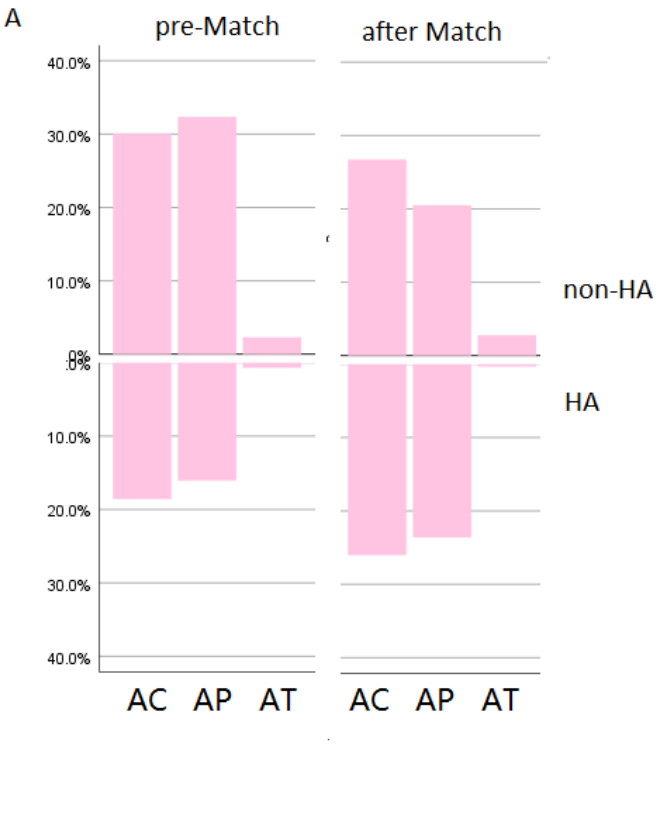

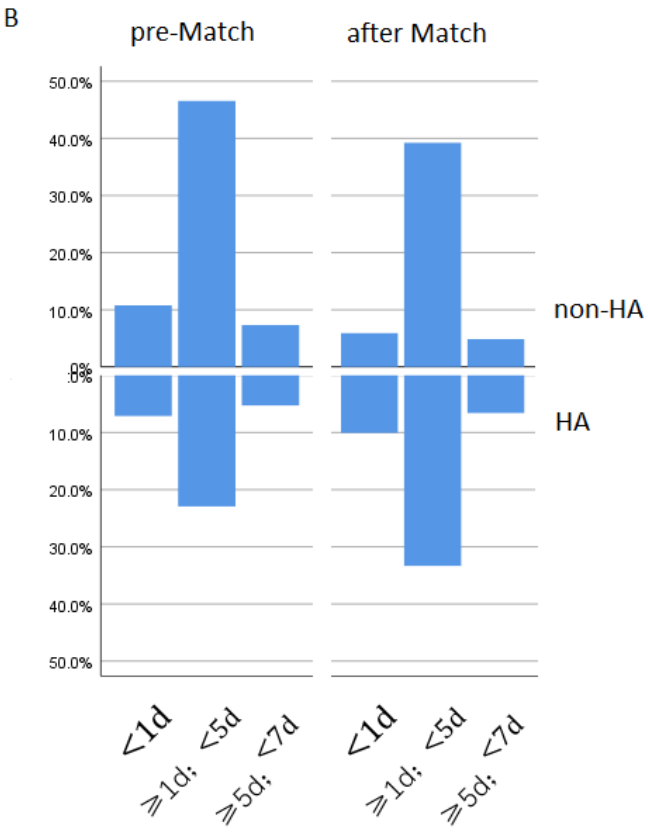

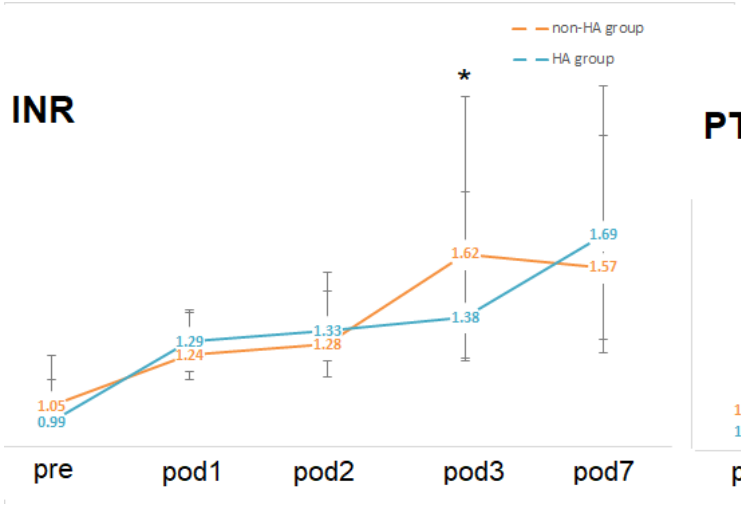

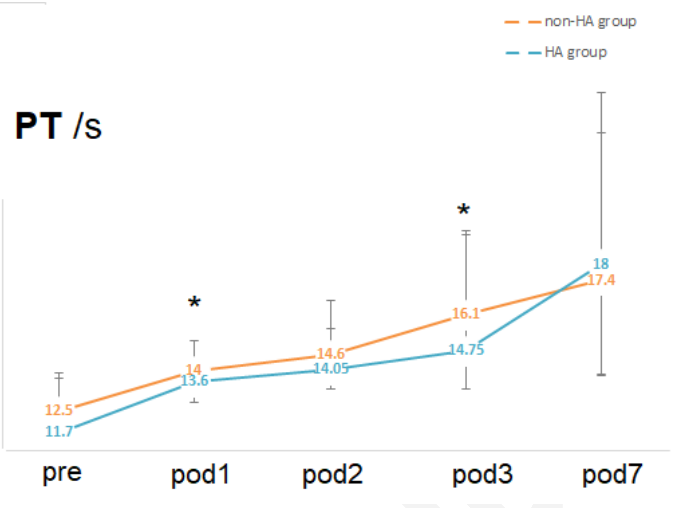

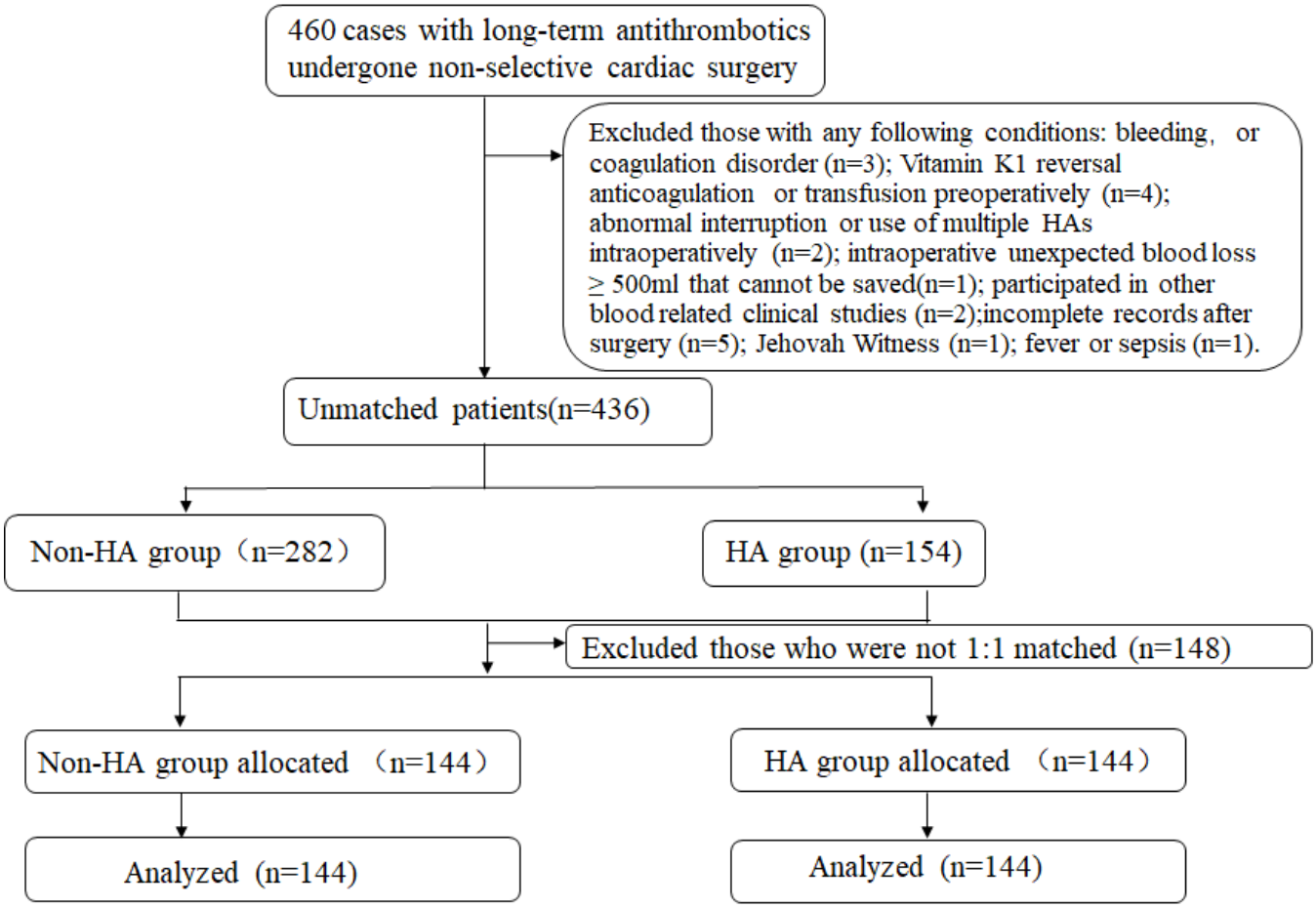

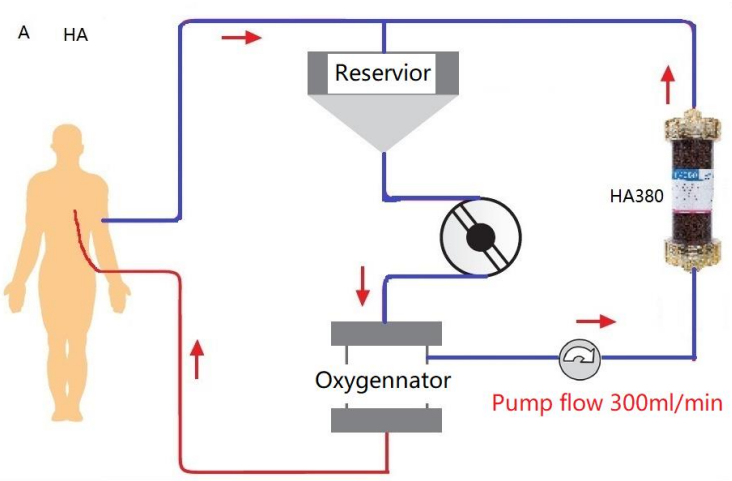

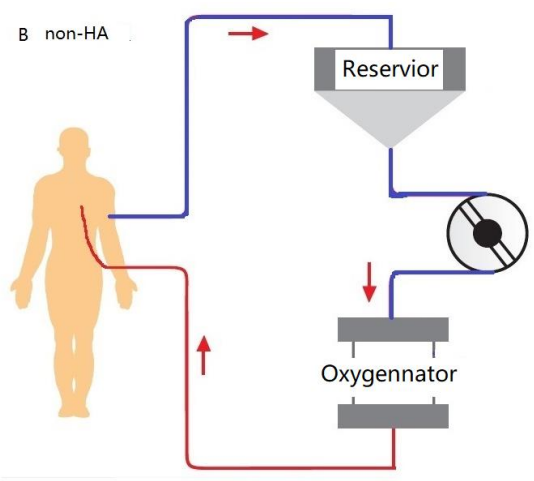

Table 1　Characteristics of two groups before and after propensity score matching

Variables	Pre-Match			After Match		
	non-HA (*n* = 282)	HA (*n* = 154)	*P*	non-HA (*n* =144)	HA (*n* =144)	*P*
Sex: Male, *n* (%)	196(69.5)	79(51.3)	0.000	85(59.0)	76(52.8)	0.285
Age, year	55(48,62)	58(53,65)	0.000	58(52,64)	57(53,65)	0.774
Weight, kg	64(55,70)	59(50,65)	0.000	60.5(53,67.75)	59(50,65.75)	0.110
BMI	23.39（21.29，25.71）	22.54(19.81,24.82)	0.003	22.86（20.53，24.98）	22.54（19.93，24.98）	0.493
Antithrombotics, *n* (%)			0.359			0.047
Anticoagulation	131(46.5)	81(52.6)		77(53.5)	75(52.1)	
Anti-platelet	141(50.0)	70(45.5)		59(41.0)	68(47.2)	
Combine	10(3.5)	3(1.9)		8(5.5)	1(0.7)	
Withdrawal duration, *n*(%)			0.302			0.072
<1d	47(16.7)	31(20.1)		17(11.8)	29	
1d≤Wd<5d	203(72.0)	100(64.9)		113(78.5)	96	
5d≤Wd<7d	32(11.3)	23(14.9)		14(9.7)	19	
Preoperative thrombocytopenia, *n*(%)	19(6.7)	5(3.2)	0.127	8(5.5)	5(3.5)	0.394
Preoperative anemia, *n*(%)	8(2.8)	8(5.2)	0.211	5(3.5)	6(4.2)	0.759
Preoperative abnormal renal function, *n*(%)	24(8.5)	19(12.3)	0.200	20(13.9)	17(11.8)	0.597
Preoperative abnormal liver function, *n*(%)	17(6.0)	6(3.9)	0.341	7(4.9)	6(4.2)	0.777
Bleeding history, *n*(%)	17(6.0)	11(7.1)	0.650	7(4.9)	11(7.6)	0.330
Stroke history, *n*(%)	24(8.5)	20(13.0)	0.138	19(13.2)	16(11.1)	0.588
NSAID or steroids history, *n*(%)	12(4.3)	5(3.2)	0.603	7(4.9)	5(3.5)	0.555
Malignant tumor, *n*(%)	4(2.1)	2(1.3)	0.918	1(0.7)	2(1.4)	0.562
Redo cardiac surgery, *n*(%)	11(3.9)	14(9.1)	0.026	9(6.3)	11(7.7)	0.643
Infective endocarditis,*n*(%)	4(2.1)	7(4.5)	0.047	4(2.8)	5(3.5)	0.735
Preoperative EF<30%, *n*(%)	21(7.4)	21(13.6)	0.036	14(9.7)	16(11.1)	0.700
Procedures, *n*(%)						
Valves	87(30.9)	84(54.5)		72(50.0)	75(52.1)	
CABG	60(21.3)	39(25.4)	0.000	23(16.0)	39(27.1)	0.012
aortic	96(34.0)	21(13.6)		40(27.7)	20(13.9)	
combine	39(13.8)	10(6.5)		9(6.3)	10(6.9)	
CPB duration, min	160(124，195)	127(102,162)	0.000	152.5(116,188)	128(103.5,163)	0.000
Cardiac ischemic time, min	91(71,125)	89(66,111)	0.168	89(68,126)	89(69,112)	0.573

HA, hemoadsorption; BMI, body mass index; Wd, Withdrawal duration; NSAID, nonsteroidal anti-inflammatory drugs; EF，ejection fraction; CABG, coronary artery bypass graft; CPB, cardiopulmonary bypass.

Table 2 Perioperative outcomes of two groups before and after propensity score matching

Variables	Pre-match			After-match		
	non-HA (*n* = 282)	HA (*n* = 154)	*P*	non-HA (*n* =144)	HA (*n* =144)	*P*
Transfusion rate, *n* (%)						
RBC	184(65.2)	72(46.8)	0.000	87(60.4)	67(46.5)	0.018
Platelet	97(34.4)	38(24.7)	0.036	40(27.8)	36(25.0)	0.593
Transfusion volume, u						
RBC	2(0,5.5)	0(0,3.6)	0.001	2(0,5)	0(0,3.88)	0.033
Platelet	0(0,1)	0(0,0.25)	0.021	0(0,1)	0(0,0.75)	0.517
Plasma	6.5(4,12)	8 (5,13)	0.065	6(4,10)	8 (5,13)	0.004
Cryoprecipitate	0(0,1)	0(0,1)	0.001	0(0,1)	0(0,1)	0.108
Inotropics, *n* (%)			0.000			0.000
0	54(19.1)	13(8.4)		24(16.7)	12(8.3)	
Dop/dof/ne	141(50.0)	55(35.7)		72(50.0)	50(34.7)	
Adr+ Dop/dof/ne	87(30.9)	86(55.8)		48(33.3)	82(57.0)	
MV, h	22(15,44)	7(13,25)	0.000	19(14,36)	17(13,25)	0.047
ICU stay, h	60(38,120)	45(25,83)	0.005	47(27,114)	45(25,75)	0.135
Posthospital stay, d	12(8,16)	8(6,10)	0.000	11(8,15)	8(6,10)	0.000
mortality, *n* (%)	17(6.0)	4(2.6)	0.110	7(4.9)	4(2.8)	0.356
Morbidity:						
EBE, *n* (%)#	78(27.7)	34(22.1)	0.202	40(27.8)	33(22.9)	0.343
ITE, *n* (%)Δ	26(9.2)	6(3.9)	0.042	16(11.1)	5(3.5)	0.013
Low cardiac output, *n* (%)	26(9.2)	10(6.5)	0.323	20(13.9)	9(6.3)	0.031
MODS, *n* (%)	17(6.0)	3(2.0)	0.052	10(6.9)	3(2.1)	0.047
Closed-chest drainage, *n* (%)	85(30.1)	43(27.9)	0.627	43 (29.9)	40(27.8)	0.696
Acute kidney injury, *n* (%)	109(38.7)	28(18.2)	0.000	54(37.5)	27(18.8)	0.000
Acute hepatic injury , *n* (%)	8(2.8)	10(6.5)	0.067	5(3.5)	9(6.3)	0.273
CNS injury, *n* (%)	61(21.6)	11(7.1)	0.000	29(20.1)	10(6.9)	0.001
Systemic infection, *n* (%)	13(4.6)	1(0.6)	0.025	6(4.2)	1(0.7)	0.056
Delayed incision healing, *n* (%)	21(7.4)	3(1.8)	0.016	9(6.3)	3(2.1)	0.077

#：cardiac surgery–related excessive bleeding events (EBE), as defined by the occurrence of 1 or more of the following 5 components during the procedure through hospital discharge: fatal bleeding; perioperative intracranial bleeding within 48 hours; surgical reexploration for the purpose of controlling bleeding; 12-hour chest tube output of more than 1L, or packed red blood cell transfusion of more than 6 units.

Δ：cardiac surgery–related ischemic /thromboembolic events (ITE), as defined by the occurrence of 1 or more of the following 6 components during the procedure through hospital discharge：myocardial infarction (MI), ischemic stroke, ischemic spinal cord injury deep vein thrombosis (DVT), pulmonary embolism (PE), local arterial embolism.

**P*<0.05; ***P*<0.001

HA, hemoadsorption; dop, dopamine; dof, dobutamine; ne, norepinephrine; adr, adrenaline; ICU, intensive care unit；MODS, multiple organs dysfunction syndrome; CNS, central nervous system.